Pathogen reduction requirements for direct potable reuse in Antarctica: evaluating human health risks in small communities

Methods

Additional information about methods used to develop and implement the model is provided below.

Dose-Response Models

The norovirus dose-response model published by Teunis et al. (2008) estimates probabilities of infection and illness as functions of dose. Fit parameters for the combined inocula dataset (8fIIa+8fIIb) were used, making no assumptions about the aggregation state of the virus particles. One of the fit parameters provided by Teunis et al. (2008) exceeds the limits of this model; therefore, the Pfaff transformation was used as a very close approximation (assuming all doses ≤33,323). The probability of norovirus infection per dose ($p_{\text{inf\_NV}}$; person^{-1} day^{-1}) was estimated as

$$p_{\text{inf\_NV}} = 1 - \left[{}_2F_1(\beta_{\text{NV}}, \frac{\lambda_{\text{NV}}(1-a_{\text{NV}})}{a_{\text{NV}}}, \alpha_{\text{NV}} + \beta_{\text{NV}}; a_{\text{NV}}) \left(\frac{1}{1-a_{\text{NV}}}\right)^{-\left(\frac{\lambda_{\text{NV}}(1-a_{\text{NV}})}{a_{\text{NV}}}\right)} \right], \quad [1]$$

where ${}_2F_1$ is a hypergeometric function, λ_{NV} is the dose of norovirus (number of organisms), α_{NV} and β_{NV} are fit parameters and a_{NV} represents the fit parameter of the (logarithmic series) aggregate size distribution. The conditional probability of illness in infected subjects ($p_{\text{ill}_{\text{inf\_NV}}}$) was modeled following Teunis et al. (2008) as

$$p_{\text{ill}_{\text{inf\_NV}}} = 1 - (1 + \eta_{\text{NV}}\lambda_{\text{NV}})^{-r\_\text{NV}} \quad [2]$$

where η_{NV} and r_nv are model parameters described in Teunis et al. (1999). The probability of illness per dose ($p_{\text{ill\_NV}}$) was defined as

$$p_{\text{ill\_NV}} = p_{\text{inf\_NV}} p_{\text{ill}_{\text{inf\_NV}}} \quad [3]$$

and using Eqs. [3, 4 and 5] the tolerable dose of norovirus, λ_{NV}, was determined.

For giardia, Teunis et al. (1996) fitted the exponential dose-response model, using

$$p_{\text{inf\_G}} = 1 - exp(-r\_\text{G}\lambda_G), \quad [4]$$

to the original data published by Rendtorff (1954) where r_G is an infectivity parameter (interpreted as the probability for one organism to initiate infection) and λ_{G} is the dose of giardia (number of organisms) consumed. The mechanism of giardia pathogenicity and host responses to infection remain unclear (Roxström-Lindquist et al., 2006), although it has been widely reported that a high proportion of giardia infections are asymptomatic; even the original study found no evidence of illness that could be connected to ingestion of giardia cysts (Rendtorff, 1954). The reported proportions of asymptomatic cases are highly variable: two community-wide studies reported 0.19 (Birkhead and Vogt, 1989) and 0.76 (Lopez et al., 1980) and studies of adults found 0.07 (Hoque et al., 2002) and 0.30 (Yakoob et al., 2010). Therefore, a Uniform distribution was used to represent the proportion of infections that result in illness. The tolerable daily probability of infection ($p_{\text{inf\_G}}$) was estimated as

$$p_{\text{inf\_G}} = \frac{p_{\text{ill\_G}}}{(inf{:}ill)}, \quad [5]$$

where *inf:ill* is the proportion of infections that are symptomatic (illness). Eq. [4] was then used to solve for the tolerable dose of giardia, λ_G.

The probability of *Campylobacter* infection per dose (p_{inf_C}; person^{-1} day^{-1}) was estimated as

$$p_{\mathrm{inf\_C}} = 1 - {}_1F_1(\alpha, \alpha+\beta; -\lambda_C), \quad [6]$$

where ${}_1F_1$ is a hypergeometric function, λ_C is the dose of *Campylobacter* (number of organisms) and α and β are fit parameters. The conditional probability of illness in infected subjects ($p_{\mathrm{ill}_{\mathrm{inf\_C}}}$) was found to be dose-dependent and was modeled following Teunis et al. (2005) as

$$p_{\mathrm{ill}_{\mathrm{inf\_C}}} = 1 - (1 + \eta_C \lambda_C)^{-r\_C} \quad [7]$$

where η_C and r_C are model parameters described in Teunis et al. (1999). We have assumed the values of η_C and r_C were incorrectly reported in Teunis et al. (2005) such that the published value of η_C is actually r_C . The probability of illness per dose (p_{ill_C}) was defined as

$$p_{\mathrm{ill\_C}} = p_{\mathrm{inf\_C}} p_{\mathrm{ill}_{\mathrm{inf\_C}}} \quad [8]$$

and using Eqs. [8, 9 and 10] the tolerable dose of *Campylobacter*, λ_C, was determined.

Estimates of municipal sewage

Measurements of norovirus in municipal wastewater are scarce which can be explained, at least in part, by the methodological challenges related to the detection of norovirus (Haramoto et al., 2006; Katayama et al., 2008; La Rosa et al., 2010; Ottoson et al., 2006a; Ottoson et al., 2006b). Only two studies reported recovery efficiencies for norovirus detection (Haramoto et al., 2006; Katayama et al., 2008); therefore, a Mixture distribution, incorporating both studies with equal weighting, was used assuming that norovirus concentrations are similar across populations with high living standards. *Giardia lamblia* cyst numbers were surveyed in raw sewage from three sewage treatment plants over a 6 to 12 month period (Van Den Akker et al., 2011). Concentration values, corrected for recovery efficiency, were similar across all three sewage treatment plants with a mean of 2.5 $\log_{10}$ cysts L^{-1}. The $\log_{10}$ mean and standard deviation were used to define a Normal distribution (by definition the antilog is Lognormal[1]) for each sewage treatment plant and the concentration of giardia in raw sewage was represented by a Mixture distribution of random values drawn from the three Normal distributions with equal weighting. There was limited information on *Campylobacter* concentrations although there is a reference in the Australian Guidelines for Water Recycling (NRMMC et al., 2006a) to unpublished research (10^2 to 10^5 cfu L^{-1} in raw sewage, 95th percentile $7x10^3$). To represent station conditions, the Guideline values (95th and estimates of 1st and 2nd percentiles) were used to estimate a Lognormal distribution.

[1] Technically, the definition uses the natural logarithm, but data were provided in base 10; it was assumed the definition still applies.

84 Table S.1 Published values of daily per capita drinking water consumption (L person^{-1} day^{-1}).

Country	Mean	Standard Deviation	Description	Reference
USA	1.098	0.922 (estimated)	adults 20 years and older	(USEPA, 2004)
USA	1.48	0.984 (estimated)	adults 25-54 years old	(USEPA, 2006)
Canada	1.2	0.8	data from 7 cross-sectional studies	(Roche et al., 2012)
USA	1.3	1.17	Lognormal distribution	(Schijven et al., 2011)
Sweden	0.873	0.541	Lognormal distribution	(Ãstrom et al., 2007)
France	1.760	0.001715		(Hunter et al., 2011)

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Table S.2 Comparison of methods used to estimate required log_{10} reductions for potable reuse of municipal sewage.

Model Parameters	Australian Guidelines: Augmentation of Drinking Water Supplies[a]	WHO: Guidelines for Drinking Water Quality[b]	Model (estimated municipal sewage)
Model type	Deterministic	Deterministic	Stochastic
Reference pathogens	RV, Cr, Cb	RV, Cr, Cb	NV, G, Cb
Pathogen concentration (# L^{-1})	95th percentile values in raw sewage RV: 8.00x10^3 = adenovirus concentration from Virginia Pipeline Scheme, SA (unpublished) Cr: 2.00x10^3; Cb: 7.00x10^3	River Water RV: 10 Cr: 10 Cb: 100	Mixture distribution for raw sewage NV: 3.12x10^6 (mean), 1.02x10^7 (95th percentile)[c] G: 2.51x10^3 (mean), 9.04x10^3 (95th percentile) Cb: 1.90x10^3 (mean), 7.19x10^3 (95th percentile)
Dose-response model	RV: simplified approx. Beta-Poisson Cr: Exponential (r=0.059) Cb: simplified approx. Beta-Poisson	RV: Beta-Poisson (α=0.2531, β=0.4265) Cr: Exponential (r=0.00467) Cb: Exponential (r=0.019)	NV: full Beta-Poisson (hypergeometric) G: Exponential (r=Triangular) Cb: full Beta-Poisson (hypergeometric)
Disease burden (DALYs case^{-1})	RV: 1.3x10^{-2}; Cr: 1.5x10^{-3}; Cb: 4.6x10^{-3}	RV: 1.4x10^{-2} Cr: 1.5x10^{-3} Cb: 4.6x10^{-3}	NV: Uniform(3.71x10^{-4}, 6.23x10^{-3}) ~ 3.30x10^{-3} (mean) G: Uniform(2.10x10^{-3}, 2.68x10^{-3}) ~ 2.39x10^{-3} (mean) Cb: Uniform(4.60x10^{-3}, 4.10x10^{-2}) ~ 2.28x10^{-2} (mean)
Susceptibility fraction	RV: 0.06 (population <5 years) Cr and Cb: 1	RV: 0.06 Cr and Cb: 1	NV: Uniform(0.8, 1.0) G and Cb: 1
Ratio of infection to illness	RV: 0.88 Cr: 0.70 Cb: 0.30	RV: 0.5 Cr: 0.7 Cb: 0.3	NV: non-linear dose-response model G: Uniform(0.24, 0.93) ~ 0.58 (mean) Cb: non-linear dose-response model
Daily per capita drinking water (L)	2	1	Lognormal(3, 1) – truncated at 2 and 6
Required log_{10} reduction	RV: 9.5 Cr: 8 Cb: 8.1	RV: 5.96 Cr: 5.89 Cb: 5.98	NV: 6.9 (95th percentile) G: 8.0 (95th percentile) Cb: 7.4 (95th percentile)

[a]Guidelines refer to Phase I Guidelines for many of the parameter values (NRMMC et al., 2006).

[b](WHO, 2011)

[c]Municipal treatment plants were different sizes. In Haramoto et al. (2006) the WWTP serves a population of ~63,000 and treats 28,000m^3 of sewage per day. In Katayama et al. (2008), samples were collected from 6 WWTPs that , ranging in size from 63,000 to 770,000 people served and average daily treated volume of 28,000 to 571,000 m^3 per day.

Note: Cb=*Campylobacter*, Cr=cryptosporidium, G=Giardia, NV=norovirus, RV=rotavirus

Table S.3. Stepwise results from reverse QMRA for required $\log_{10}$ reduction (LRV) of pathogens in sewage for potable reuse of treated wastewater. Values reported as $50^{th}[5^{th}, 95^{th}]$ percentiles.

Model Parameter	Norovirus	Giardia	*Campylobacter*
Health target (DALYs person^{-1} year^{-1})	10^{-6}	10^{-6}	10^{-6}
Sewage conc'n – municipal (# L^{-1})	$1.7x10^{6}[3.2x10^{5}, 1.0x10^{7}]$	$6.5x10^{2}[4.2x10^{1}, 9.0x10^{3}]$	$6.7x10^{2}[6.3x10^{1}, 7.2x10^{3}]$
Sewage conc'n – Davis outbreak (# L^{-1})	$5.0x10^{11}[6.5x10^{10}, 1.4x10^{12}]$	$9.7x10^{5}[7.5x10^{5}, 1.4x10^{6}]$	$1.2x10^{8}[9.6x10^{6}, 4.9x10^{8}]$
Sewage conc'n – Melbourne outbreak (# L^{-1})	$2..6x10^{10}[3.4x10^{9}, 7.2x10^{10}]$	n/a	n/a
Tolerable annual probability of illness	$3.4x10^{-4}[1.9x10^{-4}, 1.7x10^{-3}]$	$4.2x10^{-4}[3.8x10^{-4}, 4.7x10^{-4}]$	$4.4x10^{-5}[2.6x10^{-5}, 1.6x10^{-4}]$
Tolerable daily probability of illness	$3.8x10^{-6}[1.8x10^{-6}, 1.9x10^{-5}]$	$4.6x10^{-6}[3.4x10^{-6}, 6.6x10^{-6}]$	$5.0x10^{-7}[2.5x10^{-7}, 1.8x10^{-6}]$
Tolerable daily probability of infection	$4.6x10^{-3}[3.2x10^{-3}, 1.0x10^{-2}]$	$8.2x10^{-6}[4.5x10^{-6}, 1.8x10^{-5}]$	$6.2x10^{-4}[4.4x10^{-4}, 1.2x10^{-3}]$
Tolerable daily dose (#)	3.8[2.6, 8.5]	$3.3x10^{-4}[1.3x10^{-4}, 1.0x10^{-3}]$	$9.2x10^{-4}[6.7x10^{-4}, 1.7x10^{-3}]$
Tolerable drinking water conc'n (# L^{-1})	1.3[0.7, 3.0]	$1.1x10^{-4}[4.0x10^{-5}, 3.6x10^{-4}]$	$3.1x10^{-4}[1.7x10^{-4}, 6.3x10^{-4}]$
Required LRV – municipal	6.1[5.3, 6.9]	6.8[5.5, 8.0]	6.3[5.3, 7.4]
Required LRV – outbreak	11.6[10.6, 12.1]	10.0[9.4, 10.4]	11.6[10.5, 12.3]
Required LRV – Melbourne outbreak	10.3[9.4, 10.8]	n/a	n/a
Required LRV – Guideline values	9.5	8.0	8.1

Table S.4 Estimated required protozoan $\log_{10}$ reduction values (LRVs) for stepwise methodological changes from the Guideline method (NRMMC et al., 2008) to a deterministic approximation of the model using municipal sewage concentrations.

Step	RV	Model Input Parameters[a]						
		V	*c*	*B*	S_f	*inf:ill*	d-r	*n*
1.	.0	2	2000	$1.5x10^{-3}$	1	0.70	Cr[b]	365
2.	.6	2	$9.04x10^{3}$ (95^{th} G)	$1.5x10^{-3}$	1	0.70	Cr[b]	365
3.	.3	4.8 (95^{th})	2000	$1.5x10^{-3}$	1	0.70	Cr[b]	365
4.	.9	2	$9.04x10^{3}$ (95^{th} G)	$2.7x10^{-3}$ (95^{th})	1	G[c]	G[c]	365
5.	.2	4.8 (95^{th})	$9.04x10^{3}$ (95^{th} G)	$2.7x10^{-3}$(95^{th})	1	G[c]	G[c]	365
6.	.4	2	$9.04x10^{3}$ (95^{th} G)	$2.7x10^{-3}$(95^{th})	1	G[c]	G[c]	118 (95^{th} AAD)
7.	.8	4.8 (95^{th})	$9.04x10^{3}$ (95^{th} G)	$2.7x10^{-3}$(95^{th})	1	G[c]	G[c]	118 (95^{th} AAD)

[a]Model input parameters: *V* = daily water consumption (L person^{-1}), *c* = sewage pathogen concentration (# L^{-1}), *B* = disease burden (DALYs case^{-1}), S_f = susceptibility fraction, *inf:ill* = ratio of infection to illness, d-r = dose-response model, *n* = days of exposure.

[b]exponential dose-response model; $r=5.9x10^{-2}$

[c]giardia exponential dose-response model: use 95^{th} values of r (0.0468) and Inf:ill (0.8954).

The Guidelines (NRMMC et al., 2008) recommend a minimum cryptosporidium $\log_{10}$ reduction (LRV) of 8.0 for the production of drinking water from sewage while the full stochastic model, using municipal sewage concentration, obtained the same value for giardia. To compare these two methods, sequential steps in methodology from the Guideline method (Step 1) to a deterministic approximation of the model method (Step 7, using 95^{th} percentile values of all input distributions) are reported. The difference in LRVs between Steps 1 and 2 shows the effect of using Australian giardia concentrations (8.0 to 8.6). The difference between Steps 2 and 4 shows the slight increase in LRV due to the giardia dose-response model (8.6 to 8.9). The difference between Steps 4 and 5 shows the impact of using the higher drinking water volume (8.9 to 9.2) and the difference between Steps 5 and 7 shows the impact of a shorter exposure period (9.2 to 8.8). Comparing the 95^{th} percentile of the full stochastic model (8.0) with a deterministic approximation of the method (Step 7; 8.8), the difference is moderate.

Table S.5 Estimated required bacterial $\log_{10}$ reduction values (LRVs) for stepwise methodological changes from the Guideline method (NRMMC et al., 2008) to a deterministic approximation of the model using municipal sewage concentrations.

Step	RV	Model Input Parameters[a]						
		V	*c*	*B*	S_f	Inf:ill	d-r	*n*
1.	.1	2	7000	4.6×10^{-3}	1	0.30	Cb[b]	365
2.	.5	4.8 (95^{th})	7000	4.6×10^{-3}	1	0.30	Cb[b]	365
3.	.6	2	7000	3.9×10^{-2} (95^{th})	1	Cb[c]	Cb[c]	365
4.	.0	4.8 (95^{th})	7000	3.9×10^{-2} (95^{th})	1	Cb[c]	Cb[c]	365
5.	.4	2	7000	3.9×10^{-2} (95^{th})	1	Cb[c]	Cb[c]	118 (95^{th})
6.	.7	4.8 (95^{th})	7000	3.9×10^{-2} (95^{th})	1	Cb[c]	Cb[c]	118 (95^{th})

[a]Model input parameters: *V* = daily water consumption (L person^{-1}), *c* = sewage pathogen concentration (# L^{-1}), *B* = disease burden (DALYs case^{-1}), S_f = susceptibility fraction, Inf:Ill = ratio of infection to illness, d-r = dose-response model, *n* = days of exposure.

[b]simplified approximate Beta-Poisson; alpha=0.145, beta=7.58

[c]full Beta-Poisson

The Guidelines (NRMMC et al., 2008) recommend a minimum *Campylobacter* $\log_{10}$ reduction (LRV) of 8.1 for the production of drinking water from sewage while the full stochastic model, using municipal sewage concentrations, determined a 95^{th} percentile LRV of 7.4. To compare these two methods, sequential steps in methodology from the Guideline method (Step 1) to a deterministic approximation of the model (Step 6, using 95^{th} percentile values of all input distributions) are reported. The difference between Steps 1 and 2 shows the impact of using the higher drinking water volume (8.1 to 8.5). The difference between Steps 1 and 3 shows the reduction in LRV due to the full *Campylobacter* dose-response model (8.1 to 7.6) and a further reduction is shown with the implementation of the (shorter) summer exposure period (Steps 4 and 6; LRVs of 8.0 and 7.7). Comparing the 95^{th} percentile of the full stochastic model (7.4) with a deterministic approximation of the method (Step 6; 7.7), the difference is small.

141 Table S.6 Published maximum pathogen concentrations in raw sewage.
142

Country	Peak value	Units	Account for % recovery[a]	Reference
NOROVIRUS				
Brazil	~$5x10^4$	Genomic copies L^{-1}	n/a	(Victoria et al., 2010)
Finland	10^6	PCR units L^{-1}	n/a	(Von Bonsdorff et al., 2002)
France	$1x10^9$ (NV GI)	Genomic copies L^{-1}	n/a	(Da Silva et al., 2007)
Germany	$9.7*10^5$	Genomic equivalents L^{-1}	no	(Pusch et al., 2005)
Italy	$5.7x10^8$	GC/L (have assumed error in paper)	n/a	(La Rosa et al., 2010)
Japan	$1.9x10^7$ total NV (I+II)	copies L^{-1}	yes	(Haramoto et al., 2006)
Japan	$6.6x10^6$ total NV (I+II)	monthly mean RT-PCR units L^{-1}	yes	(Katayama et al., 2008)
Netherlands	$8.5x10^5$	PDU L^{-1}	no	(Lodder and De Roda Husman, 2005)
Netherlands	10^6	PCR detectable units L^{-1}	n/a	(Van Den Berg et al., 2005)
Singapore	$1x10^7$ (NV GI)	Genomic copies mL^{-1}	no	(Aw and Gin, 2010)
Sweden	3.65	$\log_{10}$ MPN PCR units L^{-1}	n/a	(Ottoson et al., 2006b)
Sweden	$4.5 x10^3$	# L^{-1}	n/a	(Ottoson et al., 2006a)
Sweden	$1x10^7$ (NV GII)	Genomic copies L^{-1}	n/a	(Nordgren et al., 2009)
UK	$1.8x10^7$	cDNA copies L^{-1}	no	(Laverick et al., 2004)

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145 Table S.6 Published maximum pathogen concentrations in raw sewage - continued.
146

Country	Peak value	Units	Account for % recovery[a]	Reference
GIARDIA				
Australia	>5.0x10^2	cysts L^{-1}	n/a	(Wohlsen and Katouli, 2006)
Canada	2.1 x10^2	cysts L^{-1}	n/a	(Chauret et al., 1999)
Japan	3.9x10^3	cysts L^{-1}	yes	(Oda et al., 2005)
Netherlands	2.6x10^3	cysts L^{-1}	yes	(Medema and Schijven, 2001)
Spain	1.4x10^4	cysts L^{-1}	yes	(Castro-Hermida et al., 2010)
Spain	8.31x10^3	cysts L^{-1}	n/a	(Castro-Hermida et al., 2008)
Sweden	5.72x10^4	cysts L^{-1}	yes	(Ottoson et al., 2006b)
Sweden	1.77x10^4	cysts L^{-1}	yes	(Ottoson et al., 2006a)
USA	1.4x10^4	cysts L^{-1}	n/a	(Gassmann and Schwartzbrod, 1991)
USA	1.3x10^2	cysts L^{-1}	n/a	(Rose et al., 1996)
USA	1.4 x10^4	cysts L^{-1}	n/a	(Sykora et al., 1991)
Australia	~900	cysts L^{-1}	yes	(Van Den Akker et al., 2011)

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149 Table S.6 Published maximum pathogen concentrations in raw sewage - continued.
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Country	Peak value	Units	Account for % recovery[a]	Reference
CAMPYLOBACTER				
Germany	>1x10^7	CFU L^{-1}	no	(Rechenburg and Kistemann, 2009)
Italy	10^5	CFU L^{-1}	no	(Stellacci et al., 2010)
Baltic Sea	1.1x10^6	CFU L^{-1}	no	(Holler, 1988)
Netherlands (combined sewers)	2.4x10^4	CFU L^{-1}	no	(ten Veldhuis et al., 2010)
Germany	10^4	CFU L^{-1}	no	(Stelzer, 1991)
USA	6.2x10^7	CFU L^{-1}	n/a	(Hellein et al., 2011)
Spain	1.5x10^5	MPN L^{-1}	no	(Rodríguez and Araujo, 2010)
Switzerland	2.3x10^6	cells L^{-1}	no	(Rinsoz et al., 2009)
France	3x10^6	genes L^{-1}	no	(Wéry et al., 2008)
UK	4.6x10^5	MPN L^{-1}		(Arimi et al., 1988)

151 [a] n/a = not stated, unclear
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