QMRA and water safety management: review of application in drinking water systems

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ABSTRACT

Quantitative microbial risk assessment (QMRA), the assessment of microbial risks when model inputs and estimated health impacts are explicitly quantified, is a valuable tool to support water safety plans (WSP). In this paper, research studies undertaken on the application of QMRA in drinking water systems were reviewed, highlighting their relevance for WSP. The important elements for practical implementation include: the data requirements to achieve sufficient certainty to support decision-making; level of expertise necessary to undertake the required analysis; and the accessibility of tools to support wider implementation, hence these aspects were the focus of the review. Recommendations to support the continued and growing application of QMRA to support risk management in the water sector are provided.

Key words | drinking water, pathogens, quantitative microbial risk assessment (QMRA), risk management

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INTRODUCTION

Compliance monitoring of fecal indicator bacteria is inadequate for the provision of consistently safe drinking water – as seen from numerous waterborne outbreaks worldwide (Hrudey & Hrudey 2004, 2014). Sampling is too infrequent and too little water is sampled to identify short-term periods of sub-optimal system performance during which the overall system integrity can be compromised (Medema *et al.* 2006; Signor & Ashbolt 2006; Smeets *et al.* 2010). The WHO guidelines for safe drinking water (WHO 2011b) recommend the implementation of water safety plans (WSP) which require a comprehensive risk-based approach to managing hazards from source to tap (WHO 2009).

Quantitative microbial risk assessment (QMRA), the assessment of microbial risks when model inputs and health impacts are explicitly quantified, is a valuable tool to support water safety planning and specific control point parameters for pathogen management (WHO 2016). The role of QMRA within the WSP context was previously explored through the EU-MicroRisk project (2003–2006, www.microrisk.com) within 10 case study drinking water systems in Europe and Australia. At that time, practical implementation of QMRA by regulators and water utilities within the WSP process was limited. Despite clear theoretical advantages, data limitations and the associated uncertainty for decision making were identified as the key challenges to widespread adoption. Since the Micro-Risk project, the role of QMRA for water safety management has continued and expanded with many peer reviewed journal publications, and large multi-partnered EU funded projects including HiWATE (Nieuwenhuijsen *et al.* 2009), TECHNEAU (www.tech-neau.org) and VISK (www.visk.nu).

Here we review research undertaken on the application of QMRA for drinking water systems to support the introduction and on-going development of drinking WSP by Environment and Sustainable Resource Development (as of 2015 renamed, Environment and Parks), Government of Alberta. Firstly, the application of QMRA for the development of national regulations was reviewed, as these

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regulations set the framework and criteria within which the WSP may be developed. Secondly, for each of five target areas where QMRA may be used to support WSP, cases from the literature that provide practical examples were identified, software tools that provide support for calculations were reviewed, and strengths and limitations of QMRA within each context are discussed. The important elements for practical implementation include: the data requirements to achieve sufficient certainty to support decision-making; level of expertise necessary to undertake the required analysis; and the accessibility of tools to support wider implementation. These factors are therefore the ultimate focus of this review.

REGULATION AND HEALTH-BASED TREATMENT TARGETS

While it is widely acknowledged that water of poorer quality requires a higher level of treatment to achieve safety, quantitatively specifying how much treatment is required, in terms of technologies or required Log_{10} pathogen reduction, is a challenge. The QMRA framework provides a systematic approach for defining treatment targets in relation to source water quality (US-EPA 2007; USDA/US-EPA 2012). The approach is illustrated in Figure 1. First, the health target is defined, depending on the required level of safety for the local context. Secondly, the model input assumptions are defined and include consumption volume (unheated water per person × day), dose-response relationship for the reference pathogens, exposure frequency (typically assumed to be daily for the entire year, however may be reduced for consideration of specific event concentrations) and Disability Adjusted Life Year (DALY) health-impact weightings. Then, for any level of contamination in the source water, the required level of pathogen reduction (by treatment and management controls) to meet the health-based (enteric pathogen) tolerable risk target can be determined by optimization. This conceptual approach is

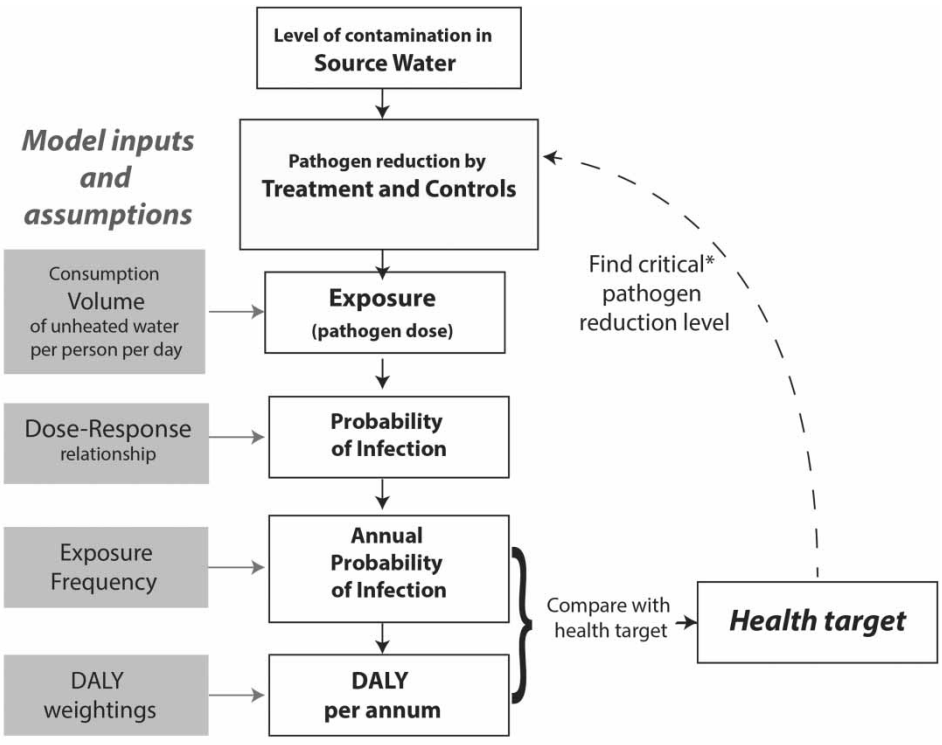

Figure 1 | Illustration of approach for defining treatment requirements based on source water pathogen concentration (Petterson *et al.* 2015).

recommended by WHO for drinking water (WHO 2011b, 2011a) and for the safe use of wastewater, excreta and greywater (WHO 2006a, 2006b), and has been used in Australia for setting recreational water access (Roser *et al.* 2006) in order to quantify the required treatment, or the necessary controls, in order to achieve the tolerable risk target. Very limited work has been undertaken for the currently unregulated problem of water-based pathogens (Ashbolt 2015), such as *Legionella pneumophila*, which may grow post treatment and largely within premise plumbing (Schoen & Ashbolt 2011).

Case study examples

The principle

In using the QMRA framework to determine treatment requirements for surface water sources, the principle was presented with the earliest QMRA studies (Regli *et al.* 1991; Rose *et al.* 1991), revision of the enhanced surface water treatment rule (US-EPA 2006) and then later extended to account for variability in pathogen concentration (Masago *et al.* 2002). The US-EPA followed by many other jurisdictions have used QMRA in this way, including Health Canada and others. In principle, the same method could be used at the water supply system-specific scale and context.

In practice

There are limited examples of where the conduct of QMRA at a water supply system specific scale is a regulatory requirement. Most notably, the Dutch Drinking Water Act requires that risk assessment be undertaken for waterborne pathogens at every water supply to demonstrate microbiologically safe water, with a health based target of less than one infection per 10,000 per year (Anonymous 2001). In 2005, the inspectorate guideline 5318 was created to define the requirements of the QMRA including the reference pathogens to be used, the data requirements, means of quantifying treatment efficacy, selection of dose-response models and other important assumptions (Anonymous 2005). Defining these requirements created a clear basis on which the water utilities could quantify their risk and compare with the target, yet certain aspects were not addressed, such as post-treatment recontamination risks during drinking water distribution.

The Australian guidelines for water recycling (NWQMS 2006) were developed in keeping with the guidance of the WHO guidelines for the safe use of wastewater, excreta and greywater (WHO 2006a). The QMRA framework was used to provide a quantitative approach within a structured framework to evaluate a diverse range of potential recycled water uses. The guidelines allow for combinations of treatment options and preventative measures to be selected so as to ensure the water is fit-for-purpose and meets the $1\ \mu DALY.person^{-1}.year^{-1}$ health based target.

Software tools

Schijven *et al.* (2011), at the National Institute for Public Health and the Environment (RIVM) in the Netherlands, developed a software tool to support the evaluation of each water supply in comparison to the Dutch regulation. The model is constructed in Mathematica® software (Wolfram Research, USA), with the assumptions and data analysis approaches as defined in the inspectorate guidelines (Anonymous 2005). Water utilities are required to collect input data for the model and the output is the annual probability of infection for treatment compliance comparison with the annual target of 1×10^{-4} infection risk 95% of the time.

Strengths, limitations and data needs

The experiences of QMRA-based regulation in both the Netherlands and Australia were evaluated by Bichai & Smeets (2013). Their analysis of experiences and perceptions across regulatory bodies, government, water utilities and scientists in both countries identified the following advantages and challenges associated with QMRA-based regulation. In their evaluation, Bichai & Smeets (2013) argue that efficiently addressing small (remote) water systems is likely to require a centralized approach where human resources, data and knowledge are shared.

Advantages

- QMRA scenario modeling provides a better assessment of water safety than the absence of fecal indicators.
- Setting a health-based risk target addresses the balance between investments and public safety.
- Helps staff responsible to better understand risks from their water sources, treatment operation and in particular, likely increased risks during hazardous events.

Challenges

- Efficient monitoring and designing sufficient monitoring to meet the requirements of the Dutch regulation.
- The need for institutional support for utilities since QMRA as a regulatory tool cannot stand alone, and effective implementation requires adapted institutional support; such as specific training, development of auditing approaches.
- Interpretation of uncertainty by regulators. Uncertainty in QMRA science needs to be balanced with the policy approach to uncertainty (i.e. to draw a 'thin line' when in reality there is a wider, fuzzier line), in order to allow decision-making and use of the approach by utilities.
- How to communicate risk to consumers in a consistent and balanced way; often boiled down to meeting best management practices and risk targets.

QMRA IN THE WATER SAFETY PLAN – SITE SPECIFIC APPLICATIONS

A hazard analysis critical control point (HACCP) form of water management was first proposed by Havelaar (1994), however it took another decade before the approach was formalized (Hrudey 2004; Hrudey *et al.* 2006) and included in guidelines published by the WHO (2004) and in Australia (NWQMS 2006). The EU MicroRisk project (Medema *et al.* 2006) (www.microrisk.com) aimed to demonstrate how QMRA may be used to aid a HACCP-type of water management that is site-specific. The WSP steps are illustrated in Figure 2, identifying how QMRA can provide valuable input for the development of the plan.

Know your system

An underlying principle of the WSP is that to manage the system effectively, it is important to 'know your system'. Systems lacking understanding and systematic evaluation of microbial risks continue to cause outbreaks (Hrudey & Hrudey 2004, 2014). Considerations include the following:

- How impacted is the source water? What are the sources of contamination and how do they vary (including various likely events (all termed hazardous events))?
- Which pathogens are most relevant for the system? In general, when sewage or septic seepage is possible, enteric viruses, bacteria and parasitic protozoa from these sources all need to be represented by reference pathogens. Whereas in the absence of these human fecal sources (best demonstrated by the absence of human-targeted microbial source markers (Harwood *et al.* 2014) and supporting sanitary survey information) generally only enteric bacteria and parasitic protozoan reference pathogens are necessary to address zoonotic pathogens.
- What is the relative importance of different pathogen sources by event types?
- How effective are the existing treatment barriers for each reference pathogen?
- What are the vulnerabilities of the drinking water treatment process?
- What are the vulnerabilities of the drinking water distribution system?
- What are the implications of these vulnerabilities to the consumer population?

These questions may be addressed qualitatively based on the expertise of the WSP team, however direct quantitative input based on scientific evidence is a valuable support to the risk identification, prioritization and management process.

Case study examples

The following examples demonstrate how the application of the QMRA framework has supported understanding of the system and risk management. By modelling the system from source to exposure, sensitive system components are identified. Most notably, source water fluctuations and

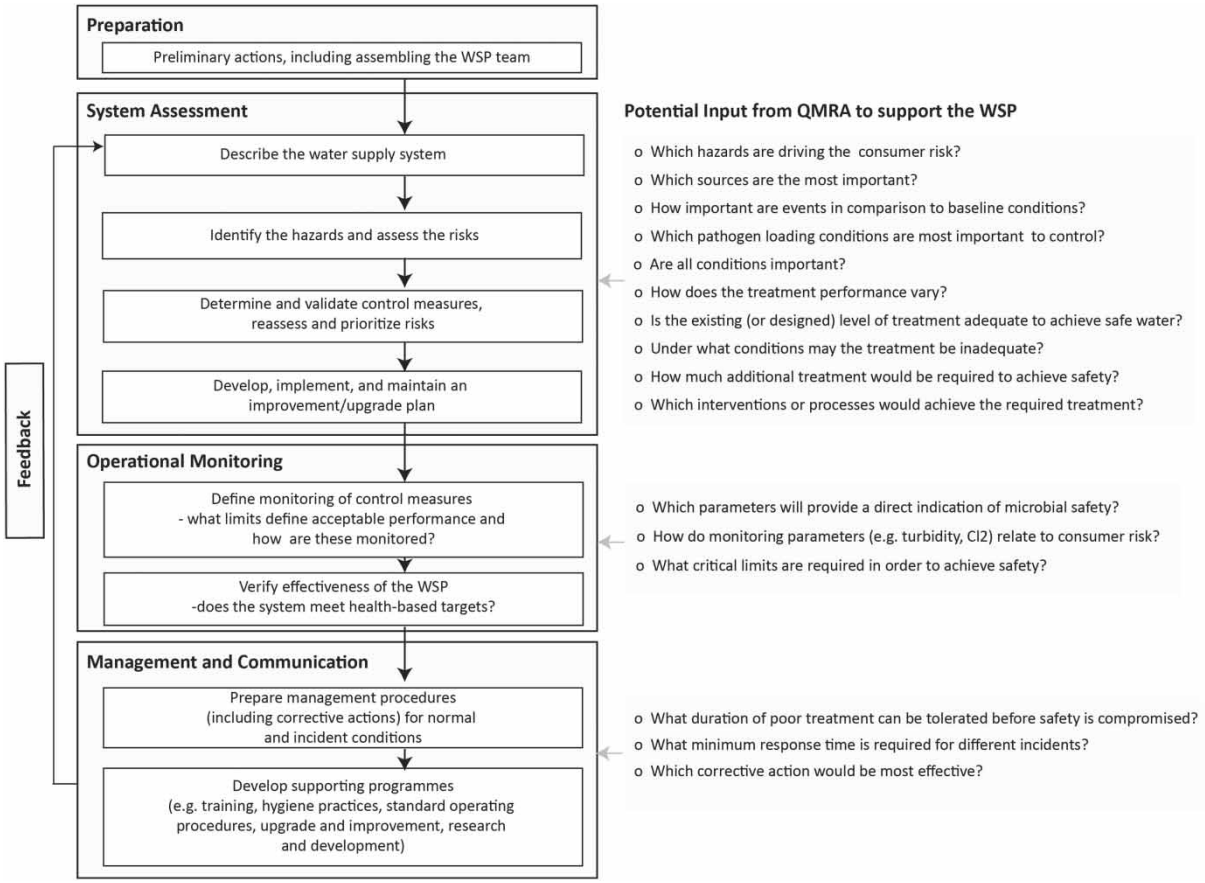

Figure 2 | Potential input from QMRA to support water safety planning.

treatment failures (Teunis *et al.* 1997; Jaidi *et al.* 2009; Cummins *et al.* 2010) were frequently identified as the most sensitive model components (noting that distribution system effects were not included in these studies, but have more recently begun to be addressed (Teunis *et al.* 2010; Besner *et al.* 2011; Yang *et al.* 2011)).

Know your source water. In investigating the source water contamination level, including the predicted pathogen concentration under baseline and event conditions, QMRA provided value with respect to:

- identification of a potential health threat associated with a particular hazard, such as the *Enterovirus* Coxsackievirus (Mena *et al.* 2003) or *Norovirus* (Petterson *et al.* 2016) when sewage contamination is likely;
- evaluation of the water quality impacts from zoonotic bacterial pathogens due to manure run-off and use of tile drain agricultural management practices (Schmidt *et al.* 2013b);
- understanding the uncertainties in risk estimates resulting from analytical recovery in predicting the magnitude of pathogen contamination (Teunis *et al.* 1999; Petterson *et al.* 2007; Schmidt *et al.* 2013a);
- considerations in the quantification (potential overestimation of infectious pathogens) of source water analysed with molecular data (Kundu *et al.* 2013; Petterson *et al.* 2015);
- application of hydrodynamic and hydrologic models to highlight short-circuiting in reservoirs, rain event pathogen loads, impacts from sewage releases etc. to facilitate the modelling of pathogen concentrations in source waters (Signor *et al.* 2005; McBride *et al.* 2012; Sokolova *et al.* 2012, 2015; Åström *et al.* 2013), and to identify the relative importance of different contamination sources/events; and

- evaluation of the relative importance of different fecal sources on the overall risk to the community, i.e. generally if sewage/septage present, human enteric viruses dominate risk estimates (Schoen & Ashbolt 2010; Soller *et al.* 2010, 2015; Schoen *et al.* 2011).

Know your treatment. QMRA provided value with respect to:

- identification of the importance of managing treatment failures to reduce consumer risk (Teunis *et al.* 1997);
- identification of the relative importance of different failure events to prioritize management options (Westrell *et al.* 2003);
- assessment of the safety or otherwise associated with recycling filter backwash water to the inlet of the water treatment plant (Loret *et al.* 2013);
- demonstration of the importance of system compliance on overall consumer risk (Hunter *et al.* 2009; Enger *et al.* 2013; Petterson 2016);
- the effectiveness of different risk management options for treatment including intake closure during hazardous events to reduce pathogen concentrations (Åström *et al.* 2007);
- evaluation of treatment performance with respect to different pathogen loading (Smeets *et al.* 2007); and
- demonstration of the value of monitoring and what to monitor to inform pathogen treatment performance (Signor & Ashbolt 2006; Smeets *et al.* 2010).

Know your distribution system. Overall, distribution systems could account for some 30% of outbreaks in North America (Craun *et al.* 2010), and premise plumbing may account for the majority of these via *Legionella* and nontuberculous mycobacterial growth and subsequent infections that dominate US hospitalization costs via drinking water exposures (Collier *et al.* 2012), and drinking water outbreak health burden in general (Beer *et al.* 2015).

Drinking water distribution systems have only begun to be accounted for within drinking water QMRA and methodologies are developing. Case studies were identified that show how QMRA has improved understanding of the risk drivers associated with the distribution network (van Lieverloo *et al.* 2007; Teunis *et al.* 2010; Besner *et al.* 2011) and how that can be translated into risk management strategies (Yang *et al.* 2011). Critical premise plumbing *Legionella* concentrations have also been estimated by a reverse QMRA approach (Schoen & Ashbolt 2011), yet there are also other opportunistic pathogens to be addressed that grow post treatment (Ashbolt 2015).

Software tools

The Swedish water and wastewater association developed a QMRA tool for drinking water supplies (Svenskt Vatten 2015) specifically to support the application of QMRA for system understanding. The tool is constructed in the Analytica® (Lumina Decision Systems, USA) software platform, and is designed to be flexible and to allow a diverse range of treatment trains to be modelled, and is available freely online (Svenskt Vatten 2015). The tool includes eight reference pathogens (*Salmonella*, *Campylobacter*, *Escherichia coli* O157, Rotavirus, *Norovirus*, *Adenovirus*, *Cryptosporidium* and *Giardia*), and each treatment step allows for different failure scenarios to be selected and investigated against nominal conditions. The software is specifically designed as an educational tool for water managers within WSP workshops to demonstrate how microbial risks travel through water supplies and hence how they may be managed. The Health Canada QMRA tool (discussed under 'System assessment' below) designed for use by municipal engineers, water treatment plant (WTP) operators, and local decision makers also serves to support system understanding. While the primary purpose of the Canadian tool is to quantify treatment plant risk for comparison with a health target, it has also been identified that 'the greatest value of using this tool may reside in the systematic evaluation of the process that WTP managers must follow to implement it' (Tfaily *et al.* 2015).

Strengths, limitations and data needs

A major strength of the QMRA framework is to pool and interpret existing data, with the overall goal to support system understanding. Within this context, the success of QMRA is not dependent on the amount of data, but rather on effective construct and implementation. The key expertise is therefore in developing representative quantitative inputs of model parameters from sometimes very limited

data. A representative quantitative input to the decision making process, even if vague due to data limitations, is superior to expert opinion alone. Perhaps most effective is when using the QMRA framework to test the validity of qualitative assumptions from the WSP team. Even with a basic sanitary survey and literature data the framework can help structure the knowledge base about system attributes and consumer risk to improve water quality management.

The development of the Swedish software tool was intended to make the QMRA approach accessible to water managers, without the need to understand detailed risk calculations. While some success was achieved, the complexity of the underlying assumptions of the model was a barrier to widespread implementation. The initial hurdles associated with understanding the QMRA approach, understanding the limitations of the microbial data and hence uncertainties, and understanding the implications of the model outcomes were underestimated. Further work is needed to communicate these fundamental concepts at an appropriate level of detail for technical professionals who are not QMRA specialists.

In contrast, the Health Canada QMRA tool only uses stochastic inputs for reference pathogens (not treatment performance), generally with default values, and largely misses the opportunity for managers/operators to explore and get to know their system. Further, while the results seem clear, because of the lack of uncertainty integrated within the tool's approach, results are very likely to be misleading and over-simplistic; giving a false sense of precision and safety. Neither tool addresses distribution systems nor premise plumbing-related pathogen risks and hence, both may fail to provide perspective for system managers to prioritize expenditures for overall pathogen management of the complete source to tap system.

System assessment

QMRA provides a clear and transparent approach for comparing system risks with a health target, making it possible to evaluate if a system or pathway is safe (Figure 1). When the system is not safe, the steps that need to be undertaken in order to achieve the required level of safety can be evaluated and compared. In addition, circumstances (or event-driven conditions) during which the safety may be compromised can be identified.

Case study examples

The following case study examples demonstrate the evaluation of risk for direct comparison with a tolerable risk target to evaluate safety:

- Medema *et al.* (2003) evaluated three separate systems for *Cryptosporidium*. In one case the risk was well below the risk target, and therefore the system was deemed safe. In the second case the risk was well above the risk target and additional control measures were identified. In the third case, the risk was of a similar magnitude to the risk target and further investigation to reduce the uncertainty was recommended.
- Stored household water in South Africa was identified as unsafe with respect to *Salmonella* (Steyn *et al.* 2004).
- Risk of *Cryptosporidium* and *Giardia* from very small water supplies in the UK and France were evaluated to be extremely high (Hunter *et al.* 2011).
- Risk from *Adenovirus* via drinking water and recreational waters exceeded health targets (van Heerden *et al.* 2005).
- For surface water impacted by sewage effluent risks were demonstrated to be tolerable, even under hazardous event conditions (van den Akker *et al.* 2011).
- Investigation of uncertainty and variability and the implications of comparing risk with a tolerable target have been presented (Pouillot *et al.* 2004; Jaidi *et al.* 2009).
- Critical level for *Helicobacter pylori* in drinking water to be protective of life-time stomach cancer via drinking water (Ryan *et al.* 2014).
- Critical values of *Legionella* (moving back 'upstream' to aid in identifying management targets) in aerosols, drinking water and actual sites of growth within biofilms associated with premise plumbing (Schoen & Ashbolt 2011).

Software tools

Health Canada (Tfaily *et al.* 2015) has developed a stochastic tool in Excel® for modeling health risks for comparison with the US-EPA used benchmark of 1×10^{-4} annual infection probability and the WHO benchmark adopted by Health

Canada of the 1 μDALY.person^{-1}.year^{-1}. Reference pathogens include *Cryptosporidium*, *Giardia*, Rotavirus, *Campylobacter* and diarrheic *E. coli*. Users are required to input the concentration of pathogens in raw water as the mean and standard deviation for characterization by a log-normal distribution, and $\log_{10}$ reductions by treatment are defined based on reported values in the literature. The Guidelines for Canadian Drinking Water Quality encourage the implementation of a risk-based multiple barrier approach that includes QMRA (Health Canada 2012; Tfaily *et al.* 2015). The tool is intended to be applied by end users to evaluate alternative strategies to satisfy regulatory requirements, evaluate the robustness of a given treatment train, or determine crucial situations in which the risk of exposure may be increased, hence there is some overlap with the purpose of supporting system understanding (previous section).

Strengths, limitations and data needs

Measures for independently identifying whether a risk pathway is 'safe' are extremely limited. Traditional epidemiologic approaches that look for elevated levels of disease associated with a particular water source or pathway lack the sensitivity for verifying the low levels of risk desired for drinking water systems (i.e. best randomized control double blinded drinking water studies can only detect illness when it exceeds 10% within the study population (Hellard *et al.* 2001) not the desired 0.01%). In addition, they lack the statistical power and flexibility for undertaking system specific evaluation of water safety across a broad range of systems and event conditions. As for chemical risk assessment, QMRA overcomes both of these limitations and is therefore extremely valuable for comparing risks for a particular system with an independently determined benchmark.

There are, however, constraints in the practical implementation of the QMRA approach. The discussion points associated with defining treatment requirements in 'Regulation and health-based treatment targets' above are also relevant to system assessment. Firstly, the target benchmark in terms of risk measure (e.g. daily probability of infection, annual probability of infection, probability of illness, DALY), and the associated statistic (e.g. mean, 95th percentile) need to be defined. There has been criticism that extremely low benchmarks (such as the WHO 1 μDALY.person^{-1}.year^{-1}) may be unnecessarily low and hence driving an imbalance in the focus on drinking water in comparison to other pathways of infection (such as the 3.5% GI illness required by recreational water criteria (EPA 2012)) – yet this harmonized approach is recognized by WHO in their overall framework for water exposure pathways (Fewtrell & Bartram 2001).

Secondly, it is important to note that the model input assumptions (exposure volumes, dose-response models, DALY weightings, etc.) can make an important impact on the quantified risk, and need to be carefully defined, particularly if a 'level playing field' is desired for comparative studies. In some cases choices between comparable inputs can make more than an order of magnitude difference in the estimated risk, and even larger changes if hazardous events are not sampled or estimated (e.g. Signor & Ashbolt 2009). The most suitable inputs for the local region and for the purpose of the assessment need to be selected, and if comparison between systems is the objective, then these inputs need to be constant among QMRAs.

Thirdly, the site-specific data collection and analysis requirements need to be carefully defined. For example, when the source water contamination level is based on a limited environmental dataset, concentrations predicted from samples collected during baseline conditions (including estimates of their standard deviations, as used in the Health Canada tool) can be expected to be much lower than concentrations/SD predicted from samples collected during events. Under the US-EPA surface water treatment rule (US-EPA 2003b) it is necessary to collect 48 samples and analyse for *Cryptosporidium*. The conditions under which these samples are to be collected are not prescribed. Given the extreme variability in *Cryptosporidium* concentration in many systems, the conditions under which samples were collected will fundamentally influence the required level of treatment to achieve safety – e.g. during dry versus wet and snow melt conditions.

Critical control points and setting critical limits

Operational limits and critical control points for water treatment plants need to be defined in order to manage the system. Parameters including turbidity (on raw water to

define coagulant needs and on finished water to determine filtration efficacy), and chlorine residual are monitored to ensure that the plant is operating effectively. Appropriate values are typically chosen based on the design requirements and expected reduction performance of the treatment plant. It is possible to use QMRA to define the critical limits so that the required level of treatment is achieved, without undue redundancy.

Case study examples

The concepts that have led to the development of using QMRA for establishing critical limits for water treatment plant operation are included in the following examples:

- In the US-EPA surface water treatment rule (US-EPA 2003a), filtration and chlorine dose is related to Log_{10} reductions for parasitic protozoa and enteric viruses (Regli *et al.* 1991; Rose & Gerba 1991).
- QMRA has been used to compare risks between different agents to balance risks associated with disinfection dosing (Havelaar *et al.* 2000; US-EPA 2001; Petterson *et al.* 2010).
- Evaluation of hydraulic requirements for achieving expected disinfection efficacy (Petterson & Stenström 2015).
- Zhang *et al.* (2012) developed a performance assessment that integrated the concepts of reliability and robustness within QMRA. This was a first step in linking measurable plant performance indicators with achievement or failure to meet health-based targets.

The concepts of using QMRA to establish critical limits has been most clearly explored through examples presented by Smeets (Medema & Smeets 2009; Smeets *et al.* 2010), however all of these examples are still conceptual, and no examples or case studies were identified in the peer reviewed literature addressing real plant operations that had adopted this approach for defining critical limits and operational targets.

Software tools

As part of the EU-HiWATE project a software tool was developed to compare the risk benefit tradeoff between free chlorine disinfection and TTHM formation (Petterson *et al.* 2010). The overall objective was to move toward defining optimal chlorine dosing in order to achieve adequate pathogen reduction without excess disinfection by-product formation. The tool was constructed using the Analytica® (Lumina Decision Systems, USA) software platform and was run for six reference pathogens (*Campylobacter*, *E. coli* O157:H7, Rotavirus, *Norovirus*, *Giardia*, and *Cryptosporidium*) and compared DALYs associated with health outcomes of gastroenteritis and bladder cancer.

Strengths, limitations and data needs

The concepts associated with using QMRA to establish critical limits are well established and make good operational sense. Without this approach there is limited confidence that the limits are appropriately set to protect public health without major redundancy. The most important limitations relate to the scientific uncertainty associated between the measurable surrogate (e.g. chlorine residual, turbidity), the achieved treatment efficacy, and hence impact on health risk. For example, turbidity or 5–20 μm particle breakthrough of filters is known to be somewhat related to pathogen breakthrough (O'Halloran *et al.* 1999), however pathogens may breakthrough well before measurable turbidity or particle counts are detected by online meters. This disconnect is a function of the poor correlation between pathogens and these physical surrogates in raw waters and that it takes a considerably lower level of pathogens than 'equivalent' measurable particles to cause an increase in risk.

Defining or evaluating monitoring requirements

Closely linked to the setting of critical limits is the characterization of monitoring requirements to verify the performance of a treatment plant. Important factors for consideration are: what should be measured, and how frequently, to ensure that health targets continue to be met. Traditional end of pipe testing that relies only on the absence of fecal indicator, is inadequate for verifying the operational integrity of the treatment train, as raised in the Introduction.

Case study examples

Only two case study examples of investigating the role of QMRA for evaluating monitoring requirements were identified for this review:

- Signor and Ashbolt evaluated the value of monitoring programs for *Cryptosporidium* and highlighted their inadequacy for protecting public health (Signor & Ashbolt 2006); and
- Nilsson and coworkers explored the limitations of relying on online SCADA data to ensure health targets are met (Nilsson *et al.* 2007).

Strengths, limitations and data needs

QMRA can provide valuable input for the development of monitoring programs. The value of monitoring for pathogens in finished water (in terms of ensuring consumer safety) can be quantitatively investigated, and compared with cost.

Monitoring will predominantly rely on process indicators rather than microbial sampling. Process indicators are often not well correlated to consumer risk, however they are well suited to identifying events within the system. The importance of events of different sizes and duration can be explored using QMRA as presented by Westrell *et al.* (2003), which was based on review of several years of operational events, concluded that source water pathogen variability/events were more important to manage (discussed later for the Åström *et al.* (2007) work associated with the same Swedish treatment works).

QMRA can demonstrate the certainty of detecting a problem associated with monitoring strategies of different frequencies (e.g. weekly, daily, hourly, online), and can therefore provide input regarding the improvement in water security achieved with respect to the additional cost associated with more frequent monitoring. Given the rapid fluctuations associated with treatment performance, online monitoring is desirable, however operational issues related to calibration and verification require ongoing attention to ensure that the system is functioning properly.

System planning and development

QMRA can be used to help identify the next best step for improving health outcomes. Scenarios, such as different potential interventions or barriers, can be modelled and their relative impact on disease can be compared. These results can be compared alongside other economic, environmental and social factors to support decision making.

Case study examples

Several examples have been identified that explore this approach:

- The Swedish Urban water project (Ashbolt *et al.* 2005) explored the application of QMRA within a multi-criteria decision making framework.
- Microbial risks were included within a sustainability framework for assessing urban water system options in Australia (Lundie *et al.* 2008; Kobayashi *et al.* 2015) and in the USA (Schoen *et al.* 2014).
- In Uganda, QMRA was applied with limited data to prioritize infrastructure spending to achieve health outcomes (Howard *et al.* 2006).
- In Ghana, QMRA was applied to estimate the risk to human health from various sources of drinking water and evaluate the cost effectiveness of different interventions (Machdar *et al.* 2013).
- When investigating a high incidence of *Cryptosporidium* in a southwestern Ontario community, Pintar *et al.* (2012) applied QMRA to effectively rule out the drinking water pathway as the cause, providing an effective communication tool and prioritizing future work.
- To determine which arsenic mitigation option presents the lowest disease burden in a particular setting (Howard *et al.* 2007).
- QMRA was applied to select among household water treatment devices in the developing context (Petterson 2016).
- To support fire protection planning following the 2003 Lost Creek Wildfire in Alberta, Canada (Emelko *et al.* 2011).
- In comparing life-cycle impacts with pathogen risks from Swedish wastewater treatment options (Harder *et al.* 2014, 2015), which could impact on source drinking waters.

Software tools

Petterson (2016) developed a software tool to support the application of QMRA as a decision support tool in selecting among household water treatment devices. Given the uncertainty and variability associated with model inputs, the tool was developed to support the exploration of model input assumptions on the outcomes of the analysis. The tool was constructed in Analytica® and used three reference pathogens (*Campylobacter*, Rotavirus and *Cryptosporidium*), one to represent each of the microbial groups.

Strengths, limitations and data needs

QMRA is unique in providing a structured approach for evaluating health impacts of hypothetical or planned future activities. It is important to include predicted health outcomes alongside other criteria to support decision-making. The outcomes of any risk assessment are dependent upon the integrity of the information underlying the calculations, and therefore the sensitivity of any decision to these input values must be tested. Additional data needs will depend on the sensitivity of these input values.

CONCLUSIONS AND RECOMMENDATIONS

The studies reviewed have demonstrated how QMRA can be applied to support water safety management and in particular the development of a WSP for a specific water supply. QMRA has unique value for providing quantitative information to support decision making; from the general objective of improved system understanding to the more specific operational requirements of the water treatment plant. While these concepts are well developed in the literature presented, there are limited examples of practical implementation within the water industry. There are several identified reasons for this, which drive the recommendations of this review.

Firstly, environmental and engineered systems demonstrate considerable variability and there is uncertainty associated with quantifying the model components for any QMRA. The data needs of applying QMRA in the WSP are summarized in Table 1, and are classified as fundamental (referring to scientific knowledge) or site specific. The current state of knowledge associated with each of the identified fundamental questions are summarized in Table 2. Some of these uncertainties are large, and appropriate consideration needs to be given in the application of QMRA. As a consequence, results need to be interpreted in the light of the certainty of the input assumptions. Confidence in how to handle uncertainty both from the perspective of the risk assessor and the regulator is essential to support implementation. The following general recommendations therefore follow:

1. When applying QMRA to support system understanding (i.e. know your system) the most important factor is to ensure that the quantitative values used to represent the scientific evidence are representative. Regardless of the amount of information available, QMRA is valuable to support the understanding of the risk drivers within the system as described/assumed, however poor interpretation of the microbial data could lead to misleading results. It is also valuable (to the extent possible) to represent the uncertainty associated with the quantitative values so that the WSP team are able to understand the level of confidence associated with the quantitative value presented.
2. When applying QMRA to determine if a system or pathway is safe (i.e. system assessment) the most important factor is to ensure that the underlying model inputs, data collection and analysis assumptions have been clearly defined. These underlying assumptions, together with the health target, define what is meant by 'safety'. To rely only on the health target, and to leave the other assumptions undefined, creates an ambiguous target and does not address uncertainties.
3. No practical cases where QMRA had been applied to determine critical limits and operational targets were identified. Rather, over-reliance on some surrogates, such as post-filtration turbidity, which is very site- and condition-specific, yet the water industry has a false sense of security in its use; turbidity is useful for filter performance, but is very loosely related to safe pathogen levels (Table 2). The uncertainty associated with the relationship between measurable surrogates and health impacts is assumed to be too great for the QMRA approach to replace existing limits. Fundamental

Table 1 | Objectives of QMRA within the WSP and associated data needs

Objective of QMRA	Specific questions that need to be defined	Data needs		Consequence of inadequate information
		Fundamental	Site specific	
Know your system Use scientific evidence to support the development of the WSP	Identification and prioritization of hazards and hazardous events	• Rather than requiring specific data, this approach allows for whatever data is available to be incorporated into the overall development of the WSP		
System assessment Compare risk with health target to determine if system is 'safe'	How will 'safety' and the model assumptions be defined?	• Determine measure for heath target • Dose-response relationship • Health impact assumptions and DALY weightings (if appropriate)	• Reference pathogen concentrations • Exposure volumes	Model assumptions and definition of safety can influence the required treatment reductions by several orders of magnitude
	What is the magnitude of contamination of the source water?	• What are the sources/hosts of pathogens? • How many are excreted by those sources/hosts? • How many are human infectious? • How well do those pathogens persist in the environment?	• Sanitary survey • Identification of pathogen mobilization events including their magnitude and frequency. • Water quality data	Quantified level of contamination may not be representative of the system, e.g. not considering all conditions (and events); or not considering only human infectious portion of pathogen loading
	How effective are the treatment barriers?	• Mechanisms of removal by different treatment barriers • Expected Log_{10} reduction by treatment barriers • Expected causes of poor performance	• What treatment barriers are in place? • How well do they perform? • What fluctuations (magnitude and frequency) are likely for the barrier?	Treatment reduction may appear adequate based on expected performance, but site-specific differences or fluctuations may undermine overall performance
Critical control points and **critical limits** Define limits for measurable surrogates	How does the measurable surrogate relate to consumer risk? What is a safe level for the surrogate?	• How does microbial indicator presence and persistence through treatment relate to pathogens?	• What level of treatment is required by all barriers? • What are the relevant surrogates for the treatment steps present at the plant to ensure each step achieves its target?	A poor understanding of the relationship between measurable surrogates and treatment performance can lead to critical limits that are not well linked with actual health risk. The result may be limits that are overly conservative, or not protective enough
	Filtration	• How does **turbidity** in finished water relate to filtration performance of pathogens?	• What is the source water turbidity? How do the principles apply to the specific plant?	

(*continued*)

Table 1 | continued

Objective of QMRA	Specific questions that need to be defined	Data needs: Fundamental	Data needs: Site specific	Consequence of inadequate information
	Disinfection	• What is the sensitivity of pathogens to **disinfectant**s and the required Ct to achieve the necessary Log_{10} reduction	• What is the residence time distribution of the disinfection contactor?	
	Distribution	• Pathogen controls via SOPs for mains break/ repairs, X-connection & back-siphoning, & reservoir cleaning	• System integrity by on-line disinfectant measures, pressure transients, source-specific faecal markers	
Define **monitoring requirements** What needs to be measured and how often to ensure consumer safety?	How does the level of the surrogate relate to consumer risk?	'As above'	'As above'	Monitoring may not be targeted toward the appropriate parameters for ensuring health targets are met, hence providing false security
	How much time is allowable before corrective action is necessary?	Based on QMRA modelling	Site-specific QMRA modelling	

Table 2 | Current state of knowledge and knowledge gaps associated with fundamental research questions of relevance to WSP

Fundamental research question	Current state of knowledge[a]		Knowledge gaps
What are the sources/hosts of pathogens in the drinking water catchment?	★★★★	Sources of human enteric pathogens within drinking water catchments are well characterized	• Emerging zoonotic pathogens
How many enteric pathogens are excreted by those sources/hosts?	★★★	The excretion density of various pathogens in different hosts is known within a few orders of magnitude	• The magnitude of asymptomatic excretion of some pathogens by humans • The variability in excretion over the course of an infection
How many of those enteric pathogens are human infectious?	★	Molecular methods enable sub-typing of samples to identify specific host links for zoonotic pathogens	• Still many unknowns with regard to the proportion of protozoa that are human infectious
How many of those pathogens are viable (detectable) and able to cause infection?	★	For culturable organisms the lower boundary of detectible organisms is well known, but not those viable but non-culturable (VBNC)	• Viability of organisms detected using modified molecular methods • The proportion of organisms that are VBNC
How well do pathogens persist in the environment	★★	Many studies under different specific conditions for a range of pathogens	• Translation of specific studies to variable environmental conditions & biotic effects • Persistence of pathogens for which there are no measures of viability
What are the mechanisms of removal by different drinking water treatment barriers	★★★★	Principles of pathogen reduction across a range of treatment barriers is well known	• Quantitative information regarding removal mechanisms is still limited • Hydrodynamic modeling is often missing to aid in estimating concentration.time (C.t) values to aid in estimating disinfection efficacy

(*continued*)

Table 2 | continued

Fundamental research question	Current state of knowledge[a]		Knowledge gaps
Expected Log_{10} reduction by different treatment barriers	★	Many studies with surrogate organisms comparing inflow and outflow concentrations	• Quantitative translation of surrogate information to pathogens is limited. Translation of site specific results to other facilities is a challenge as most studies lack a mechanistic consideration of reduction values • Appropriate quantification of treatment performance (surrogate) based on microbial data
Expected causes of poor performance	★★	Principles of compromised performance for pathogens is well known	• Quantifying how poor the performance is under different conditions is not well known • Frequency and duration of periods of poor performance
How does microbial indicator presence and persistence through treatment relate to pathogens?	★★★	Principles are well known, and some quantitative data	• Presence of microbial indicators in finished water is often a challenge to explain
How does turbidity in finished water relate to filtration performance of pathogens?	★★	Some information on relationship between turbidity/particle counts and breakthrough of protozoa; some information of total organic carbon (TOC) and virus breakthough by membrane processes	• Improved information needed for all site-specific pathogens as related to inflow turbidity/particle count levels • Not well characterized for viruses, and may be a completely inappropriate indicator of virus removal performance, depending on process
What is the sensitivity of pathogens to disinfectants and the required Ct to achieve the necessary Log_{10} reduction	★★	Many studies in the literature on pathogen and surrogate reduction by various disinfectants in laboratory studies	• Quantifying the impact of pathogen shielding on reduction efficacy, somewhat limited too because of the pathogen assay method used (i.e. may miss VBNC and persistent forms (Wood *et al.* 2013)) • Applicability of using laboratory strains to represent environmental strains is not well known • Inactivation of non-culturable organisms is not well known
Dose-response relationships for relevant pathogens	★	Human feeding studies and outbreak data available for most reference pathogens of interest	• Some studies have very limited number of datapoints at relatively high doses • Studies often only represent healthy adult volunteers – not more vulnerable groups • Studies only represent the specific strain used in the feeding study, unclear how representative
Conditions for growth of environmental pathogens	★	Warm waters, periods of stagnant flow and minimal disinfectant residual known to be important	• Specific effects of upstream microbiome and pipe materials on growth of human infectious *Legionella* and non-tuberculous mycobacteria in premise plumbing
Health impact assumptions and DALY weightings	★★	DALY weightings have been developed for most pathogens of interest	• Site specific weighting information is needed (likelihood of different disease outcomes for the local setting)
Risk based definitions of water safety (tolerable risk targets)	★★★	Tolerable risk targets have been suggested by WHO ($1 \times \mu$DALY. $Person^{-1}.year^{-1}$) and US-EPA (1×10^{-4} annual probability of infection)	• Context specific targets as the suggested targets may be too low in some circumstances to give balance to all pathways

[a]Stars provide a subjective indication of the relative level of certainty associated with each fundamental question as it relates to the representivity of risk estimates from QMRA. Four stars indicates that this aspect is well characterized and has a limited impact on the representivity in the risk outcomes; 1 star indicates that this aspect is highly uncertainty and likely to have a high impact on the representivity of the risk outcomes.

VBNC, viable but non-culturable cells.

research to overcome existing knowledge gaps is needed before this can be practically implemented.

4. When implementing QMRA as a decision support tool for system planning, the most important factor is to ensure that the sensitivity of any decision to the model input assumptions is clearly explored. Outcomes can be dependent upon input values that are highly uncertain and this needs to be transparent to the decision maker. Conversely, in many cases where scenarios are being compared, many of the uncertain inputs are common among options and therefore comparisons can be clearly and confidently made.

Secondly, QMRA calculations have historically been in the hands of specialists and researchers. The apparent complexity of the calculations has created a barrier for more widespread accessibility to the water industry. Various tools have been developed to increase accessibility of the QMRA approach to non-specialists. A range of different software platforms have been used to undertake QMRA calculations including specific Monte Carlo simulation tools (e.g. @Risk®, Crystal Ball® and Analytica®) and more generic mathematical software (R, Mathematica®, Matlab® and Excel®). The following recommendations relate to the development and application of QMRA software tools:

1. There is currently no single QMRA tool that can meet all of the needs of the water industry. Tools need to be developed and created for specific purposes. Examples of these have been identified in this review.
2. User friendly interfaces are valuable, however basic training in QMRA and understanding the underlying model assumptions is necessary to support tool implementation. Given the uncertainties that have been presented, it is important that anyone applying QMRA (even with a simple online tool) has an understanding of the framework and the objectives of the calculations including any limitations to applying the results.
3. All underlying assumptions need to be accessible and transparent to the user so that the above requirements of uncertainty can be verified. There is limited value associated with a 'black box' QMRA tool, as the greatest value is not in the result alone, but in understanding the interactions between the model parameters and relative risk estimates – so you get to know your system.

Thirdly, the cases reviewed in this study varied greatly in their level of mathematical detail. Some studies used point values and others contained detailed statistical modelling and uncertainty analysis. The more complex studies are not necessarily better, in fact, a QMRA should be as simple as possible in order to achieve the required outcomes of the analysis. Following the tiered approach presented previously (Medema & Smeets 2009), the complexity of an assessment only needs to be increased if it is required to inform management of the risk. This tiered approach can be extended for all of the different objectives presented in this paper. The most simple, conservative approach should be applied first, and then additional detail undertaken only as necessary to achieve the required outcome.

Fourthly, an important purpose of QMRA that underpins all potential applications is as a support for risk communication. Management of risk requires interaction between a diverse range of stakeholders, and the implications of scientific knowledge can be challenging to communicate. Simple outputs from QMRA such as: the reduction in risk due to interventions; or selection of one intervention over another; demonstration of a process vulnerability; or identification that a current practice is unsafe, are of great value for communication to the relevant stakeholders.

In practice, whilst the QMRA methodology is fundamentally robust, its reliability is limited by the quality of supporting data and evidence. Critics of QMRA often focus on these uncertainties. However, it should be recognized that often QMRA does provide the best-supported estimate of risk. Furthermore, QMRA permits explicit identification and quantification of uncertainties. This provides a good platform for starting with a best-supported evidence-based estimate of risk whilst highlighting research and data collection needs.

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