Balancing the Risks and Benefits of Drinking Water Disinfection: Disability Adjusted Life-Years on the Scale

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To evaluate the applicability of disability adjusted life-years (DALYs) as a measure to compare positive and negative health effects of drinking water disinfection, we conducted a case study involving a hypothetical drinking water supply from surface water. This drinking water supply is typical in The Netherlands. We compared the reduction of the risk of infection with *Cryptosporidium parvum* by ozonation of water to the concomitant increase in risk of renal cell cancer arising from the production of bromate. We applied clinical, epidemiologic, and toxicologic data on morbidity and mortality to calculate the net health benefit in DALYs. We estimated the median risk of infection with *C. parvum* as 10^{-3}/person-year. Ozonation reduces the median risk in the baseline approximately 7-fold, but bromate is produced in a concentration above current guideline levels. However, the health benefits of preventing gastroenteritis in the general population and premature death in patients with acquired immunodeficiency syndrome outweigh health losses by premature death from renal cell cancer by a factor of > 10. The net benefit is approximately 1 DALY/million person-years. The application of DALYs in principle allows us to more explicitly compare the public health risks and benefits of different management options. In practice, the application of DALYs may be hampered by the substantial degree of uncertainty, as is typical for risk assessment. *Key words*: bromate, *Cryptosporidium parvum*, disinfection, drinking water, ozone, quality of life, risk assessment. *Environ Health Perspect* 108:315–321 (2000). [Online 21 February 2000]

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The microbiologic safety of drinking water is of paramount importance to public health (*1*). Source protection is generally accepted as the primary strategy to obtain microbiologically safe drinking water. However, many sources (surface waters in particular) are highly polluted and need extensive treatment before distribution to the consumer. Chemical disinfection is prominent in these treatment schemes. Highly oxidizing chemicals such as chlorine and ozone kill a variety of pathogenic microorganisms during treatment, and chlorine is applied in many countries as an additional safeguard in the distribution system. An important drawback of the use of these chemicals is the generation of disinfection by-products, which have suspected adverse effects on human health. This situation calls for a formal quantitative framework to compare the positive and negative health effects of drinking water disinfection and to assist in the design and operation of treatment plants (*2*).

Microbiologic risks are expressed as the annual individual probability of infection for a given consumption of drinking water. Chemical risks related to genotoxic carcinogens are usually associated with an increase in cancer incidence attributable to a lifetime exposure. The public health impact of these disease end points is very different and cannot be compared directly. Hence, decision making is difficult. We evaluated the applicability of a single measure of attributable disease burden to compare and balance health risks and benefits on a public health basis. The disability adjusted life-year (DALY) consists of the loss of healthy life years due to either premature mortality or morbidity. The DALY integrates several dimensions of the public health impact, such as the number of affected persons and the severity and duration of adverse health effects, and uses time as a unit of measurement. We illustrate our approach by a case study of ozonation of a hypothetical drinking water supply using surface water. We used Monte Carlo simulation to assess the uncertainty in our risk estimates, to account for biologic and seasonal variation in exposure and effects, and to accommodate uncertainty in parameter values. In accordance with the framework proposed by the U.S. National Research Council (*3*), we discuss the four consecutive elements of the risk assessment process.

Hazard Identification

We considered a hypothetical drinking water supply that is typical for drinking water in The Netherlands. In this supply, raw water is abstracted from an international river that has been polluted by domestic and industrial sources and by agricultural run-off. The water is treated by storage in three consecutive reservoirs, coagulation, sedimentation, rapid sand filtration, ozonation (only when disinfected), granular activated carbon filtration, and ultraviolet (UV) postdisinfection. The water is then distributed to the consumer without any residual disinfectant in the distribution system. Drinking water may harbor many pathogenic microorganisms. In this paper, we considered only one pathogen and one of the many potential disinfection by-products that are associated with ozonation. We illustrated the methodology but did not make a comprehensive assessment of a particular situation. We selected a microbial and chemical agent of major public health significance in surface water supplies. Other agents occur in lower concentrations and/or induce smaller health effects. Hence, this restriction does not largely affect the validity of the final conclusions.

Cryptosporidium parvum is a protozoan parasite that produces environmentally resistant and highly infectious oocysts. Other pathogenic microorganisms, such as viruses and *Campylobacter jejuni,* may also be present in similar concentrations in water from storage reservoirs. However, these organisms are inactivated by postdisinfection processes such as UV irradiation in our scenario and hence cause smaller public health problems. Adequate control of *C. parvum* is therefore of critical importance in most surface-water supplies. Infection with *C. parvum* may result in self-limiting gastroenteritis in immunocompetent persons. In those who are immunocompromised, the infection is not easily cleared and usually results in severe life-threatening gastroenteritis. In the immunocompromised group, we only considered acquired immunodeficiency syndrome (AIDS) patients because a severe clinical course of cryptosporidiosis is associated

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with CD4 counts ≤ 53 cells/mL (*4*), which is typical only in the advanced stages of AIDS.

C. parvum has caused major outbreaks of waterborne disease in Europe and in North America (*5,6*). *C. parvum* oocysts are resistant to chlorination but may be inactivated by ozonation, which is increasingly used as an alternative disinfectant. However, ozone reacts with bromide ions to produce bromate (*7*). Bromate induces tumors in the rat kidney, thyroid, and mesothelium (*8,9*) and is a renal carcinogen in the mouse (*9*). In accordance with the World Health Organization (WHO) (*1*), we concentrated on renal cell cancer as an outcome of chronic exposure to bromate. Bromate is considered the most important by-product of ozonation (*10*). Other by-products from ozonation may include aldehydes, bromoform, and brominated acetic acids, none of which are classified as genotoxic carcinogens. Pilot plant experiments (*11*) have demonstrated that at usual ozone doses only formaldehyde is produced in measurable quantities, although at levels far below the WHO guideline of 900 µg/L (*1*).

Exposure Assessment

The model used for assessment of exposure to *C. parvum* and bromate is described in Table 1. Table 1 also shows Equations 1–9. Not all parameter values are available for one single drinking water production plant; therefore, we used data from several plants to represent a hypothetical but typical situation in The Netherlands. When necessary, we used additional data from the international literature. Table 2 presents a point estimate for each parameter as well as the probability distributions used in the uncertainty analysis.

C. parvum. We estimated the concentration of *C. parvum* oocysts in drinking water from their concentration in raw water and their reduction by treatment. The concentration of *C. parvum* oocysts, measured at the outlet of a series of storage reservoirs with a mean retention time of 5 months and corrected for recovery of the detection method and for viability (*12*) can be described by a lognormal distribution. The removal of *C. parvum* oocysts by coagulation–sedimentation–rapid sand filtration is estimated by the removal of spores of sulfite-reducing clostridia under full scale conditions (*13*). We used Equation 1 to estimate the median concentration of *C. parvum* oocysts in drinking water without ozonation as 1.1×10^{-3}/L.

We used a two-step approach to estimate the effective ozone concentration in water (*14*). Ozone was added at a constant dose of 3.1 mg/L to the first of a series of four contact chambers, then partially consumed by initial rapid oxidation reactions (ozone demand). Parameter values in the ozone demand model and the subsequent exponential decay model were based on linear regression analysis of pilot-plant data (*14*), assuming a pH of 7.5 and a temperature of 10–12°C. The SD of the residuals in the regression equation quantified the uncertainty in the predicted values (*15*). We modeled the variability in the residence time distribution in the ozone contact chambers by the inverse Gaussian distribution (*16*). The Hom formula (Equation 5B) modeled inactivation of *C. parvum* oocysts by ozone, using the geometric mean as an estimate of the effective ozone concentration (*17*). The parameters were based on linear regression analysis using the log-transformed Hom model, and were applied to data measured at approximately 10°C (*17*), again taking the SD of the residuals to quantify uncertainty. Ozonation reduced the median concentration of viable oocysts in the

Table 1. Model equations for assessment of the incidence of infection by *C. parvum* and renal cell cancer by bromate.

Description (unit)	Equation	Equation no.
Conc of *C. parvum* oocysts in drinking water (per L)	$C_{Cp,DW} = C_{Cp,RAW} \times 10^{-[DR_{Cp,CSF} + DR_{Cp,O_3}]}$	1
Ozone Conc after first contact chamber (mg/L)	$C_{O_3}(0) = \beta_0 + \beta_1 \times D_{O_3}$	2
Ozone residual (mg/L)	$C_{O_3}(T) = C_{O_3}(0) \times e^{-d \times T}$	3
Effective ozone Conc (mg/L)	$C_{O_3}(eff) = e^{\{\ln[CO_3(0)] + \ln[C_{O_3}(T)]\}/2}$	4
Disinfection of *C. parvum* oocysts		
Without ozonation	$DR_{Cp,O_3} = 0$	5A
With ozonation	$DR_{Cp,O_3} = k \times [C_{O_3}(eff)]^m \times [T]^n$	5B
Daily risk of infection with *C. parvum*	$P_{inf,Cp} = 1 - e^{-r \times C_{Cp,DW} \times V_u}$	6
Number of persons with one or more infections per year	$N_{inf,Cp} = N \times [1 - (1 - P_{inf,Cp})^{365}]$	7
Conc of bromate in drinking water (µg/L)	$C_{BrO_3^-,DW} = 1.46 \times 10^{-6} \times DOC^{1.18} \times D_{O_3}^{1.42} \times \mathrm{pH}^{5.11} \times T^{0.27} \times C_{Br^-}^{0.88}$	8
Incidence of renal cell cancer per year	$N_{RCC} = \left(N \times \frac{C_{BrO_3^-,DW} \times V_t \times q}{BW^{2/3}} \right) \Big/ 80$	9

Conc, concentration.

Table 2. Point estimates and probability distributions of model parameters for assessment of the incidence of infection by *C. parvum* and renal cell cancer by bromate.

Description (unit)	Symbol	Median value	Probability distribution[a]
Conc of *C. parvum* in raw water (per L)	$C_{Cp,RAW}$	0.044	Lognormal (-3.12, 0.97)
Decimal reduction of *C. parvum* by coagulation–sedimentation–rapid sand filtration	$DR_{Cp,CSF}$	1.6	Normal (1.6, 0.4)
Ozone dose (mg/L)	D_{O_3}	3.1	Fixed
Ozone demand parameter (intercept) (mg/L)	β_0	-0.194	Normal (pred, 0.091)
Ozone demand parameter (slope)	β_1	0.443	Normal (pred, 0.091)
Contact time (min)	T	5	Inverse Gaussian (5, 75)
Ozone decay parameter (per min)	d	0.257	Normal (pred, 0.239)
Hom intercept parameter [(L/mg)^m/min^n]	k	0.219	log (DR) = normal (pred, 0.134)
Hom parameter for concentration	m	0.899	
Hom parameter for contact time	n	1.059	
Daily consumption of uncooked drinking water (L/person/day)	V_u	0.16	Lognormal (-1.80, 0.99)
Dose–response parameter for *C. parvum*	r	0.0037	Lognormal (-5.61, 0.43)
Population served	N	10^6	Fixed
Dissolved organic carbon (mg/L)	DOC	3.5	Lognormal (1.25, 0.03)
pH value	pH	7.5	Fixed
Conc of bromide in raw water (µg/L)	C_{Br^-}	86	Lognormal (4.46, 0.20)
Daily consumption of total drinking water (L/person/day)	V_t	0.81	Lognormal (-0.21, 0.82)
Renal cell cancer risk parameter (kg$^{2/3}$/µg)	q	3.0×10^{-6}	Custom (bootstrap)
Body weight (kg)	BW	74.5	Men: lognormal (4.39, 0.15) Women: lognormal (4.21, 0.16)

Abbreviations: Conc, concentration; Pred, predicted value.
[a]Normal (mean, SD); lognormal (mean, SD on $\log_e$ scale); inverse Gaussian (mean, shape).

baseline approximately 7-fold to a median concentration of 1.6×10^{-4}/L.

Bromate. Bromate is only occasionally present in raw water in The Netherlands (*18*); therefore, all bromate in drinking water is presumably formed during the ozonation process. Dissolved organic carbon and bromide concentrations in raw water are based on measurements at an actual plant in The Netherlands, taking annual variation into account as an uncertainty factor. We used the Song et al. (*19*) model to estimate the formation of bromate as a function of the ozone dose and several water quality parameters. We calculated the median bromate concentration in our scenario as 3.8 µg/L (Equation 8 in Table 1).

Finally, we calculated the daily ingested dose of *C. parvum* oocysts and bromate ions by multiplication of their concentration in drinking water with the daily consumption V_u of uncooked drinking water (*12*) or V_t of total drinking water (*20*), respectively. The V_t commonly used default value of 2 L/person/day is close to the 95th percentile of the distribution in Table 2.

Hazard Characterization

C. parvum. We used the exponential dose–response model (*21*) to estimate the risk of infection related to the daily ingested dose of *C. parvum* and to estimate the dose–response parameter, *r*, (*22*) from volunteer challenge data (*23*). A sample of 1,000 simulations of *r*, obtained by bootstrapping, is described by a lognormal distribution. We assumed a population of 1 million inhabitants in the distribution area who randomly consume drinking water. The daily risk associated with exposure to *C. parvum* is accumulated to estimate the annual risk of infection (Equation 7).

To assess the uncertainty in the annual risk of infection, we assumed that all model parameters were independent. Five thousand replicates of the concentration of *C. parvum* oocysts in drinking water without ozonation (C_{Cp,DW^-}) were drawn from the distributions in Equations 1 and 5A. Then we calculated corresponding estimates of the concentration of *C. parvum* in drinking water with ozonation (C_{Cp,DW^+}) by multiplying each value of C_{Cp,DW^-} with a random value for the reduction factor by ozonation (Equation 5B). Samples from the distributions of C_{Cp,DW^-} and C_{Cp,DW^+} were then combined with randomly drawn samples of *r* and V_u, using identical indices for both series (with and without ozone). Equation 6 allows us to compare their values and assess the influence of ozonation on the risk of infection of any one individual on any 1 day. We estimated the annual individual risk of infection by taking a sample of 365 values of the daily risk using Equation 7. We repeated this 5,000 times to simulate the distribution of the annual risk of infection. We then computed the annual incidence of infection as the annual risk multiplied by the size of the population at risk.

The annual incidence of infection without ozonation appears to be approximately lognormally distributed with a median of 1,000 cases/million person-years (mpy) and spans a relatively small range. The 95% confidence interval (CI) for annual incidence of infection is 760–1,500 cases/mpy (Figure 1A). The introduction of ozonation leads to a reduced incidence (median 180 cases/mpy; CI, 120–260 cases/mpy).

The median values of the incidence of infection cannot be exactly reproduced by the simple substitution of median parameter values in the equations in Table 1. The additive nature of Equation 7 implies that the annual risk is mainly determined by the few occasions on which a high dose is encountered.

Bromate. Exposure to bromate in drinking water is mainly by ingestion; other routes (inhalation and dermal exposure) are not described in the literature. To estimate the excess lifetime risk of renal cell cancer from exposure to bromate, the WHO (*1*) used data by Kurokawa et al. (*24*) and fitted the linearized multistage model (LMS) to extrapolate from high to low doses (*25*). Applying this procedure while dividing the lifetime risk by an average life expectancy of 80 years results in an incidence of 0.16 cases of renal cell cancer/mpy at the calculated exposure level. For our comparison of infection and cancer risks associated with the ozonation of drinking water, the estimated uncertainty in that risk is needed. Therefore, we reanalyzed the original data to obtain the maximum likelihood estimate of excess risk (*26*). We added other data by Kurokawa et al. (*27*) and recently published data (*9*) (Figure 2). The three data sets were fitted by the LMS model, in which one of the parameters, *b*, which denoted a dose factor, was allowed to vary between the three studies. We found that the LMS model did not give a significantly better fit than the two-stage model:

$$F_i = a + (1 - a) \times [1 - e^{-b_i \times dose - c(b_i \times dose)^2}]$$

where F_i = probability of renal cell cancer in study *i*, *dose* = dose [mg $KBrO_3$/(kg body weight)$^{2/3}$], *a* (background response) and *c* (shape) = common parameters for all datasets (for this data set $a = 0.019$ and $c = 0.13$), and b_i = dose–response parameter fitted to dataset *i* ($b_1 = 0.0013$, $b_2 = 0.0028$, and $b_3 = 0.0091$ kg$^{2/3}$/mg). For each study we calculated the corresponding dose associated with a 10% response (ED_{10}). The slopes of the three straight lines from the origin to the ED_{10} are point estimates for the three conservative dose–response parameters of the individual studies ($q_1 = 0.0086$, $q_2 = 0.0026$, and $q_3 = 0.0012$ kg$^{2/3}$/mg). The geometric mean of these three values is the point estimate for the pooled dose–response parameter ($q^3 = 0.0030$ kg$^{2/3}$/mg). We estimated the uncertainty in *q* by bootstrapping (*28*), which resulted in a trimodal uncertainty distribution.

We obtained a Monte Carlo sample for the distribution of renal cell cancer incidence

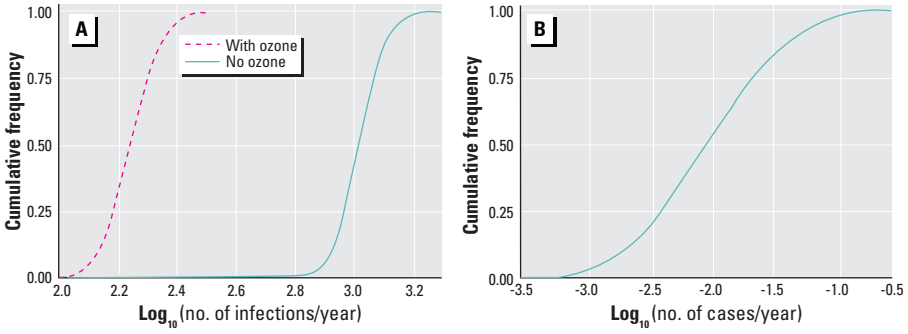

Figure 1. Cumulative frequency distributions of the incidence of (*A*) infection with *C. parvum* and (*B*) renal cell cancer/1 mpy.

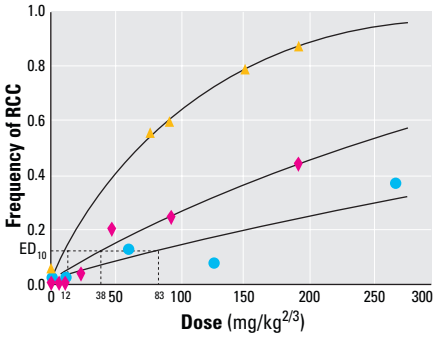

Figure 2. Dose–response data for induction of renal cell cancer (RCC) in rats by bromate [as mg $KBrO_3$/(kg body weight)$^{2/3}$] and fitted by two-stage models. Data symbolized by triangles from Kurokawa et al. (*27*); data symbolized by diamonds from Kurokawa et al. (*24*); and data symbolized by circles from DeAngelo et al. (*9*). The dose associated with a 10% response (ED_{10} values) for each study are based on a simultaneous fit of all three data sets.

by substituting 3,000 replicates from all of the underlying distributions in Equation 9. Using this model, we estimated that the median incidence of renal cell cancer was 0.009 cases/mpy, 18 times lower than the WHO estimate, as based on the LMS model. This difference is largely (a factor of 10) because we used the maximum likelihood estimate instead of the 95th percentile of the dose–response parameter and also because we used a probability distribution for the consumption of drinking water instead of a conservative point estimate (accounting for a factor of 1.8). Using three datasets instead of one has little effect on the median risk. The renal cell cancer incidence CI is relatively wide (0.001–0.075) (Figure 1B), mainly because the three experimental dose–response data sets show large differences.

Risk Characterization

General. Disease may result in the reduction of survival time (quantity of life), the reduction of the quality of life, or both. We combined these outcomes in a single measure, the DALY, as originally proposed by Murray in the global burden of disease (GBD) study (*29*). The DALY concept is designed as a generic instrument that produces results on an interval scale so that meaningful comparisons between widely different disease end points can be made. The loss of healthy life-years in a population, measured in DALYs, is calculated as:

$$DALY = LYL + YLD,$$

where *LYL* is the number of life-years lost due to mortality and *YLD* is the number of years lived with a disability, weighed with a factor between 0 and 1 for the severity of the disability. *LYL* is calculated by accumulation over all relevant diseases (*i*) of the product of *d* (the number of deaths due to a particular disease) and e^* (the standard life expectancy at the age of death due to that disease). *YLD* is calculated as the accumulated product of *N* (the number of persons affected by a non-lethal disease), *L* (the duration of this disease), and *W* (a measure for its severity). If necessary, disease processes are subdivided into several stages with different duration and severity. Murray (*29*) and Van der Maas and Kramers (*30*) provide further details. Thus, for a particular agent, the population health burden is calculated as:

$$DALY = \sum_i d_i e_i^* + \sum_i N_i L_i W_i .$$

C. parvum. Table 3 presents the distributions used for estimation of the health burden of infection with *C. parvum*. Infection with *C. parvum* leads to gastroenteritis in 71% of immunocompetent persons (*31*). The duration of cryptosporidiosis is usually reported as 1–2 weeks, but these estimates are based on cases detected in laboratory surveillance and may be biased toward longer duration. In population-based outbreak studies (*6,32*) and in volunteer experiments (*23,31*), the mean duration of gastroenteritis is reported to be only 3–6 days. Both types of study (*31,33*) report relapses of diarrhea in 40–70% of patients. To quantify the duration of cryptosporidiosis we used a lognormal distribution with a median duration of 6 days and a range between 2 and 30 days.

The disability weight for cryptosporidiosis is taken from the GBD study (*29*). In this study, a severity weight for watery diarrhea is derived using the person trade-off protocol. Panel members trade off life-years of healthy persons for healthy years gained by people in a certain state of reduced health until a point of indifference is reached. The person trade-off protocol estimates social values of different health states, and thus is considered appropriate for the evaluation of health intervention programs (*34*).

The mean mortality risk for cryptosporidiosis in the immunocompetent population is estimated as 1/100,000, based on experience from the 1993 outbreak in Milwaukee, Wisconsin (*35*). Four deaths in the nonimmunocompromised population were attributed to the outbreak, which involved approximately 400,000 persons (*35*). The large uncertainty in this estimate is accounted for by choosing a lognormal distribution with a high but arbitrary dispersion factor (log-SD = 1). This distribution has a median of 0.6, a mean of 1, and 95% of the distribution ranges between 0.1 and 4 per 100,000. To estimate the number of life-years lost by a fatal case of gastroenteritis, we used the age distribution for all gastroenteritis deaths in The Netherlands in 1993–1995 and computed the standard life expectancy in 5-year intervals (*29*). Figure 3A shows that most deaths associated with gastroenteritis occur in people older than 75 years of age.

In immunocompromised persons, particularly in AIDS patients, infection with *C. parvum* leads to gastroenteritis in virtually all cases (*38*). McGowan et al. (*39*) reported that only 30% of AIDS patients have a remission; the others suffer from cryptosporidiosis until death. We fit a lognormal model to the reported duration of disease in all patients. There is no formally derived

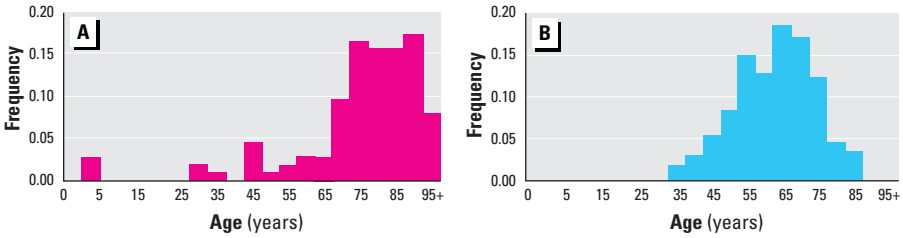

Figure 3. Age distribution of (*A*) fatal cases of gastroenteritis (*36*) and (*B*) patients with renal cell cancer (*37*) in The Netherlands.

Table 3. Point estimates and probability distributions of model parameters for assessment of the health burden of gastroenteritis by infection with *C. parvum*.

	Immunocompetent population		Population of AIDS patients[a]	
Parameter	Median value[b]	Probability distribution[c]	Median value[b]	Probability distribution[c]
P|infection	0.71	Normal (0.71, 0.08)	1.00	Fixed
Severity (*W*)	0.054	Lognormal (-2.92, 0.63)	0.16	Lognormal (-1.81, 0.63)
Duration (*L*)	0.016	Lognormal (-4.14, 0.67)	0.13	Lognormal (-2.03, 0.92)
Case fatality ratio	0.06 per 10,000	Lognormal (-2.80, 1.00)	0.70	Normal (0.70, 0.08)
Life expectancy (e^*)	8.2	Custom[d] (13.2, 15.0)	1.0	Lognormal (0.00, 0.83)

[a]Prevalence 4:10,000. [b]Duration and life expectancy have unit year; all other parameters are dimensionless. [c]Normal (mean, SD); lognormal (mean, SD on $\log_e$ scale). [d]See Figure 3A.

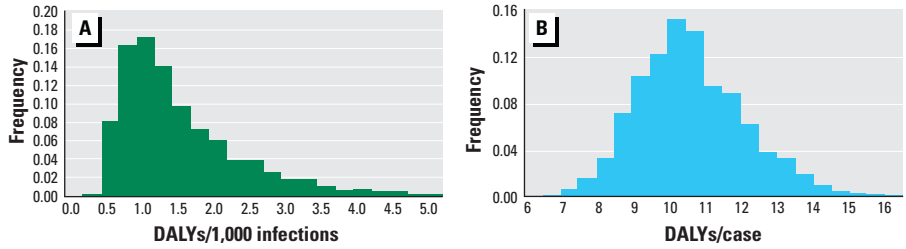

Figure 4. Health burden of (*A*) infection with *C. parvum* (per 1,000 cases of infection) and (*B*) renal cell cancer (per case).

severity weight for cryptosporidiosis in AIDS patients. Because enteritis is more severe in AIDS patients than in immunocompetent persons, leading to significant weight loss and abdominal pain, a larger weight is justified. The median survival times for patients with and without cryptosporidiosis are 11.5 and 66 weeks, respectively. Hence, active cryptosporidiosis reduces the life expectancy of 70% of AIDS patients by approximately 1 year (median value). The uncertainty in this value depends mainly on the survival of the remission group, which is poorly known because most patients were still alive when the study ended. With this restriction, we fit a lognormal distribution to the reported survival times. The average prevalence of AIDS is 0.4/1,000 as for the city of Amsterdam (*40*).

Drawing 3,000 replications using the probability density functions in Table 3 simulates the probability distribution of the health burden of gastroenteritis resulting from infection by *C. parvum* in drinking water (Figure 4A). The distribution is highly skewed to the right, with a median value of approximately 1.1 healthy life-years/1,000 cases of infection and a small but important probability of a loss of up to five healthy life-years/1,000 cases of infection.

Table 4. Point estimates and probability distributions of model parameters for assessment of the health burden of renal cell cancer.

Parameter	Age class	
	< 70 years	≥ 70 years
Percent in class	62 (50–65)[a]	38 (35–50)[a]
No resection	18 (10–20)	37 (25–40)
Postoperative death	4 (3–5)	4 (3–5)
Metastases	19 (15–30)	14 (10–20)
Death within 5 years (no metastases)	25 (20–30)	48 (40–60)
Life expectancy	24.7 (7.4)[b]	10.5 (2.9)[b]

Values in percent except where noted.
[a]All triangular distributions: most likely value (minimum, maximum). [b]Discrete distribution; mean (SD), in years. derived from Figure 3B.

Bromate. The survival of patients with renal cell cancer depends primarily on age, fitness for resection, postoperative survival, and the presence of metastases (Table 4) (*41,42*). Patients with one or more unfavorable prognostic factors have a short survival. Those patients who survive for 5 years after diagnosis have a normal life expectancy. To estimate the number of life-years lost from a case of renal cell cancer, we combined these prognostic factors with the age distribution at diagnosis (Figure 3B) and calculated standard life expectancies. The morbidity burden due to renal cell cancer is small as compared to the mortality burden because death usually occurs within a few months after diagnosis of a fatal case, and because the quality of life after a successful operation is not negatively influenced. Disability weights for the clinical phase of unrelated cancers in the Dutch Public Health Status and Forecast Report (*32*) are used to approximate the severity of renal cell cancer during the first year after diagnosis to account for the effects of surgery, therapy, and emotional stress on the quality of life of survivors. The health burden/case of renal cell cancer is simulated by 3,000 samples from the probability distributions in Table 4. The median health burden/case of renal cell cancer is 10 DALYs, with a relatively symmetrical distribution (Figure 4B).

Integration. Table 5 presents point estimates of the health impacts of supplying drinking water with or without ozonation. The median incidence of infection with *C. parvum* of 1,000 cases/mpy leads to 710 cases of gastroenteritis in the immunocompetent population and an additional 0.40 cases of cryptosporidiosis in AIDS patients. The mortality in the immunocompetent population is low; the AIDS population had 0.29 premature deaths/mpy. Multiplication of these incidence estimates with disability weights and the duration of the health states results in an estimate of the health loss in the scenario without ozonation. Disability by acute gastroenteritis is the most important source of health loss for this pathogen (0.61 DALYs), whereas AIDS patients add 0.29 DALYs, mostly due to premature death. By summation of all effects, we estimated a health loss by infection of 0.93 DALYs/mpy in the scenario without ozonation. The introduction of an ozonation step in the treatment chain does not completely eliminate health risks, although it reduces the median health loss by gastroenteritis to 0.17 DALYs/mpy. Hence, the median health benefit of ozonation is 0.76 DALYs/mpy. The production of bromate leads to 0.01 additional cases of renal cell cancer/year. The health loss of morbidity from renal cell cancer is negligible; premature death adds 10 life-years lost/fatal case or 0.06 DALYs/mpy, which is > 10-fold lower than the health benefits by reducing the risk of infection. The median net health benefit in this scenario is estimated as 0.70 DALYs/mpy.

Uncertainty and sensitivity analysis. Figure 5 shows the uncertainty in the estimated health effects. The population health loss by exposure to *C. parvum* is simulated by multiplying the matched pairs of incidence of infection (with and without ozonation) with samples from the health burden/case. The median without ozonation is 1.2 DALYs/mpy (CI, 0.36–4.6) and is reduced a factor of approximately 6 (equal to the reduction of oocyst concentration) to a median of 0.20 DALYs/mpy (CI, 0.06–1.1) by ozonation. These values are again different from the point estimates by simple substitution of median values as given in Table 5.

Multiplication of the incidence distribution with the health burden distribution of renal cell cancer results in the estimated health loss in the population by exposure to bromate in the case of ozonation. The median health loss has a value of 0.10 DALYs/mpy (CI, 0.01–1.1).

Parallel to these simulations, we calculated the net health benefit of ozonation as the health loss by gastroenteritis (in the case

Table 5. Balancing the risks of drinking water disinfection (point estimates based on median values).

Hazards	Morbidity				Mortality			
	N	*L*	*W*	*YLD*	*d*	*e**	*LYL*	*DALY*
No ozone								
Immunocompetent persons	710	0.016	0.054	0.61	0.004	8.2	0.03	0.64
AIDS patients	0.40	0.16	0.16	0.01	0.28	1.0	0.28	0.29
With ozone								
Immunocompetent persons	130	0.016	0.054	0.11	0.001	8.2	0.01	0.12
AIDS patients	0.07	0.13	0.16	0.00	0.05	1.0	0.05	0.05
Bromate, renal cell cancer	0.01	See text	See text	0.00	0.006	10	0.06	0.06
Health benefit[a]								
Immunocompetent persons	–	–	–	0.50	–	–	0.02	0.52
AIDS patients	–	–	–	0.01	–	–	0.23	0.24
Bromate, renal cell cancer	–	–	–	0.00	–	–	-0.06	-0.06
Total	–	–	–	0.51	–	–	0.19	0.70

Abbreviations: *d*, number of deaths (per mpy); *e**, standard life expectancy at the age of death; *L*, duration (years); *LYL*, life years lost; *N*, number affected (per 1 mpy); *W*, severity weight; *YLD*, years lived with disability.
[a]No ozone minus with ozone.

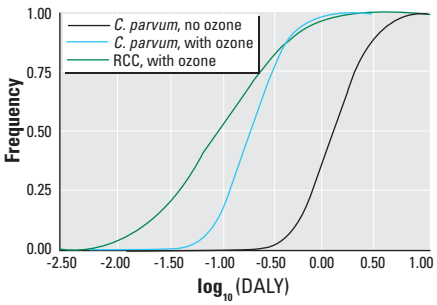

Figure 5. Health loss in a population of 1 million by *C. parvum* and bromate in drinking water, with and without ozonation in the production process. RCC, renal cell cancer.

without ozonation) minus the sum of the residual health loss by gastroenteritis and the health loss of renal cell cancer (in the case with ozonation). We estimated the net median health benefit by the probabilistic model as 0.82 DALYs/mpy; the benefit is mainly determined by a reduction of the risk of infectious disease. Figure 6 shows the uncertainty distribution of the net health benefit, which is skewed to the right; the CI ranges between -0.22 and 3.7. There is a 5% chance that the net effect is negative and a 50% chance that it is > 0.82 DALYs/mpy.

Univariate sensitivity analysis (data not shown) demonstrates that the net health benefit is most sensitive to (in order of importance) decimal reduction of *C. parvum* by coagulation/sedimentation/filtration (CSF); dose–response parameter of *C. parvum*; consumption of unboiled drinking water; concentration of *C. parvum* in raw water ($C_{Cp,RAW}$); pH; and probability, duration, and severity of enteritis in immunocompetent individuals. We varied these parameters by wide but plausible ranges to evaluate the robustness of the overall conclusions and the magnitude of the net health benefit. In comparison to the baseline scenario, only some extreme parameter values resulted in the conclusion that ozonation leads to a net health loss in the population: high efficiency of CSF (decimal reduction of *C. parvum* ≥ 2.4) and low severity weight for gastroenteritis in immunocompetent individuals (≤ 0.005) in combination with a low prevalence of AIDS (≤ 0.5/10,000). Other variations in parameter values result in increased estimates of health gain. Increasing $C_{Cp,RAW}$ or reducing the efficiency of CSF result in health benefits up to 8–12 DALYs/mpy (Figure 7 A, B). The dose–response parameter *r* for *C. parvum* is based on experimental data with healthy adult volunteers. Other subgroups of the population (infants and the elderly) might be more susceptible to infection. A 10-fold increase in *r* results in an approximately 10-fold increase in the net health benefit to approximately 8 DALYs/mpy. Similarly, increasing the unboiled water consumption to 1 L/day increases the net health benefit to 3 DALYs/1 mpy. The results are less sensitive to the total water consumption; to reduce the net health gain to 0 would require per capita consumption of 5 L/day. The prevalence of AIDS was also of interest in our study. In our scenario, the health loss in AIDS patients was smaller than in the immunocompetent population. If the AIDS prevalence is higher, e.g., 4/1,000 [which is typical of larger U.S. metropolitan areas (*38*)], the health loss in AIDS patients is much larger, and results in a larger net benefit of 3 DALYs/mpy.

Discussion

This study evaluates the feasibility of integrated measures of public health, such as the DALY, as a means to assist in the complex decision-making problem of risk balancing in drinking water disinfection. A major advantage of the proposed method is that it leads to a logical, transparent, and comprehensive evaluation of health gains and losses in terms of established public health concepts (quality and quantity of life and social magnitude) using time as a unit of measurement. The DALY measure is superior to comparisons based on annual mortality rates because it also includes nonlethal end points and explicitly addresses life and health expectancy. Information from microbiology, toxicology, epidemiology, environmental, and the clinical sciences is integrated in one single estimate that accounts for the probabilities of different end points occurring. A similar measure (the quality adjusted life-year) is extensively used in economic assessment of medical technologies and in clinical decision making. The explicit introduction of values and preferences when attributing weights to different diseases adds a new and possibly controversial dimension. Because highly prevalent health responses of limited severity were the most important variables for the final result, this aspect deserves detailed attention and communication with both decision makers and the public. Sensitivity analysis demonstrates that variation of the severity weight of gastroenteritis in the immunocompetent population does not affect the conclusion that the health benefits of ozonation outweigh the health losses, but the magnitude of the net effect varies considerably.

DALYs specifically address the health dimension of a risk management problem. They do not capture social and cultural values that are important determinants of risk perception in the public (e.g., equity, voluntariness, and dread) or economic and technical factors (e.g., costs, benefits, and feasibility). Such factors will also be taken into account when taking risk decisions.

Many potential flaws of the DALY approach are not unique for this method, but bear upon health impact assessments in general, given the present lack of knowledge and availability of data. Important but almost inevitable shortcomings are the imprecision of population exposure assessments, the unknown and possibly unknowable shape of the dose–response curves at low environmental levels of exposure, and the translation of this information from rodents to humans as well as within the human population. Another important issue is the internal and external validity of epidemiologic results.

The limited availability of data leads to extensive use of simple models to arrive at final estimates. Many assumptions are made both qualitatively (which models to use) and quantitatively (the choice of distributions and parameter values). The uncertainty in the microbiologic health risk assessment relates predominantly to the precision of model parameters and to a lesser extent to the models themselves. Because relevant health risks occur at concentrations of microorganisms that are far below the limit of detection of current analytical methods, validation of model predictions by comparison with measured data is not possible. On the other hand, the uncertainties of the chemical risks pertain to the level of construct validity. Is carcinogenesis in laboratory animals exposed

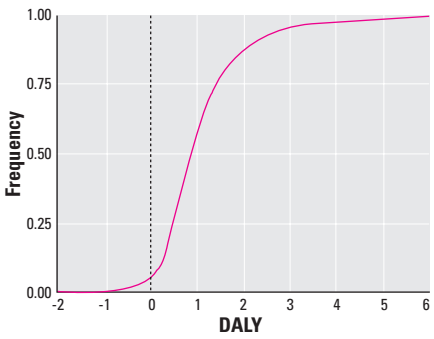

Figure 6. Net health benefit of ozonation of drinking water.

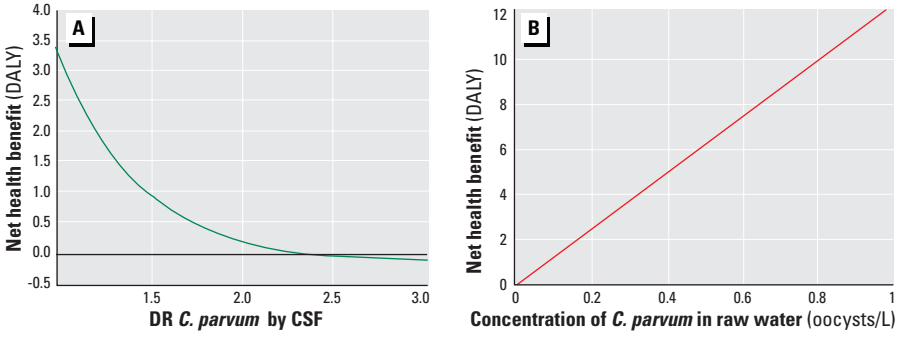

Figure 7. Sensitivity of net health benefit of ozonation to (*A*) CSF and (*B*) the occurrence of *C. parvum* in raw water. DR, decimal reduction.

to high doses of bromate really predictive of effects in humans who are exposed to concentrations many orders of magnitude lower and, if so, what is the actual risk? The difference in this study between the conventional conservative approach designed to derive safe maximum allowable concentrations, and the probabilistic approach designed to estimate the probability distribution of the response parameter for renal cell cancer, illustrates one of the consequences of this uncertainty. Not only does the risk of renal cell cancer appear to be reduced by a factor of 18, but the final conclusion is also strongly affected by the choice of the extrapolation method. None of the models in this study can be rigorously validated, but we believe that they reflect the best available knowledge. The DALY methodology adds a public health dimension to the process of risk assessment that may make the outcomes more useful for risk managers. Also, our method does not impose any constraints on allowing the incorporation of future information.

In our standard scenario, the estimated health benefits by pathogen reduction appear to outweigh the health losses by bromate formation. The absolute level of the net health benefit is approximately 1 DALY/1 mpy, which is a relatively small fraction of the total healthy life expectancy. For comparison, we refer to the commonly accepted 10^{-6} lifetime cancer risk by exposure to genotoxic carcinogens. Using renal cell cancer data as an example, this risk equals a health loss of $10^{-6} \times 10$ DALYs/80 life-years = one-eighth DALY/mpy. The health benefit in our case study is larger than this value; therefore, ozonation is indicated. The cost-effectiveness of achieving this benefit has not yet been evaluated.

Several factors may influence the size of the final health benefit. The microbiologic risks are most sensitive to the concentration of oocysts of *C. parvum* in the raw water. Many drinking water supplies in the world are challenged with considerably higher levels than our hypothetical supply, and in these cases ozonation would yield a considerable public health benefit. However, there are also many drinking water supplies in which the concentration of bromate would be higher than our estimate, leading to higher health losses in achieving the desired disinfection goal. Bromate levels can be partially controlled by the adjustment of pH and optimization of the dose/contact time combination. If a high level of inactivation of *C. parvum* oocysts must be achieved, it will certainly lead to increased toxicologic risks. Our results highlight the need for raw water quality protection and a multiple barrier approach in treatment to reduce the need for disinfection as much as possible.

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