Risk Analysis, Vol. 33, No. 12, 2013 DOI: 10.1111/risa.12077

A Decision Support Tool to Compare Waterborne and Foodborne Infection and/or Illness Risks Associated with Climate Change

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Climate change may impact waterborne and foodborne infectious disease, but to what extent is uncertain. Estimating climate-change-associated relative infection risks from exposure to viruses, bacteria, or parasites in water or food is critical for guiding adaptation measures. We present a computational tool for strategic decision making that describes the behavior of pathogens using location-specific input data under current and projected climate conditions. Pathogen-pathway combinations are available for exposure to norovirus, *Campylobacter, Cryptosporidium*, and noncholera *Vibrio* species via drinking water, bathing water, oysters, or chicken fillets. Infection risk outcomes generated by the tool under current climate conditions correspond with those published in the literature. The tool demonstrates that increasing temperatures lead to increasing risks for infection with *Campylobacter* from consuming raw/undercooked chicken fillet and for *Vibrio* from water exposure. Increasing frequencies of drought generally lead to an elevated infection risk of exposure to persistent pathogens such as norovirus and *Cryptosporidium*, but decreasing risk of exposure to rapidly inactivating pathogens, like *Campylobacter.* The opposite is the case with increasing annual precipitation; an upsurge of heavy rainfall events leads to more peaks in infection risks in all cases. The interdisciplinary tool presented here can be used to guide climate change adaptation strategies focused on infectious diseases.

KEY WORDS: Climate change; epidemiology; food and waterborne diseases; quantitative microbial risk assessment

1. INTRODUCTION

Concerted action is needed to assess and address public health issues related to climatic change, such as a shifting distribution of infectious diseases or changes in infectious disease burden.[(1)] For example, temperature has been found to be positively associated with food poisoning[(2–7)] and wound and ear infections,[(8,9)] while excess rainfall has been associated with drinking-water-related outbreaks.[(10,11)]

Humans are exposed to a wide range of climate-sensitive pathogens (bacteria, viruses, parasites, and algae) through food, drinking water consumption, and recreational water use. At elevated temperatures, some pathogens proliferate, whereas other (often enteric waterborne) pathogens show faster die-off or inactivation.[(12,13)] Humans may be exposed to these pathogens through food or drinking water consumption or recreational water use. Interdisciplinary

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links between climate variability and the pathogens in water and food have been identified and warrant further quantification.[14] Quantitative knowledge about infection pathways and the fate of microbial pathogens associated with rainfall and temperature is key to predicting risks.

Climate change models project higher temperatures, heat waves, excessive precipitation, storm surges, and droughts.[15] Because the exposure pathways of waterborne and foodborne pathogens are subject to climatic conditions, future human exposures may differ significantly from current patterns as the climate changes. Such changes pose considerable challenges to existing public health infrastructures.

Amid competing demands, allocating scarce resources to myriad pressing needs is a predicament of public health. In 2008, member states of the World Health Organization passed a World Health Assembly Resolution in 2008 acknowledging the importance of climate change and specifying five areas of research priority.[16] One such priority area was the development of decision support tools for assessing vulnerability and health impacts from climate change.[17] In response to this call, we developed a decision support tool than can estimate changes in infection risk for selected food- and waterborne diseases due to climate change.

Predicated upon quantitative microbial risk assessment (QMRA), this tool can assist decision-makers in prioritizing different adaptation options. QMRA has traditionally been used to estimate health impacts from exposure to pathogens[18,19] and has been applied to climate change.[12] The tool, called CC-QMRA (Climate Change Quantitative Microbial Risk Assessment), quantifies the anticipated impacts in terms of relative infection risks under climate change scenarios for norovirus, *Campylobacter, Cryptosporidium*, and noncholera *Vibrio* species. Realistic scenarios are described in detail here to illustrate the interplay of the effect of changes in temperature, annual precipitation, and frequency of heavy rainfall.

2. DESCRIPTION OF THE CC-QMRA TOOL

The CC-QMRA tool is programmed in Mathematica 8 (Wolfram Research Inc., Champaign, IL, USA), is freely available, and runs in computable document format (CDF) with the free Wolfram CDF player (Fig. 1). In total, the CC-QMRA tool enables 12 pathogen-pathways to construct from 16 separate modules (Table I) and to perform QMRA for various location-specific climate conditions and changes. All calculations are conducted for a whole year in which Monte Carlo samples from distributions are generated for each day in a year. The tool is built for use with location-specific variable such as climate conditions, microbial data, wastewater treatment, and dimensions of a river, but where users might not have the full range of data to input, the tool includes default values based upon the literature.

Climate conditions that the tool can model include air and water temperatures and precipitation (Fig. 1). The dates for the coldest and warmest day in the year can be set as well as the values of minimum and maximum average daily air and water temperatures. Temperature increases linearly from day to day from minimum to maximum temperature and back again to mimic seasonality. Temperature change between current and future conditions can be set from –6 °C to +6 °C, surpassing Intergovernmental Panel on Climate Change (IPCC) scenarios to enable more extreme location-specific changes. Annual precipitation as well as the occurrence of heavy rainfall days per quarter of the year for current and future climate conditions can also be set. The current annual precipitation is r_y mm with n heavy rainfall days per year with r_{peak} mm precipitation per day and $365 - n$ days with $r_{\text{low},0}$ mm daily low precipitation:

$$r_{\text{low},0} = \frac{r_y - n r_{\text{peak}}}{365 - n}. \tag{1}$$

Under future climate conditions, annual precipitation changes f_r times and there are $365 - n f_{\text{peak}}$ days with low precipitation:

$$r_{\text{low},1} = \frac{f_r r_y - f_{\text{peak}} n r_{\text{peak}}}{365 - f_{\text{peak}} n}. \tag{2}$$

Heavy rainfall days can be randomly allocated to each quarter of the year.

3. MODULES

3.1. Wastewater Treatment Plant (WTP)

Waterborne enteric pathogen concentration in wastewater is C_{ww} (N/L). Z_{wtp} is the fraction of pathogens passing wastewater treatment. Assuming complete mixing, the treated wastewater in surface water is diluted $\frac{Q_{\text{ww}}}{Q_{\text{sw}}}$ times, where Q_{ww} is the waste water discharge and Q_{sw} is the surface water flow rate. During n heavy rainfall days, combined sewer overflow (CSO) is assumed to occur whereby untreated wastewater discharges lead to peak pathogen

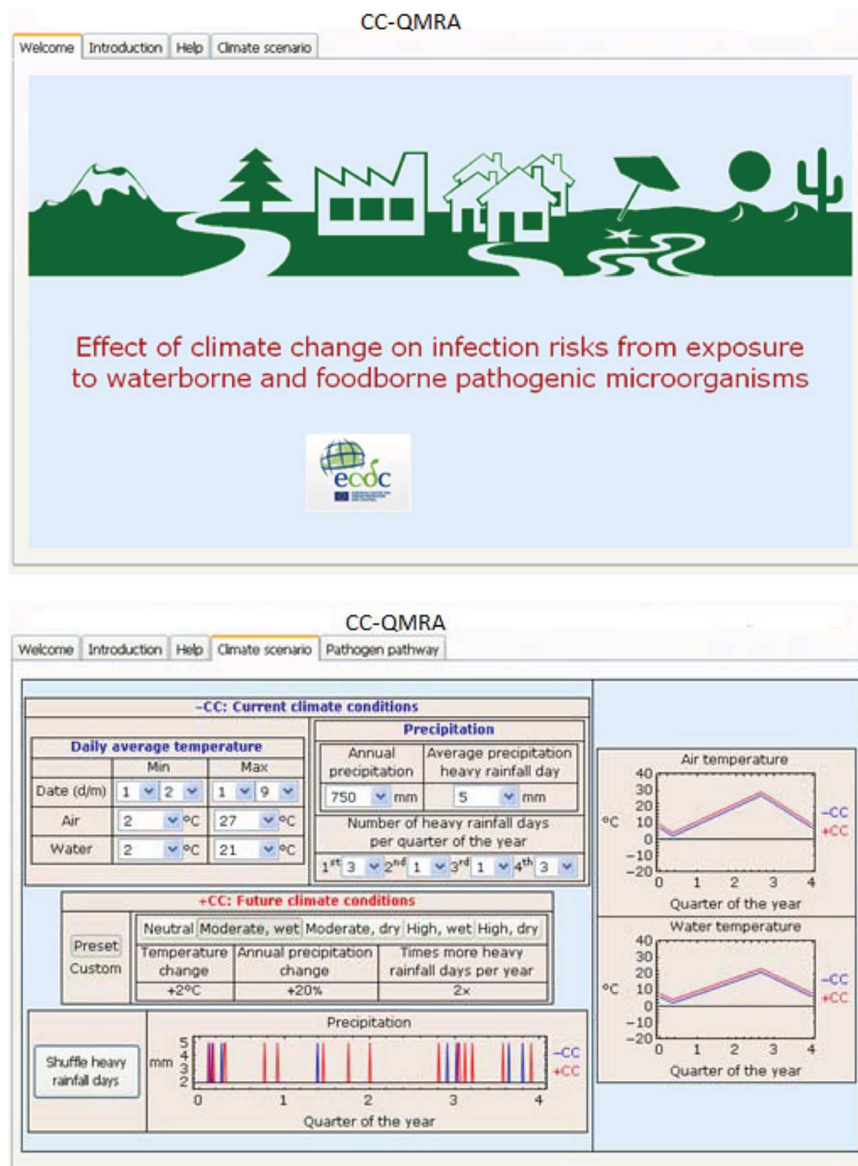


Fig. 1. Screenshots of the welcome and climate scenario pages of CC-QMRA.

concentrations in surface water. For the days with and without CSO under current (index 0) and future (index 1) climate conditions, four equations describe the pathogen concentration in the surface water at the discharge point, C_{sw}. During heavy rainfall, pathogen concentrations in wastewater can increase/decrease f_{ww} times.

Under current climate conditions, there are $365 - n$ days without overflow where

$$C_{sw,0} = C_{ww} Z_{wtp} \frac{Q_{ww}}{Q_{sw}}, \tag{3}$$

and n days with overflow where

$$C_{sw,0} = f_{ww} C_{ww} \left(Z_{wtp} + \frac{r_{peak}}{r_{low,0}} - 1 \right) \frac{Q_{ww}}{Q_{sw}} \frac{r_{low,0}}{r_{peak}}. \tag{4}$$

Under future climate conditions with $365 - f_{peak} n$ days without overflow and $f_{peak} \times n$ days with overflow, $r_{low,0}$ is replaced by $r_{low,1}$ and Q_{sw} by $f_r\, Q_{sw}$ in Equations (3) and (4).

Default values for pathogen concentrations in raw wastewater and removal by wastewater treatment are taken from the literature for norovirus,[20]

Table I. Pathogen-Pathway Selections

Pathogen	Pathway	Modules
Norovirus	Drinking water	WTP→ISW→TDW→VDW→DR→Risk of infection
	Bathing water	WTP→IBW→VBW→DR→Risk of infection
	Oysters	WTP→ISW→IOY→COY→DR→Risk of infection
Campylobacter	Drinking water	WTP→RO→ISW→TDW→VDW→DR→Risk of infection
	Bathing water	WTP→RO→IBW→VBW→DR→Risk of infection
	Oysters	WTP→RO→ISW→IOY→COY→DR→Risk of infection
	Chicken fillet	PPF→CCF→DR→Risk of infection
Cryptosporidium	Drinking water	WTP→RO→ISW→TDW→VDW→DR→Risk of infection
	Bathing water	WTP→RO→IBW→VBW→DR→Risk of infection
	Oysters	WTP→RO→ISW→IOY→COY→DR→Risk of infection
Noncholera *Vibrio* Species	Bathing water	GBW→VBW→DR→Risk of infection
	Oysters	GOY→COY→DR→Risk of infection
WTP	Wastewater treatment plant	
RO	Runoff from agricultural land	
ISW	Inactivation in surface water	
GSW	Growth in surface water	
IBW	Inactivation in bathing water	
GBW	Growth in bathing water	
IOY	Inactivation in oysters	
GOY	Growth in oysters	
PPF	Prevalence in poultry flocks	
TDW	Treatment of drinking water	
VDW	Volume of unboiled drinking water	
VBW	Volume of swallowed bathing water	
COY	Consumption of oysters	
CCF	Consumption of raw/undercooked chicken fillet	
DR	Dose response	
Risk of Infection	Risk of infection	

Campylobacter,[21] and *Cryptosporidium*.[22] Wastewater treatment is applied as average $\log_{10} Z_{\text{wtp}}$ with a standard deviation. Default values for flow rate Q_{sw}, width w_{sw}, and depth d_{sw} of a small, medium-sized, and large river are provided.[23]

3.2. Runoff (RO)

Manure on agricultural land contains zoonotic pathogens, such as *Campylobacter* and *Cryptosporidium*. Runoff to the surrounding surface water depends on soil-specific cover characteristics contained in a so-called runoff curve number, CN,[24] which is used to calculate the runoff water volume RO:

$$RO = \frac{\left(r - 0.2\left(\frac{1,000}{CN} - 10\right)\right)^2}{r + 0.8\left(\frac{1,000}{CN} - 10\right)}. \tag{5}$$

Substituting r with the three different daily precipitations, $r_{\text{low},0}$, $r_{\text{low},1}$, and r_{peak}, into Equation (5) gives three corresponding runoff volumes: $RO_{\text{low},0}$, $RO_{\text{low},1}$, and RO_{peak}.

Runoff occurs from an area of agricultural land along the riverbank of length l_{rb} and width w_{a}. Pathogen runoff concentrations C_{ro} are diluted in surface water to concentrations C_{swro}.

Under current climate conditions, there are $365 - n$ days where

$$C_{\text{swro},0} = C_{\text{ro}} \frac{l_{\text{rb}} w_{\text{a}} R0_{\text{low},0}}{Q_{\text{sw}}}, \tag{6}$$

and n heavy rainfall days where

$$C_{\text{swro},0} = C_{\text{ro}} \frac{l_{\text{rb}} w_{\text{a}} R0_{\text{peak}}}{Q_{\text{sw}}} \frac{r_{\text{low},0}}{r_{\text{peak}}}. \tag{7}$$

Under future climate conditions with $365 - f_{\text{peak}} n$ days with $RO_{\text{low},1}$ and $f_{\text{peak}} \times n$ days with RO_{peak}, $r_{\text{low},0}$ is replaced with $r_{\text{low},1}$ and Q_{sw} by $f_r Q_{\text{sw}}$ in Equations (6) and (7). By default, the tool provides wastewater concentrations as runoff concentrations for *Campylobacter* and *Cryptosporidium*.

3.3. Inactivation in Surface Water, Bathing Water, and Oysters (ISW, IBW, IOY)

With the exception of some enteric bacteria, enteric pathogens in surface water do not replicate, but gradually inactivate or die off at a rate that depends on the type of microorganism and that is faster at higher temperature. A first-order temperature-dependent inactivation or die-off rate is used:[25]

$$C_{t,T} = C_0 \exp\left[-\frac{\ln 10}{10^{a_0+a_1 T}} t\right], \qquad (8)$$

where C_0 is the initial concentration (N/L), t is the time (days), T is the temperature (°C), and a_0 (log10 day) and a_1 ($\log_{10}$ day °C^{-1}) are inactivation rate parameters.

Distance and travel time affect the pathogen concentration in surface water that ends up in drinking water, a bathing area, or an oyster bank. After a travel time of m days, pathogen concentration $C_{m,T}$ is calculated:

$$C_{m,T} = C_0 \exp\left[-\ln 10 \sum_{i=1}^{m} \frac{1}{10^{a_0+a_1 T_i}}\right], \qquad (9)$$

where T_i is the temperature (°C) on the ith day. The values for a_0 and a_1 are, respectively, 2.3 and –0.035 for norovirus,[25] 0.53 and –0.017 for *Campylobacter*,[26] and 3.1 and –0.078 for *Cryptosporidium*.[27]

Oysters accumulate pathogens by filter feeding. Oysters accumulated bacteriophages with an accumulation factor ranging from 3 to 99 and the accumulation factor for bacteria roughly 4.[28] The default accumulating factor set in CC-QMRA is 10.

Depuration has not been shown to reduce the levels of bacteriophage and of human pathogenic virus in the United Kingdom and Spain, though *Escherichia coli* levels were reduced 83–176 times.[29] Oysters depurate *Cryptosporidium* oocysts very inefficiently.[30] In the CC-QMRA tool, it is assumed that during depuration, pathogen concentrations decrease due to inactivation at the same rate as in surface water. Default depuration time is five days.[29]

3.4. Growth in Surface Water, Bathing Water, and Oysters (GSW, GBW, and GOY)

At water temperatures over 17–20 °C, *Vibrio*s are capable of multiplication[31] and at lower temperatures they persist without replication.[32] Noncholera *Vibrio* species grow in brackish to salt water.[33] Growth of *Vibrio parahaemolytics* strains has been modeled as a function of temperature, pH, and salinity.[34–36] They all showed rapid growth at temperatures above 16 °C with lag times of less than one day, independent of pH and salinity. Growth of noncholera *Vibrio* species is highly variable between species, and since it is very complex to include species-dependent models, a simple model was implemented in the tool for any *Vibrio* species. In this model, lag times for growth and inactivation are neglected and it is assumed that noncholera *Vibrio* species at low temperatures are present at a minimum concentration that can be set to 0.01–100 colony-forming units/liter (cfu/L). Above 17–20 °C, rapid growth occurs to maximum concentrations that can be set to 10^4–10^7 cfu/L.[35–38] At the set temperature threshold, the module switches between minimum and maximum concentrations.

3.5. Prevalence in Poultry Flocks (PPF)

A relation between temperature and *Campylobacter* incidence in broiler flocks in Denmark was used.[38] A logistic model was fitted to these data and implemented to calculate prevalence P as a function of temperature T:

$$P(T) = \left(1 + e^{\ln\left(\frac{1}{P_{\text{ref}}}-1\right)+0.007T_{\text{ref}}^2-0.007t^2}\right)^{-1}, \qquad (10)$$

where P_{ref} and T_{ref} are an observed location-specific prevalence and temperature. To allow for the large variability between locations in Europe (European Food Safety Authority (EFSA), 2010), a location-specific value for prevalence can be set.

During slaughter, uncontaminated flocks can become cross-contaminated. It is not expected that climate change affects the contamination level of chicken meat during the slaughter process in a conditioned environment. Nevertheless, any climate change effect that is present at the farm level might change in the slaughterhouse, for example, due to cross-contamination. Hence, prevalence in flocks after slaughter is calculated by using the analytical formulas for the maximum effect of random or logistic slaughter.[39] After slaughter, the fraction of contaminated chicken fillets of contaminated flocks can be given. The concentrations of *Campylobacter* on chicken fillets can be set to reported ranges.[40–42]

3.6. Treatment of Drinking Water (TDW)

The efficiency of drinking water treatment steps (filtration and disinfection) is highly location-specific.[43,44] Z is the fraction of pathogens that is able to pass drinking water treatment. It is entered as $\log_{10} Z$ and is assumed to follow a normal distribution. An overview of $\log_{10} Z$ values is given in the WHO drinking water quality guidelines.[45]

3.7. Volume Drinking Water (VDW)

The module uses a lognormal distribution for unboiled water consumption in liters per person per day based on Dutch data with parameters 1.85779 and 1.07487,[46] or on USEPA[47] data with parameters 0.03598 and 0.77218, or a fixed value of 2 L per person per day.

3.8. Volume of Bathing Water (VBW)

The module uses data for men bathing in fresh water, which is gamma-distributed with parameters $\alpha = 0.45$ and $\beta = 60$ (average swallowed volume of 27 mL of water per bathing event).[48]

3.9. Consumption of Oyster, Chicken Fillet (COY, CE, CCF)

By default a meal of raw/undercooked oysters is 200 g[49] and a (undercooked) chicken fillet meal amounts 50, 100, or 200 g.

3.10. Dose Response and QMRA

From the pathogen concentrations in water or food and the amount of swallowed water or consumed food, the dose D (exposure) is calculated. The infection risk P_{inf} is calculated as follows:[50]

$$P_{\text{inf}} = 1 - {}_1F_1(\alpha, \alpha + \beta; -D), \tag{11}$$

where α and β are pathogen-specific infectivity parameters (Table II) and ${}_1F_1$ is the confluent hypergeometric function. The dose-response parameters for *Vibrio parahaemolyticus* are for illness, however, and not infection as they are based on outbreak data from oyster consumption.[49] These values are applied here to the swallowing of bathing water. In the case *V. parahaemolyticus*, where $\beta >> \alpha$, P_{inf} is approximated:[51]

$$P_{\text{inf}} = 1 - \left(1 + \frac{D}{\beta}\right)^{-\alpha}. \tag{12}$$

Table II. Dose-Response Parameters

Pathogen	α	β	Reference
Norovirus	0.04	0.055	50
Campylobacter	0.038	0.022	51
Cryptosporidium	0.106	0.295	48
Vibrio parahaemolyticus	0.6	1.3×10^6	49

[a]These are illness dose-response parameters.

So, for the year under current and future climate conditions, infection risks per person per event are calculated for each day in the year. The relative infection risk due to climate change is calculated as the pair-wise per day ratios of current and future infection risks, so for each year-day a relative infection risk is calculated. In the case of infection risks from swimming in recreational water, this is limited to the days above a minimum swimming water temperature that can be set in the CC-QMRA tool.

In the case of drinking water consumption, the infection risk for drinking water consumption is calculated as per person per year by Monte Carlo sampling from a subset of 365 per day probabilities:[50]

$$P_{\text{inf,year}} = 1 - \prod_{i=1}^{365} (1 - p_i). \tag{13}$$

4. RISK ASSESSMENT VALIDATION

The CC-QMRA tool was validated by comparing the output of the risk assessments with published data. The results of these comparison are summarized in Table III for drinking water, bathing water, and oysters. Parameter values for discharges of wastewater in the tool (WTP module) were set to simulate the same concentrations of pathogens in source waters and in oysters as those published. Mean values were compared, but it should be noted that ranges of calculated risks are inherently subject to fluctuations in Monte Carlo simulations.

4.1. QMRA for Drinking Water

QMRA for *Cryptosporidium* has been conducted in surface waters of Arizona in the United States.[52] The CC-QMR tool produces a risk that is 10-fold higher than this published value, which can be explained by the difference in applied infectivity parameters (Table III). Comparison of infection risks for *Campylobacter* and *Cryptosporidium*

Table III. Validation: Comparison of Infection Risk of the Tool with Published Data

Drinking Water, P_{inf} per Person per Year								
				Consumed Volume, L			P_{inf}	
Reference		Concentration (#/L) in Source Water	Log Treatment	Reference	CC-QMRA	Dose-Response Reference	Reference	CC-QMRA
52	*Cryptosporidium*	0.0015	3	2	2	Exponential, $r = 0.028$	3×10^{-5}	3×10^{-4}
53	*Campylobacter*	130	2	0.27	0.27	Table II	0.05	0.05
	Cryptosporidium	0.002	4	0.27	0.27	Table II	3×10^{-5}	4×10^{-5}

Bathing Water, P_{inf} per Person per Event							
			Swallowed Volume, mL			P_{inf}	
Reference		Concentration (#/L) in Bathing Water	Reference	CC-QMRA	Dose-Response Reference	Reference	CC-QMRA
54	Norovirus	2.1	33	27	Table II	0.029	0.027
	Campylobacter	0.2	33	27	Hypergeometric, (0.024, 0.011)	0.025	0.004 (10^{-5}–10^{-2})
	Cryptosporidium	1	33	27	Exp 0.09	7×10^{-4}	0.007 (10^{-6}–10^{-2})
55	*Cryptosporidium*	0.02–0.07	27	27	Table II	(1–5) $\times 10^{-4}$	(1–7) $\times 10^{-4}$
56, 57, 58	*Vibrio parahaemolyticus*	12 days 10^4/L+46 days 1/L	–	27	–	rare	$<10^{-4}$

Oysters, P_{inf} per Person per Event							
			Consumption, g per Meal			P_{inf}	
Reference		Concentration (#/L) in Bathing Water	Reference	CC-QMRA	Dose-Response Reference	Reference	CC-QMRA
49, 61	*V. parahaemolyticus*	6–622	–	50–500	–	(1–44) $\times 10^{-5}$	10^{-4} (10^{-5}–10^{-3})
62	*Campylobacter*	0.05	200	200	Table II	0.05–0.20	0.30

using the data from five Dutch drinking water production locations with the drinking water risk assessment tool QMRAspot[53] demonstrated excellent agreement between CC-QMRA and QMRAspot.

4.2. QMRA for Bathing Water

QMRA was conducted for norovirus, *Campylobacter*, and *Cryptosporidium* in fresh bathing water.[54] The tool calculated risk values in the same order of magnitude. It should be noted that the tool calculates a wide range. Estimated infection risks due to exposure of swimmers to *Cryptosporidium* in three recreational lakes[55] are reproduced with the tool. Here, the same swallowed volume distribution and dose-response relationship was used.

Vibrio-associated gastroenteritis due to bathing water exposure is rare.[56] The tool calculated an infection risk of at most 10^{-4} per person per swimming event for *V. parahaemolyticus*. It should be noted that other noncholera *Vibrio* species, like *V. alginolyticus* and *V. vulnificus*, also occur frequently.[57,58] However, these species tend to be associated with wound infections rather than with gastroenteritis.

4.3. QMRA for Oysters

The most important predictor of the presence of *V. parahaemolyticus* in oysters is water temperature.[49] In the summer, *Vibrio* levels in shellfish can often be more than 100-fold greater than

those in the water.[59,60] In the GOY module, this information is not applied to *Vibrio*. Instead, minimum and maximum numbers of *Vibrio* per gram of oyster meat were set. The minimum concentrations correspond to values below 15 °C and are near detection limits, whereas the maximum concentrations correspond to concentrations at 15–30 °C.[49] After harvesting, *V. parahaemolyticus* continues to grow until the oysters are chilled. This postharvest growth was modeled giving a 1 to 2 $\log_{10}$ concentration increase, but also 1 $\log_{10}$ decrease due to cold storage.[49] In the GOY module, it is assumed that if a particular water temperature is exceeded, the noncholera *Vibrio* species concentrations in oysters switch from the default of 0.1 per gram to 10 per gram, which are the same magnitudes for oysters at the moment of consumption.[49] There is an uncertainty of about two orders in magnitude, attributable to differences in the U.S. regions where the study was conducted,[49] hence 10 times lower or 10 times higher concentrations can be set in the GOY module. These values also correspond well with those reported for *Vibrio* most probable numbers per gram in oysters of 6–622 at the Oosterschelde production areas in the Netherlands and 200 to over 300 in fish shops.[61] *Vibrio* was not detected when water temperatures were below 13.5 °C.[55] A mean illness risk per meal was estimated with the tool of about 10^{-4}, which is in good agreement with the FDA[49] mean predictions of 10^{-5} to 4.4×10^{-4} for six regions in the United States during the summer.

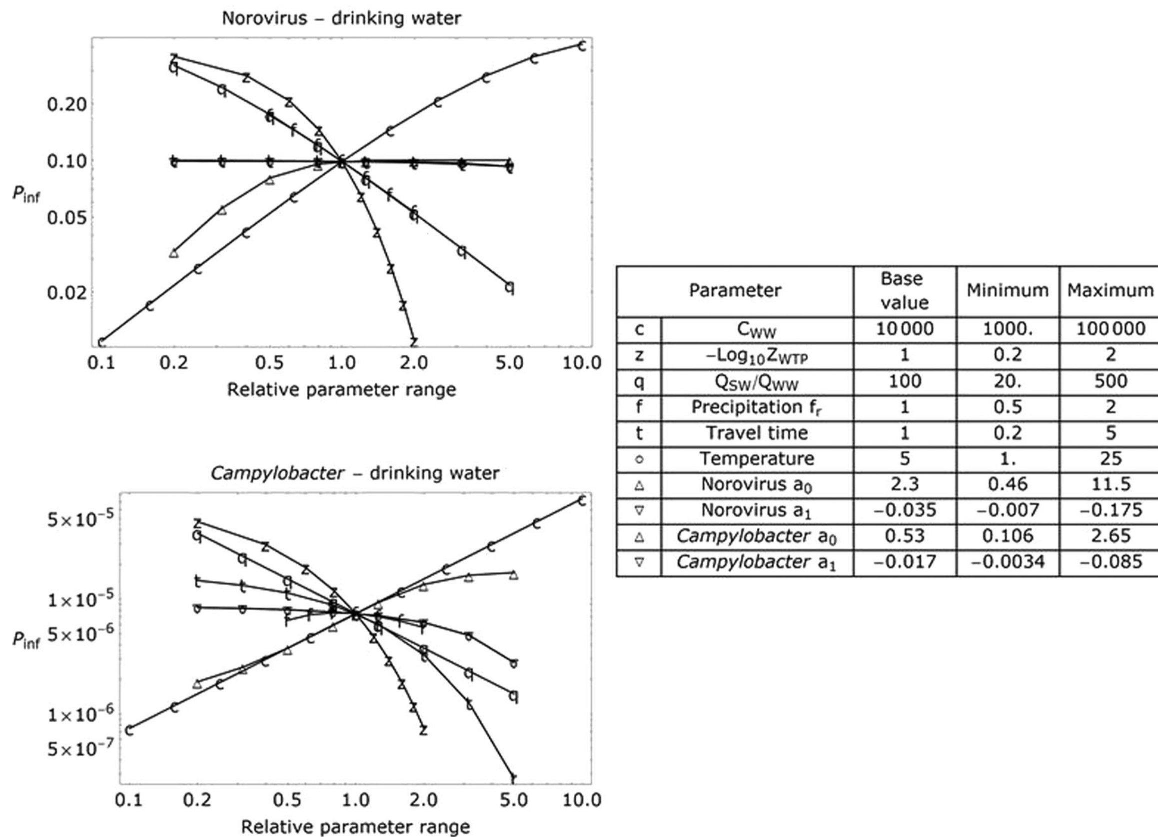
A strong seasonal variation of the level of *Campylobacter* in Dutch shellfish was reported.[62] The contamination level of mussels (<1/g) was higher than in oysters. The dominant species in Dutch shellfish is *C. lari* but little is known about its infectivity in humans. Applying infectivity of *C. jejuni* to *C. lari*, an infection risk of 5–20% (95% CI 0.01–60%) for consumption of a single portion of raw mussels and 60% (95% CI 7–99%) for repeated exposures throughout a year was estimated.[62] Risks for consumption of raw oysters were slightly lower than for consumption of raw mussels. The tool can be used to simulate 100–1,000 *Campylobacter* per liter in the surface water at the oyster bank. Following the same default settings as for *Cryptosporidium*, this leads to an infection risk of 30%, which is in good agreement with the literature.[62]

4.4. QMRA for Campylobacter in Chicken Fillet

Most essential for this QMRA is the relation between temperature and *Campylobacter* incidence as observed in broiler flocks in Denmark,[63] which predicts prevalence of *Campylobacter* in chicken flocks of 0.2 during the coldest time of the year and almost 1 during the warmest time of the year. Such a range in prevalence is also reported for 510 broiler farms in Germany.[63] From observed prevalence of 60% at 22 °C and 5% at 5 °C from a Dutch study,[64] almost the same values for the intercept of the logistic formula (Equation (16)), namely, 3.1 and 3.0, respectively, can be derived. This suggests that the temperature dependence of *Campylobacter* incidence from the Danish study may apply to other countries as well.

5. SENSITIVITY ANALYSIS

A one-at-a-time sensitivity analysis was conducted in which each model parameter was varied within the range of possible values the model parameters can have. Fig. 2 shows the results of this sensitivity analysis for the models in the risk assessment from exposure to norovirus and *Campylobacter* by drinking consumption together with the applied parameter variations. Norovirus and *Campylobacter* were selected to represent a temperature-insensitive and a temperature-sensitive microorganism, respectively. Consumption of drinking water and dose-response parameters were not varied. Also, log removal in drinking water treatment was kept constant. The sensitivity of the model outcome (infection risk) for log removal by drinking water treatment is the same as that of log removal by wastewater treatment. As can be seen in Fig. 2, the infection is for both pathogens highly sensitive to changes in wastewater concentrations. This relation becomes nonlinear for the higher risks. Even stronger, and in the opposite direction, is the sensitivity toward log removal by wastewater treatment, followed by the sensitivity to dilution of wastewater in the river. For norovirus, the effect of a change in precipitation, factor f_r, is the same as that of dilution, but for *Campylobacter* it is stronger. More precipitation adds to the dilution of wastewater in the river, but also shortens travel times. In the case of norovirus, inactivation is insignificant; therefore, only dilution counts, but in the case of *Campylobacter*, which inactivates faster, the shorter travel time partly compensates the extra dilution. Because of the negligible decay of norovirus PCR-detectable particles, changes in travel time, temperature, and inactivation parameters a_0 and a_1 do not affect the infection risk. On the contrary, infection risk for *Campylobacter* is



	Parameter	Base value	Minimum	Maximum
c	C_{WW}	10 000	1000.	100 000
z	$-\text{Log}_{10}Z_{WTP}$	1	0.2	2
q	Q_{SW}/Q_{WW}	100	20.	500
f	Precipitation f_r	1	0.5	2
t	Travel time	1	0.2	5
∘	Temperature	5	1.	25
△	Norovirus a_0	2.3	0.46	11.5
▽	Norovirus a_1	−0.035	−0.007	−0.175
△	*Campylobacter* a_0	0.53	0.106	2.65
▽	*Campylobacter* a_1	−0.017	−0.0034	−0.085

Fig. 2. Sensitivity analysis of QMRA of drinking water consumption for norovirus and *Campylobacter*. The relative parameter range (the *x*-axis) runs from the minimum value/base value to the maximum value/base value.

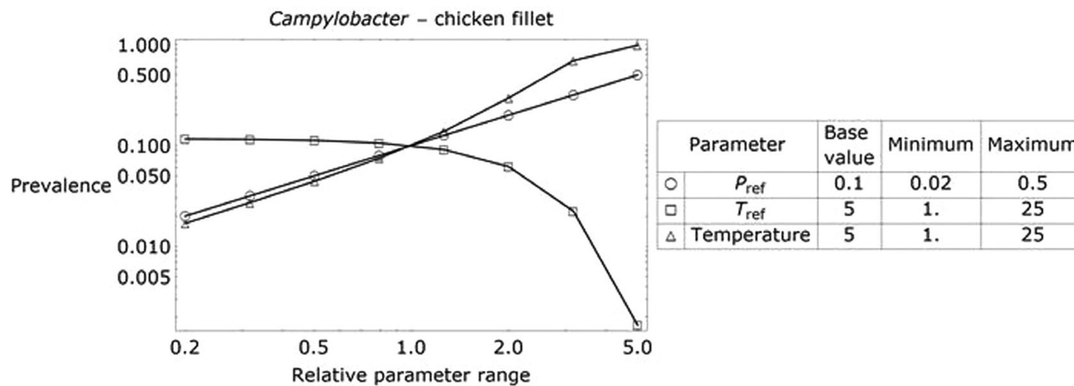
highly sensitive to changes in travel time and also is more sensitive to the higher temperatures and a_1 values.

Sensitivity analysis for the bathing water and oyster pathways shows similar sensitivities, albeit that inactivation in oysters plays a more pronounced role because of longer residence times. Sensitivity analyses did not include runoff because the model parameters for runoff are highly uncertain. Changes in pathogen concentrations in the river from runoff are expected to affect infection risk in the same way as pathogen concentrations from wastewater discharges.

Fig. 3 shows the results from sensitivity analysis of the prevalence of *Campylobacter* in chicken fillet (Equation (10)). It shows similar high sensitivity of prevalence to the location-specific prevalence P_{ref} and temperature. Prevalence is relatively insensitive to values of the location-specific temperature T_{ref} at which P_{ref} was observed for values of T_{ref} less than about 5 °C, but becomes progressively more sensitive to changes in T_{ref} above 5 °C. Random or logistic slaughtering was found not to affect infection risk. Chicken fillet consumption and concentrations of *Campylobacter* in chicken fillet, make up the dose, were proportionally related to the lower values of infection risk, but for the higher doses, infection risk was less affected, which is a well-known relation.

6. SCENARIOS: CALCULATION OF CLIMATE CHANGE EFFECTS

In order to demonstrate the interplay of climate changes and the behavior of pathogens, relative risks were calculated for five pathogen-pathway combinations, temperature changes of –2 °C, 0 °C, and +2 °C, change in annual precipitation of –50%, 0%, and +50%, and, finally, no change in heavy rainfall frequency and three higher heavy rainfall frequency. Default values for the climate conditions were minimum air and water temperature 2 °C; maximum



	Parameter	Base value	Minimum	Maximum
○	P_{ref}	0.1	0.02	0.5
□	T_{ref}	5	1.	25
△	Temperature	5	1.	25

Fig. 3. Sensitivity analysis of the prevalence of *Campylobacter* in chicken fillet. The relative parameter range (x-axis) runs from the minimum value/base value to the maximum value/base value.

air temperature 27 °C; maximum water temperature 21 °C; annual precipitation 750 mm; average daily heavy rainfall precipitation 5 mm; number of heavy rainfall days per quarter of the year under current conditions 3, 1, 1, and 3 times for the subsequent quarters of the year. Fig. 4 summarizes the results of the calculations in a bubble chart for which the diameter of a bubble is proportional to the relative infection risk, including the mean value and the 95% range.

Cryptosporidium oocysts are environmentally stable[29] and their numbers in surface water are insensitive to temperature changes. Changes in annual precipitation strongly affect the infection risks from exposure to oocysts in drinking water that was produced by treating surface water. If there is 50% more precipitation, infection risks are 30% lower because concentration of oocysts from discharged wastewater are diluted more in surface water, and if there is 50% less rain, then infection risks are almost twice as high because oocyst concentrations in discharged wastewater are diluted less. The heavy rainfall frequency strongly affects the infection risks from exposure to *Cryptosporidium* because the number of peak concentrations of oocysts in surface water has increased, and this effect is stronger if there is less annual precipitation. Here, 95% ranges are wide because of large variation in concentrations of oocysts in surface water.

Relative infection risks from exposure to norovirus in oysters follow the same trends, but the increases in infection risks are not as strong as for *Cryptosporidium*. This can be explained by the fact that infection risks are high and cannot increase so much anymore. In this case a default concentrating factor of 10 times by oyster filtration was applied. If this factor is set to 1, then relative risk changes are very similar in value as the ones given here for *Cryptosporidium* drinking water.

In comparison with *Cryptosporidium* and norovirus, *Campylobacter* shows different trends. *Campylobacter* is temperature sensitive.[28] Higher temperatures imply more inactivation and; hence, lower concentrations in surface water. This effect is stronger if travel times between wastewater discharge and, in this example, bathing water areas are larger. Here, there is an intricate interplay between effects of temperature, dilution, and travel times. In the case of more annual precipitation, discharged wastewater concentrations are diluted more, but travel times in surface water are shorter, giving less time for inactivation. The latter effect outweighs the effect of dilution; hence, relative risks have increased two to three times. In this line, risk is reduced if there is less annual precipitation. Although there is less dilution of wastewater, travel times are so much longer, that the net effect is lower concentration in the bathing water because there was more time for inactivation. An increase in heavy rainfall events with more peak concentrations of *Campylobacter* in the surface water leads to higher upper values of the 95% ranges. This effect is enhanced if there is more annual precipitation. Infection risks from exposure to noncholera *Vibrio* species in bathing water are independent of rainfall. The temperature decrease leads to a smaller risk, and the temperature increase to a larger risk. The latter is so large because the growth opportunities (more days above the temperature threshold for growth) have increased.

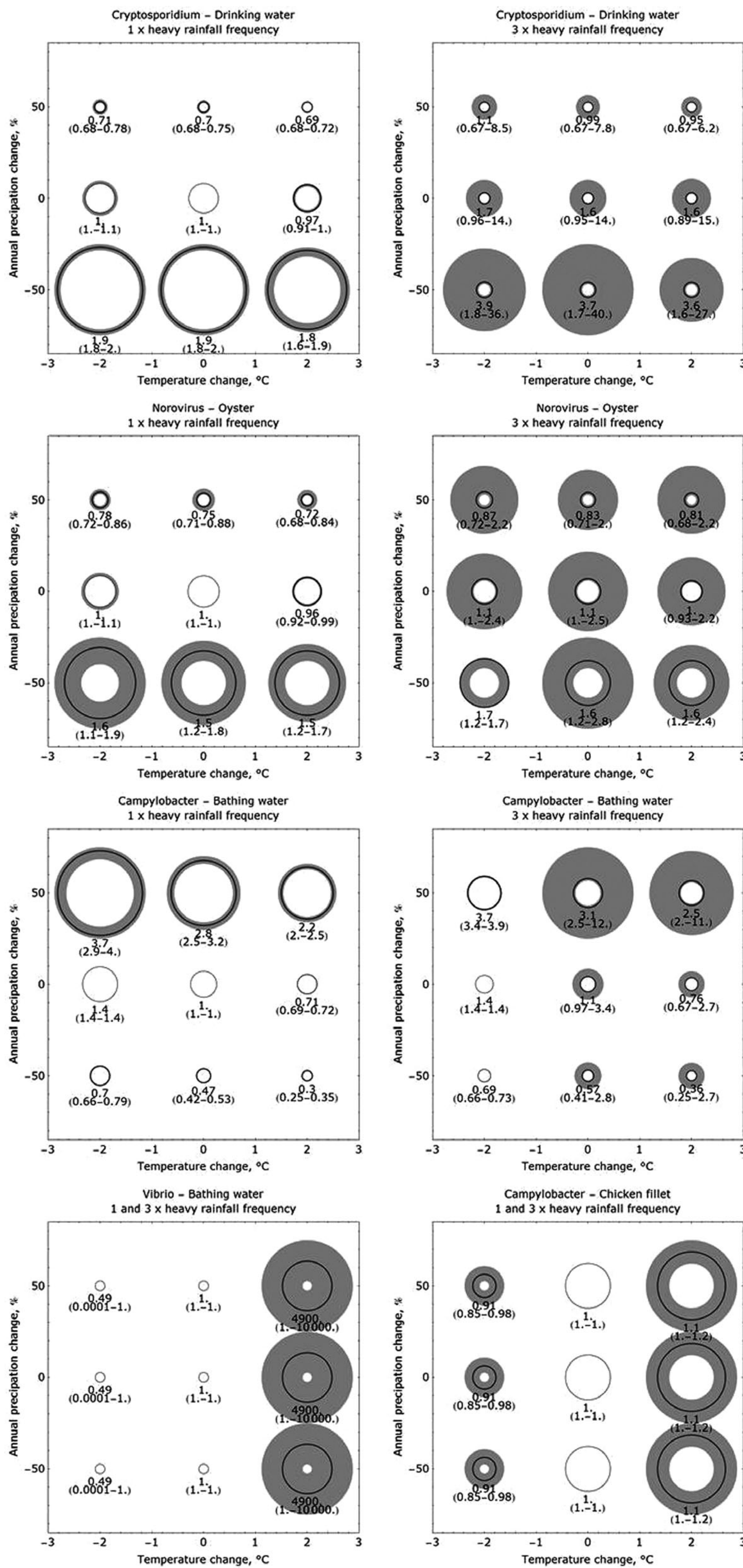


Fig. 4. Simulations of climate change effects. Bubble diameters are proportional to the relative infection risk due to climate change scenarios. Black circle line: mean relative infection risk; gray circle area: 95% range. Climate change scenarios: –2 °C, 0 °C, and +2 °C; annual precipitation change: –50%, 0%, and + 50%; one and three times more heavy rainfall frequency.

Obviously, infection risks from exposure to *Campylobacter* in chicken fillet are independent of rainfall. The simulations show a 10% decrease in infection risk when temperatures have decreased 2 °C, and a 10% increase with a 2 °C increase.

7. DISCUSSION

CC-QMRA is a climate change adaptation tool for strategic decision making. It quantifies relative infection risks for selected waterborne and foodborne pathogens at specific locations under different climate change scenarios. A variety of settings and climatic scenarios can be simulated to compute health impacts and guide policymakers in the decision-making process. Its versatility and applicability can help assessments of different intervention and adaptation options. The tool is data-driven and, therefore, requires location-specific data. If unavailable, the tool can be used to guide future data collection.

It should be noted that the tool contains simplifications that impose limitations to the interpretation of the findings. For example, the wastewater treatment module uses a simple hydrologic model with complete mixing and discharge and flow rates that are proportional to the amount of rainfall. The runoff module uses constant pathogen concentrations that runoff from land to surface water. Nevertheless, realistic levels of waterborne pathogen in surface water can be generated. It must be emphasized that the user should have knowledge about a specific location including pathogen levels. Default values are provided, but location-specific values may be quite different, and, consequently, risk outcomes may differ. In the end, the tool is a calculator that relies on quality input data. The tool has no built-in warning to prevent unrealistic settings. Experience with already developed tools for QMRA of drinking water[65] and groundwater protection[66] showed that close guidance from, for example, environmental inspectors and drinking water companies yields optimal tool outcomes and interpretation.

The tool uses a mixture of fixed values and Monte Carlo sampling. The use of fixed values (averages) is justified if model outcomes are relatively insensitive to those values, and in scenarios (Fig. 4). The Monte Carlo samplings were limited to 365 samples (one for each day in a year), to prevent long computation times, but realizations vary. However, this variation is less pronounced in the relative risk—the desired output of the tool. The user can check variability in the outcomes by repeating the Monte Carlo calculations several times.

Although realistic estimates of infection risk are produced by the tool, given the model simplifications, the limited number of Monte Carlo samplings, and the uncertainties in many of the model inputs (including the dose-response parameters), the absolute infection risk outcomes of the tool should be considered as indicative. Nevertheless, the relative risk outcomes can be used to define and evaluate interventions and mitigation strategies. It provides insight into what parts of the pathways are most vulnerable to climate changes.[13] Waterborne pathogens that are very temperature sensitive, like *Campylobacter* and *Vibrio*, will be affected considerably by temperature change.[67] Infection risk from exposure to *Campylobacter* will decrease with temperature increase due to increased inactivation, but those from exposure to *Vibrio* increase due to increased growth opportunities. Drought generally increases infection risk from exposure to slowly inactivating pathogens such as norovirus and *Cryptosporidium* due to less dilution of wastewater discharges.

Climate change will have differential impacts on infectious diseases in Europe that call for changes in public health practice.[68–70] The tool can be used to evaluate the effectiveness of interventions such as upgrading wastewater and drinking water treatment, determining the distance from wastewater discharges and agricultural land to beaches and strengthening drinking water and bathing water regulations. For example, if relative infection risks were to increase a hundred times for drinking water consumption, one may install extra treatment to reduce pathogen concentrations a hundred times or more. With regards to bathing water, more efficient wastewater treatment may be recommended together with prevention of overflows. Similarly, for foodborne diseases one may revise regulations for food production, processing, transport, and storage education programs on appropriate food handling.

In conclusion, here we have presented the freely available CC-QMRA tool and verified the risk outcomes against published models. The tool can be tested in a wide range of settings in Europe and beyond to evaluate impacts of climate change on infection risks from waterborne and foodborne pathogens.

ACKNOWLEDGMENTS

Research under this project was funded by the European Centre for Disease Prevention and Control (ECDC) and performed under an

ECDC Specific Contract (Tender OJ/2008/04/11 – PROC/2008/005).

REFERENCES

1. Semenza JC, Menne B. Climate change and infectious diseases in Europe. Lancet Infectious Diseases, 2009; 9(6):365–375.
2. D'Souza RM, Becker NG, Hall G, Moodie KB. Does ambient temperature affect foodborne disease? Epidemiology, 2004; 15(1):86–92.
3. Patrick ME, Christiansen LE, Waino M, Ethelberg S. Madsen H *et al.* Effects of climate on incidence of Campylobacter spp. in humans and prevalence in broiler flocks in Denmark. Applied and Environmental Microbiology, 2004; 70(12):7474–7480.
4. Kovats RS, Edwards SJ, Charron D, Cowden J, D'Souza RM *et al.* Climate variability and campylobacter infection: An international study. International Journal of Biometeorology, 2005; 49(4):207–214.
5. Kovats R, Edwards SJ, Hajat S, Armstrong BG, Ebi KL, Menne B. The effect of temperature on food poisoning: A time-series analysis of salmonellosis in ten European countries. Epidemiology and Infection, 2004; 132:443–453.
6. Naumova EN, Jagai JS, Matyas B, DeMaria A, Jr., MacNeill IB *et al.* Seasonality in six enterically transmitted diseases and ambient temperature. Epidemiology and Infection, 2007; 135(2):281–292.
7. Lake IR, Gillespie IA, Bentham G, Nichols GL, Lane C, Adak GK, Threlfall EJ. A re-evaluation of the impact of temperature and climate change on foodborne illness. Epidemiology and Infection, 2009; 137(11):1538–1547.
8. Andersson Y, Ekdahl K. Wound infections due to Vibrio cholerae in Sweden after swimming in the Baltic Sea, summer 2006. Eurosurveillance, 2006; 11(8):E060803 2.
9. Schets FM, Berg van den HHJL, Meulmeester de AA, Dijk van E, Rutjes SA, Hooijdonk van HJP, de Roda Husman AM. Vibrio alginolyticus infections in the Netherlands after swimming in the North Sea. Eurosurveillance Weekly, 2006; 11:11.
10. Semenza JC, Nichols G. Cryptosporidiosis surveillance and water-borne outbreaks in Europe. Eurosurveillance, 2007; 12(5):E13–E14.
11. Nichols G, Lanem C, Asgari N, Verlander NQ, Charlett A. Rainfall and outbreaks of drinking water related disease and in England and Wales. Journal of Water and Health, 2009; 7(1):1–8
12. Schijven JF, de Roda Husman, AM. Effect of climate changes on waterborne disease in the Netherlands. Water Science and Technology, 2005; 51(5):79–87.
13. Semenza JC, Höser C, Herbst S, Rechenburg A, Suk JE, Frechen T, Kistemann T. Knowledge mapping for climate change and food and waterborne diseases. Critical Reviews in Environmental Science and Technology, 2012; 42:378–411.
14. Rose JB, Epstein PR, Lipp EK, Sherman BH, Bernard SM, Patz JA. Climate variability and change in the United States: Potential impacts on water- and foodborne diseases caused by microbiologic agents. Environmental Health Perspectives, 2001; 109(Suppl 2):211–221.
15. Pachauri RK. Climate change 2007. In Pachauri RK, Reisinger A. (eds). Synthesis report. Contribution of Working Groups I, II and III to the Fourth Assessment Report. Geneva: IPCC, 2008.
16. WHA (World Health Assembly). Sixty-First World Health Assembly, WHA61.19. Climate Change and Health, 2008. Available at: http://apps.who.int/gb/ebwha/pdf_files/A61/A61_R19-en.pdf, Accessed April 9, 2012.
17. WHO (World Health Organization). Protecting Health from Climate Change: Global Research Priorities, 2009. Available at: http://whqlibdoc.who.int/publications/2009/9789241598187_eng.pdf, Accessed April 9, 2012.
18. Haas CN, Gerba CP. Quantitative Microbiological Risk Assessment. New York: Wiley and Sons, 1999.
19. Vose D. Risk Analysis: A Quantitative Guide, 2nd ed. West Sussex: John Wiley and Sons, 2000.
20. Lodder WJ, de Roda Husman AM. Presence of noroviruses and other enteric viruses in sewage and surface waters in the Netherlands. Applied and Environmental Microbiology, 2005; 71(3):1453–1461.
21. Havelaar AH. Campylobacteriosis in the Netherlands. RIVM Report 250911001, 2001 [in Dutch].
22. Hoogenboezem W, Medema GJ, Schijven JF, Rijs G. Presence and sources of *Cryptosporidium* and *Giardia* in the Netherlands. H2O, 2000; 23:17–18 [in Dutch].
23. Schijven JF, Rijs G, Verstappen G, de Roda Husman AM. Estimation of the risk of infection of dairy cows by food and mouth disease virus spread by way of surface water. Risk Analysis, 2005; 25(1):13–21.
24. U.S. Soil Conservation Service. Technical Release 55: Urban Hydrology for Small Watersheds, 2nd ed. Washington, DC: US Department of Agriculture, 1986.
25. Bertrand I, Schijven JF, Sanchez G, Wyn-Jones P, Ottoson J, Morin T, Muscillo M, Verani M, Nasser A, de Roda Husman AM, Myrmel M, Sellwood J, Cook N, Gantzer C. The impact of temperature on the inactivation of enteric viruses in food and water: A review. Journal of Applied Microbiology, 2012; 112(6):1059–1074.
26. Havelaar AH. Campylobacteriosis in the Netherlands. RIVM Report 250911001. Bilthoven, The Netherlands: National Institute of Public Health and the Environment, 2001 [in Dutch].
27. Ives RL, Kamarainen AM, John DE, Rose JB. Use of cell culture to assess Cryptosporidium parvum survival rates in natural groundwaters and surface waters. Applied and Environmental Microbiology, 2007; 73(18):5968–5970.
28. Burkhardt W, Calci K. Selective accumulation may account for shellfish-associated viral illness. Applied and Environmental Microbiology, 2000; 66(4):1375–1378.
29. Formiga-Cruz M, Allard AK, Conden-Hansson AC, Henshilwood K. Hernroth BE, Jofre J, Lees DN, Lucena F, Papapetropoulou M, Rangdale RE, Tsibouxi A, Vantarakis A, Girones R. Evaluation of potential indicators of viral contamination in shellfish and their applicability to diverse geographical areas. Applied and Environmental Microbiology, 2003; 69(3):1556–1563.
30. Graczyk TK, Lewis EJ, Glass G, Dasilva AJ, Tamang L *et al.* Quantitative assessment of viable Cryptosporidium parvum load in commercial oysters (*Crassostrea virginica*) in the Chesapeake Bay. Parasitology Research, 2007; 100(2):247–253.
31. Morris JG. Cholera and other types of vibriosis: A story of human pandemics and oysters on the half shell. Clinical Infectious Diseases, 2003; 37:272–280.
32. Roszak DB, Colwell RR. Survival strategies of bacteria in the natural environment. Microbiology Reviews, 1987; 51:365–379.
33. Oliver JD, Kaper JB. Vibrio species. Pp. 228–264 in Doyle M, Beuchat LR, Montville TJ (eds). Food Microbiol: Fundamentals and Frontiers. Washington, DC: ASM Press, 1997.
34. Nishina T, Wada M, Ozawa H, Hara-Kudo Y, Konuma H, Hasegawa J, Kumagai S. Growth kinetics of *Vibrio parahaemolyticus* O3:K6 under varying conditions of pH, NaCl concentration and temperature. Journal of the Food Hygienic Society of Japan, 2004; 45(1):35–37.
35. Fujikawa H, Kimura B, Fuji T. Development of a predictive program for *Vibrio parahaemolyticus* growth under various environmental conditions. Biocontrol Science 2009; 14(3):127–131.

36. Zhenquan Y, Xinan J, Ping L, Zhiming P, Jinlin H, Ruixia G *et al.* Predictive model of *Vibrio parahaemolyticus* growth and survival on salmon meat as a function of temperature. Food Microbiology, 2009; 26:606–614.
37. Koh EG, Huyn JH, LaRock PA. Pertinence of indicator organisms and sampling variables to Vibrio concentrations. Applied and Environmental Microbiology, 1994; 60(10):3897–3900.
38. Patrick ME, Christiansen LE, Waino M, Ethelberg S, Madsen H. *et al.* Effects of climate on incidence of Campylobacter spp. in humans and prevalence in broiler flocks in Denmark. Applied and Environmental Microbiology, 2004; 70(12):7474–7480.
39. Evers EG. Predicted quantitative effect of logistic slaughter on microbial prevalence. Preventive Veterinary Medicine, 2004; 65(1–2):31–46.
40. Calistri P, Giovanni A. Quantitative risk assessment of human campylobacteriosis related to the consumption of chicken meat in two Italian regions. International Journal of Food Microbiology, 2008; 128:274–278.
41. Ellerbroek LI, Lienau JA, Klein G. Campylobacter spp. in broiler flocks at farm level and the potential for cross-contamination during slaughter. Zoonoses and Public Health, 2010; 57:e81–e88.
42. Nauta M, Christensen B. The impact of consumer phase models in microbial risk analysis. Risk Analysis, 31(2): 255–265.
43. Hijnen WAM, Beerendonk EF, Medema GJ. Inactivation credit of UV radiation for viruses, bacteria and protozoan (oo)cysts in water: A review. Water Research, 2006; 40(1):3–22.
44. Schijven JF, de Roda Husman AM. Analysis of the microbiological safety of drinking water. Experiences with Handling Records 2006–7 RIVM-Report 703719038. Bilthoven, The Netherlands: National Institute of Public Health and the Environment, 2009 [in Dutch].
45. WHO. Guidelines for Drinking-Water Quality: Incorporating 1st and 2nd Addenda, 4th ed. Geneva, CH: World Health Organisation, 2011.
46. Teunis PFM, Medema GJ, Kruidenier L, Havelaar AH. Assessment of the risk of infection by Cryptosporidium or Giardia in drinking water from a surface water source. Water Research, 1997; 31(6):1333–1346.
47. USEPA. Economic Analysis for the Final Ground Water Rule. United States Environmental Protection Agency. EPA 815-R-06–014, 2006, Available at: http://water.epa.gov/lawsregs/rulesregs/sdwa/gwr/regulation.cfm, Accessed May 17, 2013.
48. Schets FM, Schijven JF, de Roda Husman AM. Exposure assessment for swimmers in bathing waters and swimming pools. Water Research, 2011; 45(7):2392–2400.
49. FDA. Quantitative Risk Assessment on the Public Health Impact of Pathogenic *Vibrio parahaemolyticus* in Raw Oysters. Center for Food Safety and Applied Nutrition. Food and Drug Administration U.S. Department of Health and Human Services, 2005.
50. Teunis PFM, Moe CL, Liu P, Miller SE, Lindesmith L *et al.* Norwalk virus: How infectious is it? Journal of Medical Virology, 2008; 80:1468–1476.
51. Teunis PFM, Havelaar AH. The beta Poisson model is not a single hit model. Risk Analysis, 2000; 20:511–518.
52. Ryu H, Abbaszadegan, M. Log-term study of Cryptosporidium and Giardia occurrence and quantitative microbial risk assessment. Journal of Water Health, 2008; 06(2):263–273.
53. Schijven JF, Teunis PFM, Rutjes SA, Bouwknegt M, de Roda Husman AM. QMRAspot: A tool for QMRA from surface water to potable water. Water Research, 2011; 45(17):5564–5576.
54. Soller JA, Bartrand T, Ashbolt NJ, Ravenscroft J, Wade TJ. Estimating the primary etiologic agents in recreational freshwaters impacted by human sources of faecal contamination. Water Research, 2010; 44:4736–4747.
55. Schets FM, Van Wijnen JH, Schijven JF, Schoon H, & de Roda Husman AM. Monitoring of waterborne pathogens in surface waters in Amsterdam, The Netherlands, and the potential health risk associated with exposure to Cryptosporidium and Giardia in these waters. Applied and Environmental Microbiology, 2008; 74(7):2069–2078.
56. Schets FM, Berg van den HHJL, Marchese A, Grabom S, de Roda Husman, AM. Human pathogenic vibrios in marine and fresh bathing waters related to environmental conditions and disease outcome. International Journal of Hygiene and Environmental Health, 2011; 214(5):399–406.
57. Masini L, DeGrandis B, Principi F, Mengarelli C, Ottaviania D. Research and characterization of pathogenic vibrios from bathing water along the Conero Riviera (central Italy). Water Research, 2007; 41:4031–4040.
58. Vezzulli L, Pezzati E, Moreno M, Fabiano M, Pane L *et al.* Benthic ecology of Vibrio spp. and pathogenic Vibrio species in a coastal Mediterranean environment (La Spezia Gulf, Italy). Environmental Microbiology, 2009; 58(4):808–818.
59. DePaola A, Jonesm JL, Woods J, Burkhardt W, Calci KR *et al.* Bacterial and viral pathogens in live oysters: 2007 United States Market Survey. Applied and Environmental Microbiology, 2010; 76(9):2754–2768.
60. Kaysner CA, Abeyta C, Stott RF, Krane MH, Wekell MM. Enumeration of Vibrio species, including V. cholerae, from samples of an oyster growing area, Grays Harbor, Washington. Journal of Food Protection, 1990; 53(4):300–311.
61. Schets FM, vanden Berg HH., Rutjes SA, de Roda Husman AM. Pathogenic Vibrio species in Dutch shellfish destined for direct human consumption. Journal of Food Protection, 2010; 73(4):734–738.
62. Teunis P, Havelaar A, Vliegenthart J, Roessink G. Risk assessment of Campylobacter species in shellfish: Identifying the unknown. Water Science and Technology, 1997; 35(11–12): 29–34.
63. Ellerbroek LI, Lienau JA, Klein G. Campylobacter spp. in broiler flocks at farm level and the potential for cross-contamination during slaughter. Zoonoses and Public Health, 2010; 57:e81–e88
64. Bouwknegt M, Dam-Deisz WDC, Wannet WJB, Van Pelt W, Visser G, Van de Giessen AW. Surveillance of zoonotic bacteria in farm animals in the Netherlands: Results from January 1998 until December 2002. RIVM Report 330050001. Bilthoven, The Netherlands: National Institute of Public Health and the Environment, 2004.
65. Schijven JF, Teunis PFM, Rutjes SA, Bouwknegt M, de Roda Husman AM. QMRAspot: A tool for QMRA from surface water to potable water. Water Research, 2011; 45(17):5564–5576.
66. Schijven JF, Hassanizadeh SM, de Roda Husman AM. Vulnerability of unconfined aquifers to virus contamination. Water Research, 2010; 44(4):1170–1181.
67. Semenza JC, Herbst S, Rechenburg A, Suk JE, Höser C, Schreiber C, Kistemann T. Climate change impact assessment of food and waterborne diseases. Critical Reviews in Environmental Science and Technology, 2012; 42:857–890.
68. Semenza JC, Suk JE, Estevez V, Ebi KL, Lindgren E. Mapping climate change vulnerabilities to infectious diseases in Europe. Environmental Health Perspectives, 2012; 120(3):385–392.
69. Lindgren E, Andersson Y, Suk JE, Sudre B, Semenza JC. Climate change and infectious diseases: Monitoring emerging risks in Europe. Science, 2012; 336(6080):418–419.
70. Semenza JC, Domanović D. Blood supply under threat. Nature Climate Change, 2013; 3:432–435.