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Sensitivity of quantitative microbial risk assessments to assumptions about exposure to multiple consumption events per day

N. Van Abel, E. J. M. Blokker, P. W. M. H. Smeets, J. S. Meschke and G. J. Medema

ABSTRACT

Quantitative microbial risk assessments (QMRAs) of contaminated drinking water usually assume the daily intake volume is consumed once a day. However, individuals could consume water at multiple time points over 1 day, so the objective was to determine if the number of consumption events per day impacted the risk of infection from *Campylobacter jejuni* during short-term contamination events. A probabilistic hydraulic and risk model was used to evaluate the impact of multiple consumption events as compared to one consumption event on the health risk from the intake of contaminated tap water. The fraction of the population that experiences greater than 10^{-4} risk of infection per event at the median dose was 6.8% (5th–95th percentile: 6.5–7.2%) for one consumption event per day, 18.2% (5th–95th: 17.6–18.7%) for three consumption events per day, and 19.8% (5th–95th: 14.0–24.4%) when the number of consumption events varied around 3.49 events/ day. While the daily intake volume remained consistent across scenarios, the results suggest that multiple consumption events per day increases the probability of infection during short-term, high level contamination events due to the increased coincidence of a consumption event during the contamination peak. Therefore, it will be important to accurately characterize this parameter in drinking water QMRAs.

Key words | *C. jejuni*, consumption, drinking water, risk assessment

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INTRODUCTION

Distribution system contamination has been responsible for a significant number of waterborne disease outbreaks and the proportion of waterborne disease outbreaks associated with distribution system problems is increasing (National Research Council (NRC) 2006). In the USA, distribution deficiencies were associated with approximately 30% of outbreaks in community water systems and since 1991 there has been an increased proportion of waterborne disease outbreaks associated with contaminants entering the system after treatment (Craun & Calderon 2001; Craun *et al.* 2006). While outbreaks highlight the failures in the distribution system, they do not tell the whole story because many smaller contamination events are likely occurring on a more regular basis (Van Lieverloo *et al.* 2006). In general, there are multiple types of main breaks that vary in severity and evaluation of risk from the different types of breaks needs to be completed (NRC 2006).

Distribution systems are the final component of public water supplies and the last barrier in the water-treatment process. Many events associated with the repair and maintenance of drinking water distribution systems can contribute to pathogen contamination, such as replacing a pipe or a negative pressure event when the system must be closed off for repairs (Karim *et al.* 2003; LeChevallier *et al.* 2003; Lambertini *et al.* 2011). These failures can lead to loss of physical or hydraulic integrity in systems from a few

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seconds to a few hours for a negative pressure event or from 2 to 6 hours for a water main repair (Kirmeyer *et al.* 2001; Besner *et al.* 2011). This can result in short-term contamination events that can lead to adverse health impacts for customers.

Assessing the potential health impacts from drinking water contamination events requires understanding the fate and transport of contaminants through the distribution system, the exposure of consumers to contaminated water, and the response of the individuals to the exposure (Davis & Janke 2009). The estimation of the potential risk from short-term contamination events can be done by quantitative microbial risk assessment (QMRA) coupled with hydraulic modeling. This method was previously used to evaluate the risk from microbial intrusion during negative pressure events that led to contamination of distribution systems. In these previous studies, the daily intake volume was assumed to be consumed completely at one point and any time during the day by a customer (Teunis *et al.* 2010; Yang *et al.* 2011). However, individuals could ingest water at multiple time points over 1 day drawn from the tap at several moments during the day.

Ingestion is generally assumed to be a main contributor to exposure, so accurately characterizing this parameter is important (Besner *et al.* 2011). A similar issue, the issue of timing, was previously examined though the use of a hydraulic model combined with numerous exposure models to estimate the impact on dose. In this analysis, the authors looked at a variety of exposure models, such as ingesting water every hour of the day or during every meal, for the potential impact on dose (Davis & Janke 2008). However, this work did not investigate combining a hydraulic model with an exposure and risk model to look at the impact of the number of consumption events on the probability of infection of a pathogen in a community. Therefore, the goal of this work was to determine if the number of consumption events per day had an impact on the risk of waterborne infection from *Campylobacter jejuni* during short-term contamination events.

METHODS

A multi-component probabilistic model that included hydraulic and risk analyses was used to evaluate the impact of multiple consumption events as compared to one event on the health risk from the intake of contaminated drinking water from the home tap. The probability of infection from the consumption of contaminated tap water during different numbers of consumption events was estimated.

Problem formulation

The simulated network in this analysis was Zandvoort in the Netherlands, which is a Dutch town situated on the sea. This network was built in the 1950–60s with around 10 km of pipe including 3.5 km of polyvinyl chloride pipes and 5.7 km of lined cast iron pipes. The network is composed of 448 nodes, which represents approximately 1,000 homes, two hotels, and 30 beach clubs. The network is supplied from one pumping station and has no tanks. Water use as determined from historic flow patterns is on average 24 m^3/hr (Blokker *et al.* 2010a).

Campylobacter jejuni was the reference pathogen. The simulated scenario assumed a short-term contamination event where *C. jejuni* entered the system at the pumping station from midnight until 2 am on the first day at a concentration of 10^8 bacteria/L. The concentration was kept constant for the entire 2 hour contamination period. This large initial concentration assumes that raw sewage was pumped into the distribution system. While this would be an extreme contamination incident, this high concentration was selected for modeling purposes so the movement of the contaminant cloud through the distribution system could be observed.

Hydraulic analysis

A hydraulic model (EPANET, United States Environmental Protection Agency (USEPA), Cincinnati, Ohio) was coupled with a water demand model (SIMulation of water Demand, and End-Use Model (SIMDEUM), KWR Watercycle Research Institute, Nieuwegein, The Netherlands) to estimate the distribution of the contaminant throughout the distribution system. EPANET 2.0, which is hydraulic modeling software developed by the USEPA, was used to simulate hydraulic and water quality behavior in pipe networks and was used to estimate the concentration of a contaminant throughout a distribution network (Rossman 2000). EPANET 2.0 assumes plug flow where water volumes are transported through pipes by bulk velocity and completely mix at junction nodes; thus, dispersion is ignored (Shang *et al.* 2008; Teunis *et al.* 2010). The scenario simulation was run for 3 days with a hydraulic and water quality time step of 1 min. The contamination event was assumed to occur at the start of the first day of the 3 day analysis from 12 to 2 am (2 hr). Disinfectant residual was disregarded because the distribution system modeled was in the Netherlands and residual chlorine disinfection following drinking water treatment is not used. This is in agreement with a similar study that ran hydraulic simulations for 24 hr, because within that time period the contaminated material was assumed to have left the system (Teunis *et al.* 2010). With a smaller distribution system and similar contamination level (10^8 bacteria/L), 3 days was assumed to be enough time for the contamination to be removed from the system. No die-off was assumed, but pathogen concentration was reduced at nodes where demand occurred.

For the hydraulic analysis to properly reflect system performance, accurate water demands must be incorporated. Thus, the end-use water demand model SIMDEUM developed by KWR Watercycle Research Institute in the Netherlands was used. SIMDEUM simulates water demand over the course of the day on a per-second basis. In this approach, each end-use is simulated as a rectangular pulse from probability distribution functions for the intensity, duration, and frequency of use of water-using appliances. This information is collected from surveys with information at the household level such as number of members in the household, number of water-using appliances, and intensity, frequency, and duration of use of appliances. SIMDEUM is programmed in MATLAB (MathWorks, Natick, MA) and works in tandem with EPANET (Blokker *et al.* 2010b).

The end-use model SIMDEUM was previously populated for Zandvoort with specific data collected for household composition and water-using appliances. In the initial Zandvoort model, there were two kinds of residences including type A (often apartments without gardens and no outdoor water use) and type B (villas). The detailed input information was previously published and the average water use for residences ranged from approximately 0.129 for type A residences to 0.149 m^3/person/day for type B residences (Blokker *et al.* 2010a). For the risk model we did not differentiate between the two types of residences; thus, it was assumed that the average daily demand was 0.139 m^3/person/day for Zandvoort.

The output from EPANET + SIMDEUM was the water demand (m^3/hr), time of day (minute), and concentration (bacteria/L) at each node in the distribution system. A wide distribution in the contaminant concentration (0 to 10^8 bacteria/L) at the nodes was observed because the contaminant is moving through the distribution as a highly skewed contaminant plume. The pathogen concentration at each node was then fed into the risk analysis (exposure and dose-response analyses).

Risk analysis

The probabilistic risk model including exposure and dose-response analyses was built in MATLAB (R2012b, Mathworks, Natick, MA) and estimated the dose and probability of infection for the population of Zandvoort, The Netherlands. The probabilistic risk model was run for 500 iterations.

Exposure analysis

The exposure analysis determines the amount of microorganisms that corresponds to a single dose to which a person is exposed (NRC 1983; Haas *et al.* 1999). The exposure analysis estimated the dose in drinking water based on the number of consumption events per day, the concentration in the consumed water, and the volume of water. The exposure analysis parameters are presented in Table 1.

The concentration of pathogens at the tap, the Consumed Concentration, was output from EPANET and varied per node over the 3 days from 0 to 10^8 bacteria/L. Each person in a household had an equal chance of opening the tap and consuming contaminated tap water; thus, the coincidence of opening the tap and the passing of contaminated water through the tap was estimated (Teunis *et al.* 2010). First, the demand pattern was converted to a cumulative frequency distribution (CFD) from 0 at 0:00 hr to 1 at 24:00 hr. Then, a random number was generated from a

Table 1 | Exposure analysis parameters

Parameter	Description	Units (cfu)	Data	Distribution	Reference
Consumed concentration	Concentration of *C. jejuni* at the tap	bacteria/L	$0–10^8$	Output from EPANET	–
Daily intake volume	Mean of 0.27 liters of water consumed per person per day	L	$\mu = -1.9$ $\sigma = 1.1$	Lognormal	Teunis *et al.* (1997); Schijven *et al.* (2011)
# Consumption events	Number of consumption events	# events	1,3 or varied ($\lambda = 3.49$)	None or Poisson	Assumption; Mons *et al.* (2007)

uniform standard distribution (0, 1), found on the water demand CFD, and matched to time. This time point has an associated pathogen concentration in water that was used in the estimation of the dose (Figure 1). Timing of the consumption event was drawn from a cumulative frequency distribution representing a 24 hour period.

A lognormal distribution was used to estimate the volume of water consumed during a drinking water event. For the Netherlands, the lognormal distribution has $\mu = -1.9$ and $\sigma = 1.1$, which corresponded to a mean of 0.27 liters of water consumed per person per day (Teunis *et al.* 1997; Schijven *et al.* 2011). Use of a lognormal distribution will never yield zero consumption. Thus for each person at a node, a random volume was selected from the lognormal distribution for each drinking water consumption event.

In previous studies, the entire daily intake volume was assumed to be consumed completely at a single random point during the day by a customer (Yang *et al.* 2011). However, individuals likely consume water at multiple discrete

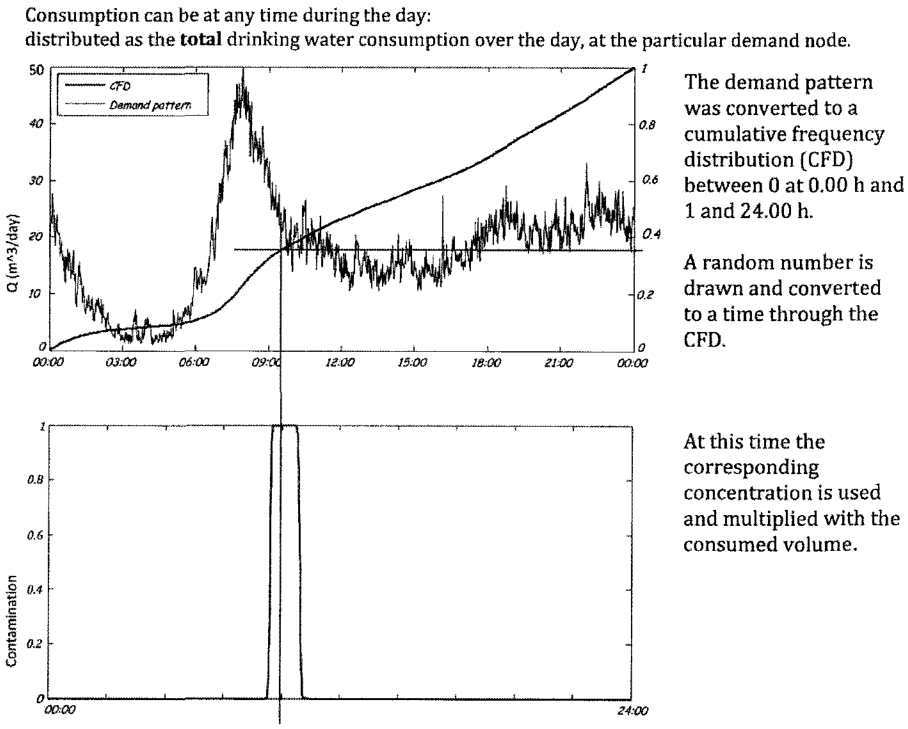

Figure 1 | Example of coincidence of tap water consumption and passing of contamination.

time points over 1 day. The number of drinking water consumption events in this model was held constant at one time per day, three times per day, or allowed to vary over multiple discrete events throughout the day. The varied number of events was obtained from a Poisson distribution with a lambda of 3.49 (Mons *et al.* 2007), which was determined from Australian data where it was inferred that the number of consumption events followed a Poisson distribution with a $\lambda = 3.49$ glasses/day. One glass was assumed to equal one event and the volume of each event was determined by sampling from a lognormal distribution. The use of a Poisson distribution may sometimes yield zero demand.

While an individual may consume water at multiple time points per day, it was assumed that the person would only consume a fraction of their total daily volume intake at any consumption event. If the person was assumed to drink tap water at more than one event per day, then the total drinking water volume selected from the lognormal distribution was divided by the number of discrete consumption events to yield a fraction of water consumed at that discrete event. The total volume of water consumed in 1 day and the number of consumption events were selected independently in each iteration. A cumulative daily dose was calculated by combining number of intake (consumption) events into one daily dose by multiplying this consumption volume by the corresponding pathogen concentration in the drinking water and summing over all the consumption events.

$$\text{Dose (bacteria)} = \sum_{1}^{\#\text{Events}} \text{Consumed Concentration} \left(\frac{\text{bacteria}}{L}\right) * \left(\frac{\text{Daily intake volume (L)}}{\#\textit{Consumption events}}\right)$$

Dose-response analysis

Dose-response analysis uses a mathematical relationship with the input of dose to yield the probability of an adverse effect (Haas *et al.* 1999). In the dose-response analysis, the probability of infection was determined from cumulative daily dose using the approximate beta-Poisson relationship for *C. jejuni* with $\alpha = 0.145$ and $\beta = 7.59$ (Medema *et al.* 1996).

$$\text{Probability of infection} \approx 1 - \left(1 + \frac{\text{dose}}{\beta}\right)^{-\alpha}$$

The impact on risk from the differing number of consumption events was compared at 10^{-4} probability of infection. Less than 1 infection per 10,000 individuals per year is the guideline for potable water for the USA and is part of the Dutch Drinking Water Act of 2001 adopted in the Netherlands for pathogenic microorganisms (Staatsblad 2001; American Academy of Microbiology 2007). A catastrophic main break or contamination episode that leads to 10^8 bacteria per liter entering the system is highly unlikely and was assumed to occur no more than one time per year. Thus, evaluating the risk at 10^{-4} was done.

RESULTS

Figure 2 shows the difference in microbial risk when different numbers of consumption events per day were modeled. A lower risk is observed when only one consumption event per day is modeled as compared to multiple events per day, even though the total consumed volume was equal.

The results of the risk model are presented in Table 2. For one consumption event per day, the fraction of the population that experiences greater than 10^{-4} risk of infection at the median dose was 6.8% (5th–95th percentiles for 500 iterations of 6.5 to 7.2%). For three consumption events per day, the fraction of the population that experiences greater than 10^{-4} risk of infection at the median dose was 18.2% (5th–95th: 17.6 to 18.7%), which was higher than for 1 consumption event. When the number of consumption events was varied, the fraction of the population that experiences greater than 10^{-4} risk of infection at the median dose was 19.8% (5th–95th: 14.0 to 24.4%), which was higher than for 1 or three consumption events per day.

Figure 3 shows the difference in microbial risk when different numbers of consumption events per day as well as different initial concentrations were modeled. At an initial concentration of 1 colony-forming unit (cfu) per

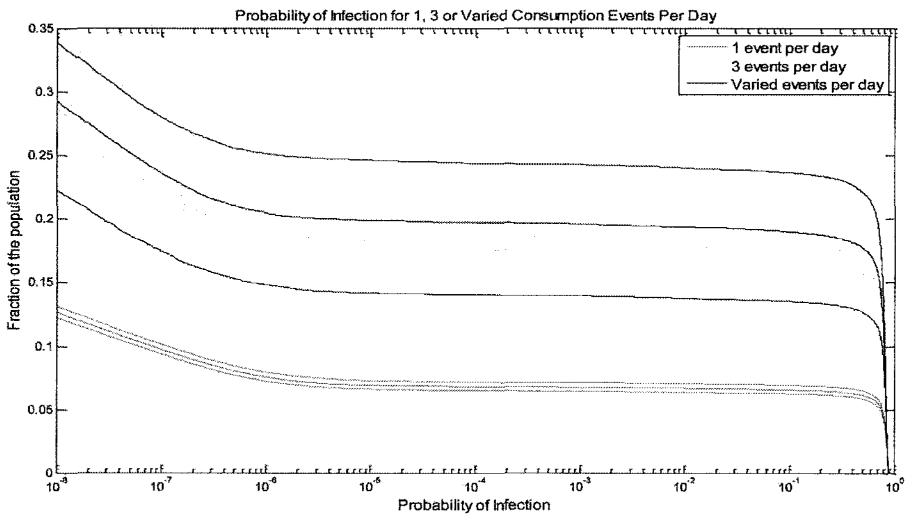

Figure 2 | Risk from the intake of contaminated water at different number of consumption events per day for 10 iterations.

Table 2 | Fraction of population at risk for $>10^{-4}$ probability of infection

	Fraction of population $>10^{-4}$ probability of infection (%)		
# Events	**At median dose**	**At 5th %tile dose**	**At 95th %tile dose**
1 event	6.8	6.5	7.2
3 events	18.2	17.6	18.7
Varied	19.8	14.0	24.4

liter, a lower fraction of the population is at risk of infection at the 10^{-4} level as compared to a dose of 10 or 10^{8} cfu/L.

The results indicate that at an initial concentration of 10 cfu per liter the fraction of the population that experiences greater than 10^{-4} risk of infection at the median dose was 5.4% (5th–95th percentiles for 500 iterations of 5.1 to 5.7%) for one consumption, 13.9% (5th–95th: 13.4–14.4%) for three consumption events per day, and 15.3% (5th–95th: 11.3–18.8%) when the number of consumption was varied. At an initial concentration of 1 cfu per liter, the fraction of the population that experiences greater than 10^{-4} risk of infection at the median dose was 4.3% (5th–95th percentiles for 500 iterations of 4.1 to 4.6%) for one consumption, 10.0% (5th–95th: 9.6 to 10.4%) for three consumption events per day, and 10.6% (5th–95th: 8.8 to 12.1%) when the number of consumption events was varied.

DISCUSSION

Particularly for short-term events and high dose thresholds, assumptions about ingestion exposure can have a significant influence on estimated impacts in distribution systems (Davis & Janke 2008). The results indicate that the number of consumption events per day does have an impact on the probability of infection during short-term contamination events. At a probability of infection greater than 10^{-4}, the fraction of the population at risk increased from 7% at the median dose if only one consumption event was considered to 18% at the median dose if three consumption events per day were considered. Thus, an underestimation of the risk was observed when only one consumption event was modeled.

The concentration of pathogens in drinking water, the volume of drinking water consumed, and when an individual ingests tap water are important factors when assessing the dose of pathogens delivered through drinking water (Mons *et al.* 2007; Davis & Janke 2008). In this model, a large concentration of *C. jejuni* was assumed to enter the system at the pumping station, which facilitates a highly skewed cloud of contaminant (0 to 10^{8} cfu/L) moving throughout the distribution system. If an individual opens the tap at the time when the contaminant plume passes, then they are at risk of infection. When the number of

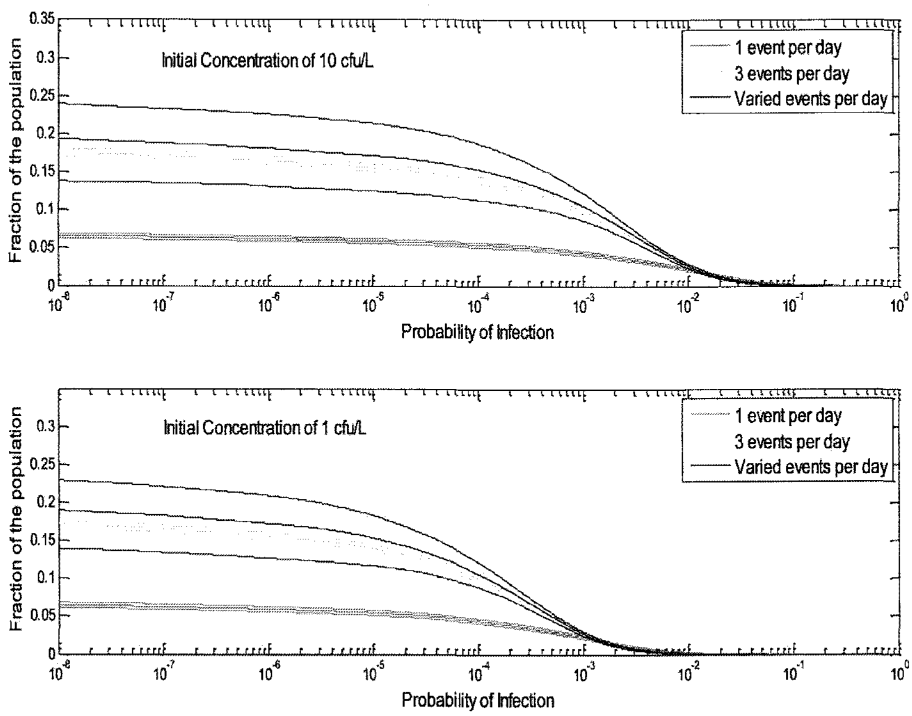

Figure 3 | Risk from the intake of contaminated water at different number of consumption events per day and multiple initial concentrations for 10 iterations.

times a tap is opened per day (consumption events per day) is increased, then the likelihood of coinciding with contaminated drinking water is increased. This ultimately leads to an increased estimation of the probability of infection for individuals. This is in agreement with previously published research which also demonstrated that the timing (or coincidence) of ingestion was important during contamination events because if the contaminated water was present at the time of ingestion, then an impact on dose and probability of infection was observed (Davis & Janke 2008; Teunis *et al.* 2010). In one study, individuals were assumed to consume water every hour for 24 hours or five times per day. It was observed that individuals who ingested water 24 times a day were exposed any time the water was contaminated while individuals who ingested water five times per day were not exposed if the contamination event was short, i.e. 1 hour (Davis & Janke 2008). Another study found that exposure to waterborne pathogens was highly heterogeneous with a strong influence of temporal coincidence of water intake and pathogen presence leading to one household member being exposed while others were not (Teunis *et al.* 2010). Thus, an increased number of consumption events per day will lead to more exposure, but a conclusion on an upper threshold of events cannot be determined because of dependence on the duration of the contaminant entering the system, which would differ depending on the contamination scenario.

Due to the high initial contaminant concentration, consumption is an important consideration because the dose and dose-response in this scenario are such that a contaminated consumption event leads to an infection. For *C. jejuni*, at a dose of 1 cfu the estimated probability of infection is 0.018 with a 95% confidence interval of 0 to 0.6, which is quite uncertain because of the extrapolation to a low dose (Medema *et al.* 1996). The probability of infection increases to 0.11 if 10 cfu are consumed and to 0.31 if 100 cfu are consumed. The probability that a customer consumes contaminated tap water is small, but when they do the microbial concentration tends to be high so the risk of infection can be quite significant (Teunis *et al.* 2010). With a less skewed contaminant plume, lower doses or other dose-response relationships, results may be different.

In this model, the approximate beta-Poisson was used, but the $_1F_1$ hypergeometric has also been proposed for use in QMRA. The proposed $_1F_1$ hypergeometric function involves a reconsideration of *C. jejuni* dose-response by combining human feeding study data with outbreak data (Teunis *et al.* 2005). Both curves provide valid fits to the dose-response data as determined by goodness of fit testing; however, the estimated probability of infection varies between the two proposed curves because there is considerable uncertainty especially at low dose levels. For a dose of 1 cfu, the probability of infection is 0.018 using the approximate beta-Poisson and is 0.44 if the $_1F_1$ hypergeometric dose-response is assumed (Medema *et al.* 1996; Teunis *et al.* 2005). This reiterates that the conclusions of this scenario are dependent on the chosen dose-response relationship as well as on the high concentration of *C. jejuni* released into the distribution system.

One consideration with this QMRA model was that the consumption events could occur at any time of day although the consumption events are related to water demand as modeled by SIMDEUM. Since coincidence of consuming tap water and the passage of contaminant are important in QMRA, realistic assumptions about the timing of consumption events should be made when estimating the dose (Davis & Janke 2008). It has been suggested that the timing of the ingestion of food is a good proxy for the timing of tapping water for consumption and a probabilistic model for the timing of ingestion of tap water was developed (Davis & Janke 2009). This model used data collected in the USA to develop the model and was not a good proxy for the Dutch scenario modeled in this paper. The use of the probabilistic model can be investigated for use in timing of water consumption events in future models of US distribution systems. Despite the limitation of consumption timing, the results would not have changed significantly; however, when applying this paper's technique to other distribution systems, a sensitivity analysis should be performed.

Another consideration is the hydraulic model assumption of plug flow. Under this assumption, dispersion of the pathogen is ignored, which could impact the risk of infection in two ways. First, dispersion could dilute pathogen concentrations, which would lower the dose during a water intake and result in lower probability of infection. Second, dispersion could increase the duration of the presence of the pathogen in the distribution system, which would increase the probability of consuming contaminated water (Yang *et al.* 2011). More research on the impacts of dispersion on pathogens needs to be investigated and incorporated into available hydraulic models. Currently, EPANET and other conventional hydraulic softwares only model transport by advection and ignore dispersion (Besner *et al.* 2011).

A final consideration is the initial concentration of contaminant introduced into the distribution system. Figure 2 demonstrates that at a large initial concentration (10^8 cfu/L) the fraction of the population at risk is constant from a probability of infection of 1 to about 10^{-7}. Thus, at such a high initial concentration in drinking water, if the opening of the tap coincides with the contaminant plume then a certain percentage of the population will be infected. At lower initial concentrations of 1 or 10 cfu/L, the fraction of the population potentially at risk drops off to 10^{-1} and 10^{-2} for initial concentrations of 10 cfu and 1 cfu/L, respectively. In addition, at an initial concentration of 10^8 cfu/L, the impact on the probability of infection from increased consumption events is more pronounced. At this initial concentration, if the number of consumption events is increased from one to three then approximately 2.7 times as much of the population has a 10^{-4} probability of becoming infected. When the initial concentration is reduced to 10 or 1 cfu/L, then approximately 2.5 or 2.3 times as many people have a 10^{-4} probability of becoming infected, respectively. Even when the initial contaminant concentration is decreased, the number of consumption events per day leads to an increased risk.

CONCLUSIONS

In conclusion, the number of consumption events per day does have an impact on the probability of infection during short-term contamination events. When only one consumption event per day was modeled, a larger fraction of the population had a lower probability of infection as compared to when three consumption events per day were modeled. This has implications for QMRA because it demonstrates that when the number of consumption events per day is greater than one, the microbial risk increases. Therefore, it will be important to accurately characterize this parameter in drinking water QMRAs.

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