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Selecting Household Water Treatment Options on the Basis of World Health Organization Performance Testing Protocols

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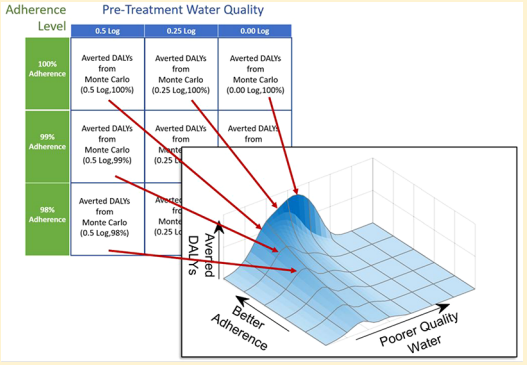
Supporting Information

ABSTRACT: The World Health Organization's International Scheme to Evaluate Household Water Treatment Technologies serves to benchmark microbiological performance of existing and novel technologies and processes for small-scale drinking water treatment according to a tiered system. There is widespread uncertainty around which tiers of performance are most appropriate for technology selection and recommendation in humanitarian response or for routine safe water programming. We used quantitative microbial risk assessment (QMRA) to evaluate attributable reductions in diarrheal disease burden associated with water treatment technologies meeting the three tiers of performance under this Scheme, across a range of conditions. According to mean estimates and under most modeling conditions, potential health gains attributable to microbiologically improved drinking water are realized at the middle tier of performance: "comprehensive protection: high pathogen removal (★★)" for each reference pathogen. The highest tier of performance may yield additional marginal health gains where untreated water is especially contaminated and where adherence is 100%. Our results highlight that health gains from improved efficacy of household water treatment technology remain marginal when adherence is less than 90%. While selection of water treatment technologies that meet minimum WHO efficacy recommendations for comprehensive protection against waterborne pathogens is critical, additional criteria for technology choice and recommendation should focus on potential for correct, consistent, and sustained use.



INTRODUCTION

In 2015, an estimated 2.1 billion people lacked access to a safely managed water service, defined by the WHO/UNICEF Joint Monitoring Programme (JMP) as a water supply that is "located on premises, available when needed and free from contamination".[1] Unsafe drinking water is a leading cause of preventable disease, with the burden borne primarily by children in low- and middle-income countries (LMICs). Pathogens transmitted in drinking water account for an unknown but presumed significant percentage of the estimated 240 million disability-adjusted life years (DALYs) associated with diarrheal diseases[2] and the estimated 500,000 deaths attributable to inadequate water in LMICs.[3] Enteric infections are among the top causes of disease and death in children globally.[4]

Providing safe, reliable, piped-on-plot water to every household is an important normative goal, yielding health gains and contributing to Sustainable Development Goal targets for water and sanitation (SDG 6) as well as across a range of categories, including child and maternal health, poverty reduction, and gender equality. However, increased access to piped water supplies does not guarantee the microbiological safety of drinking water, for a variety of reasons,[5] and fecal contamination of all "improved" water supplies, including sources like protected wells, is known to be widely prevalent.[6−8] Even sporadic degradation of the quality of water from water supplies, or intermittent exposure to less safe sources,[9,10] can undermine the health benefits of drinking water supplies.[11]

Water quality interventions, including household water treatment (HWT), are now commonly promoted to improve water safety at the point of consumption. The available evidence suggests that these technologies can reduce exposures to waterborne pathogens and potentially reduce enteric infections among users,[12] though the epidemiological evidence for sustained health effects is debated[12,13] due to the lack of

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Table 1. Overview of Model Input Used To Estimate Averted DALYs, Dose Reduction, and Risk Reduction Attributable to Household Water Treatment Technologies in Various Application Contexts

model input	units	probability density function (pdf) for independent variables	values (independent variables) or formulas (dependent variables)
		Treatment Technology Efficacy	
$\log_{10}$ reduction value (LRV)	unitless	point estimate per WHO scheme[15]	three-star: *Campylobacter* 4, rotavirus 5, *Cryptosporidium* 4
			two-star: *Campylobacter* 2, rotavirus 3, *Cryptosporidium* 2
			one-star (no virus): *Campylobacter* 2, rotavirus 0,*Cryptosporidium* 2
			one-star (no protozoa) *Campylobacter* 2, rotavirus 3, *Cryptosporidium* 2
		Application Context Variables	
pretreatment water quality (C_R), expressed as counts of reference pathogens	$\log_{10}$ microbes per liter	point estimate	−4 $\log_{10}$ to 3 $\log_{10}$ at 0.25 $\log_{10}$ increments
adherence or consistency of drinking water treatment (A)	percent of water volume consumed that is treated (%)	point estimate	100% to 0% at 1% increments
		Simulation Variables	
drinking-water quality (C_D)	organisms per liter	calculated	eq 1
consumption of drinking water (V)	liters per person per day	uniform distribution[18,21]	1 to 2
dose by drinking water (D)	microbes ingested per day via treated and untreated drinking water	calculated	eq 2
daily probability of infection ($P_{inf,d}$)	probability per day	*Campylobacter*: beta Poisson D-R, Medema et al.;[22] Teunis et al.[23]	eq 3: $\alpha = 0.144$, $N_{50} = 890$; $\alpha = 0.038$, $N_{50} = 1.84 \times 10^6$
		rotavirus: beta Poisson D-R	eq 3: $\alpha = 0.253$, $N_{50} = 6.17$
		Cryptosporidium: exponential D-R[25]	eq 4: $k = 0.0572$
annual probability of infection ($P_{inf,y}$)	per year	calculated	eq 5
probability of diarrheal illness given infection (P_{illinf})	unitless	*Campylobacter*: point estimate[18,26]	0.3
		rotavirus: point estimate[18,26]	0.5
		Cryptosporidium: point estimate[18,26]	0.7
annual probability of diarrheal illness ($P_{ill,y}$)	per year	calculated	eq 6
DALY weighting per case of illness (DW)	DALYs per case	*Campylobacter*: point estimate	4.6×10^{-3}
		rotavirus: uniform distribution	0.014 to 0.48
		Cryptosporidium: point estimate	1.5×10^{-3}
susceptible fraction (S)	percentage of population	*Campylobacter*: point estimate	100%
		rotavirus: uniform distribution	1% to 6%
		Cryptosporidium: point estimate	100%
diarrheal disease burden per 100,000 person-years	DALYs per year per 100,000 persons	calculated	eq 7
		End Point Calculations	
dose reduction	reduction in microbes ingested per day attributable to water treatment	calculated	eq 8
risk reduction	reduction in annual probability of infection attributable to water treatment	calculated	eq 9
averted disease burden per 100,000 persons	DALYs per year per 100,000	calculated	eq 10

blinded trials and potential for bias associated with subjective health outcome measures (e.g., self-reported diarrhea).[14]

A wide range of products and approaches now exist for HWT. Lack of international and national regulations and widespread uncertainty over which products are effective in reducing microbial exposures, and therefore which should be recommended for use, in both emergency and nonemergency settings, has led to the creation of the World Health Organization (WHO) International Scheme to Evaluate Household Water Treatment Technologies, beginning in 2015. The Scheme encourages standardized, laboratory efficacy testing of existing and novel technologies for small-scale and decentralized water treatment, including HWT. Manufacturers submit expressions of interest (EoIs), which are reviewed by WHO for relevance to the Scheme. Priority technologies for laboratory challenge testing are those that are "market ready", relatively low-cost, and appropriate for low-income settings where risks are highest. Testing is performed in centralized laboratories according to standardized protocols, with laboratory evaluation and interpretation of testing data supported by a panel of independent experts. The Scheme ranks technologies on a tiered scale.[15] In the upper tier (★★★) are technologies that reduce bacteria at least 99.99% (4 $\log_{10}$) from pretreatment counts, viruses at least 99.999% (5 $\log_{10}$), and protozoa at least 99.99% (4 $\log_{10}$). A middle tier (★★) includes technologies reducing bacteria 99% (2 $\log_{10}$), viruses 99.9% (3 $\log_{10}$), and protozoa 99% (2 $\log_{10}$). The lowest tier (★) describes technologies that reduce two of the three microbial classes by at least 99% (2 $\log_{10}$). Technologies

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not meeting the lowest performance tier are unranked by the Scheme.

The relationship between efficacy of HWT[10] and adherence[9] (correct, consistent, and sustained use) has been previously described via quantitative microbial risk modeling. These studies have shown that, under most modeling conditions, there are decreasing marginal health gains as microbiological performance increases and adherence (also referred to as *compliance*) is generally more important than efficacy given the fact that intermittent exposures to unsafe water control overall waterborne infection risk.[11] In this paper, we build on this work to focus specifically on the question of technology choice within the WHO Scheme to assess predicted health impacts attributable to technologies meeting each tier of performance. Our hypotheses are (i) that predicted attributable health impact is a function of pretreatment microbial water quality and adherence as well as microbial reduction and (ii) that, *ceteris paribus*, increasing $\log_{10}$ reductions of waterborne pathogens results in decreasing marginal gains in health. These decreasing gains would have particular relevance to HWT technology recommendations on the basis of the WHO Scheme. Our objective in this modeling exercise is to provide needed context to support the growing use of the WHO Scheme for water treatment technology performance characterization, selection for field implementation, and recommendation of treatment technologies across a wide range of settings from cholera outbreaks to routine longer-term safe water programs.[15]

METHODS

Overview. We constructed a quantitative microbial risk assessment (QMRA) model to simulate household water treatment under a range of application scenarios that are characterized by fixed pretreatment microbial counts and adherence levels. For each scenario described by a combination of pretreatment water quality, adherence level, and treatment efficacy, as ranked by the WHO Scheme, we executed Monte Carlo simulations utilizing published estimates for dose−response relationships for reference pathogens, per-case disability-adjusted life year (DALY) weighting, and population susceptibility. We executed our Monte Carlo simulations in Oracle Crystal Ball, Fusion Edition (release 11.1.2.1.000, www.oracle.com) using a Monte Carlo sampling method with an initial seed value of 999. Following 10,000 simulations within each scenario, we exported model output for each end point and utilized the "contourf" and "surf" functions in Matlab (MathWorks, Inc.: Natick, MA, 2017) to generate the contour and surface figures shown. Here, we briefly describe the methods and summarize our calculations. All model input is summarized in Table 1.

Reference Pathogens. The reference pathogens we selected for the model were *Campylobacter jejuni*, *Cryptosporidium*, and rotavirus; we used these fecal−oral pathogens not because they necessarily present the greatest microbial waterborne exposure risks globally but because they are risk-conservative proxies for each of the major waterborne pathogen classes and because they are supported by relatively well-characterized dose−response relationships derived from human populations.[16] They are further characterized by moderate to long persistence in water supplies, high infectivity, and moderate to high resistance to chlorine.[17] We list assumptions for pathogen-specific per-case DALY weighting, population susceptibility, and risk of illness following infection in Table 1.[18]

Treatment Technology Log Reduction Value. Microbial log reduction values (LRV) for household water treatment technologies can vary over time and may depend on a range of factors, including interacting physical, chemical, and biological characteristics of water; changes to the treatment device (e.g., membranes, seals, media) over time; temperature; other variables. We modeled performance for each reference pathogen according to the tiered levels articulated in the WHO Scheme as previously described.

Pretreatment Water Quality. Waterborne pathogen counts in drinking water sources are a function of many factors that include infection and illness prevalence and severity and therefore vary substantially over space and time. No systematically produced, internationally representative mean estimates are available for pathogen occurrence in these sources. On the basis of a synthesis of published data sets regarding *Campylobacter*[19] and rotavirus,[20] we assumed a range of reference pathogen counts to account for variability across plausible water sources and settings where HWT is applied. To estimate the health impacts of HWT in each of these scenarios, we fixed pretreatment water quality (C_R) at $\log_{10}$ count values for each reference pathogen ranging from −4 $\log_{10}$ to 3 $\log_{10}$ in 0.25 $\log_{10}$ increments. We then simulate HWT in each of these pretreatment water quality scenarios by running a Monte Carlo simulation for each one. With the pretreatment water quality and the log reduction value for the technology fixed within each model, the concentration of each reference pathogen in the treated drinking water (C_D) in $\log_{10}$ units is calculated per eq 1.

$$C_D = 10^{C_R - LRV} \quad (1)$$

Adherence and Drinking Water Consumption. For HWT to translate into health gains, the percentage of water consumed on a volumetric basis that is subjected to treatment is an important factor: here, we refer to this percentage as adherence. For each modeled HWT scenario, we fix the adherence as a point estimate with values ranging from 0% adherence, equivalent to no treatment of the daily drinking water volume, to 100% adherence, equivalent to treatment of the entire daily drinking water volume, in 1% increments. The daily dose of each reference pathogen resulting from a given adherence percentage is calculated in the model per eq 2. As an example, for a user consuming 1 L of water daily at an adherence of 50% with a pretreatment water quality of 100 rotaviruses per liter and a HWT LRV of 3, the dose from the treated drinking water, the first term in eq 2, would be 0.5 L per day times 0.1 rotaviruses per liter or 0.05 rotaviruses per day. The dose from the untreated drinking water, the second term in eq 2, would be 0.5 L per day times 100 rotaviruses per liter or 50 rotaviruses per day. The resulting combined dose would be 50.05 rotaviruses per day. We modeled the daily volume of drinking water ingested, V, as a stochastic variable with a uniform distribution from 1 to 2 L per day.[18,21]

$$D = C_D VA + C_R V(1 - A) \quad (2)$$

Probabilities of Infection. The probability of infection following the ingestion of a dose of *Campylobacter* has been found to be best characterized by a Beta-Poisson dose−response function. For our Monte Carlo simulations, we used both the Medema et al. best-fit parameters[22] and the Teunis et al. best-fit parameters[23] to estimate *Campylobacter*-related end

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points. Probability of infection following ingestion of a dose of rotavirus has also been found to be best fit by a Beta-Poisson function.[24] The Beta-Poisson function, approximate version shown in eq 3, is characterized by the median infectious dose, N_{50}, and the parameter alpha, α. The probability of infection following ingestion of *Cryptosporidium* oocysts is best characterized by an exponential dose−response function,[25] shown in eq 4 and characterized by parameter k. The input dose for each dose−response function is calculated per eq 2 as previously described.

$$P_{\text{inf}}(d) = 1 - \left[1 + \frac{d}{N_{50}}(2^{1/\alpha} - 1)\right]^{-\alpha} \tag{3}$$

$$P_{\text{inf}}(d) = 1 - e^{(-k \times d)} \tag{4}$$

After the daily probability of infection is calculated, the annual probability of infection is calculated per eq 5.

$$P_{\text{inf,y}} = 1 - \prod_{1}^{n} (1 - P_{\text{inf,d}}) \tag{5}$$

Diarrheal Disease Burden. In the absence of well-established parameters, the risks of diarrheal illness given infection for each reference pathogen were input into the model as point estimates based upon values used in WHO guidance documents.[18,26] We modeled the per-case DALY weight[27] (DW) and susceptible fractions of the population[18,26] (S) for *Campylobacter* and *Cryptosporidium* as point estimates from previous efforts to quantify the burden of disease associated with waterborne diarrheal disease. The *Campylobacter* DW includes both gastroenteritis and death associated with gastroenteritis (1/10,000 cases) as well as more rare sequelae associated with Guillain-Barré Syndrome (GBS) (1/10,000 cases) including reactive arthritis and death (2.3% of GBS cases). The DW for *Cryptosporidium* includes both water diarrhea and death (1/100,000 cases). In an effort to reflect the global rollout of rotavirus vaccines and the resulting transient state of the burden of disease for rotavirus, we modeled both the per-case DW and the susceptible portion of the population as stochastic variables. For rotavirus, we modeled the per-case DW as a uniform distribution between the high-income and low-income country DW.[27] This DW includes both diarrheal disease and death results from diarrhea with the majority of the DW accounted for by a case fatality ratio of 0.6% in low-income countries and 0.015% in high-income countries. We modeled the rotavirus susceptible fraction of the population as a uniform distribution between the high-income and low-income country point estimates.[18] The annual probability of diarrheal illness is calculated as the product of the annual probability of infection, eq 5, and the probability of illness given infection, as shown in eq 6.

$$P_{\text{ill,y}} = P_{\text{inf,y}} \times P_{\text{ill|inf}} \tag{6}$$

The annual diarrheal disease burden in DALYs is then calculated, as shown in eq 7, by multiplying the annual probability of diarrheal illness from eq 6 by the susceptible fraction (S) and per-case DALY weight (DW) appropriate for each reference pathogen. For convenience, we scale this annual burden by multiplying by a factor of 100,000 persons for a final unit of DALYs per 100,000 person-years (py).

$$\text{DALYs (DALYs/100,000 person-years)} = P_{\text{ill,y}} \times S \times \text{DW} \times 100{,}000 \tag{7}$$

End Point Estimates. To assess the effects of household water treatment technologies in various application scenarios, we considered three end points. First, we considered the reduction in the daily ingestion of reference pathogens attributable to HWT, which we define as the dose reduction. As shown in eq 8, the dose reduction is the difference between the daily dose (eq 2) of each reference pathogen ingested via drinking water without treatment and the daily dose of each reference pathogen ingested with drinking water treatment at a specified LRV and adherence level. This end point is calculated for each reference pathogen on a daily basis so that the daily probability of infection can be calculated.

$$\text{dose reduction (\#/day)} = \text{dose}_{(\text{no treatment})} - \text{dose}_{(\text{with treatment})} \tag{8}$$

Second, we considered the annual reduction in the probability of infection with a reference pathogen attributable to HWT, which we define as the risk reduction. The risk reduction is the difference in the annual probability of infection (eq 5) for each reference pathogen with no treatment and the annual probability of infection with treatment at a specified LRV and adherence level (eq 9).

$$\text{risk reduction } (P_{\text{inf,y}}) = P_{\text{inf,y(no treatment)}} - P_{\text{inf,y(with treatment)}} \tag{9}$$

Lastly, we consider the averted diarrheal disease burden attributable to HWT. As shown in eq 10, we calculated the averted diarrheal disease burden (aDALYs) as the annual diarrheal disease burden (eq 7) attributable to drinking water with no treatment minus the annual diarrheal disease burden attributable to drinking water with treatment at a specified LRV and adherence level for each reference pathogen.

$$\text{averted DALYs (aDALYs/100,000 person-years)} = \text{DALYs}_{(\text{no treatment})} - \text{DALYs}_{(\text{with treatment})} \tag{10}$$

Since all stochastic input variables are modeled as uniform distributions with each value being equally likely, we used the mean as the summary statistic for all simulation end points.

Sensitivity Analysis. To facilitate a robust sensitivity analysis, we constructed a separate Monte Carlo simulation that included pretreatment water quality (as specified in Table 1), adherence (uniform distribution from 0 to 1), and log reduction values for each reference pathogen (uniform distribution from 0 to 7) in addition to all other stochastic variables. We assessed sensitivity by measuring the Spearman's rank-order correlation[22] between model input and each end point for a 10,000-draw Monte Carlo simulation of this same model. Using this model, we also conducted a one-at-a-time perturbation analysis to determine the relative sensitivity of each end point to input variables by varying the range of each input variable. To assess the robustness of the one-at-a-time analysis, we performed three separate analyses for each reference pathogen and each end point with inputs allowed to vary from their 20th to 80th percentile, 10th to 99th percentile, and 1st to 99th percentile while holding all other variables at their median and measuring the change in each end point.

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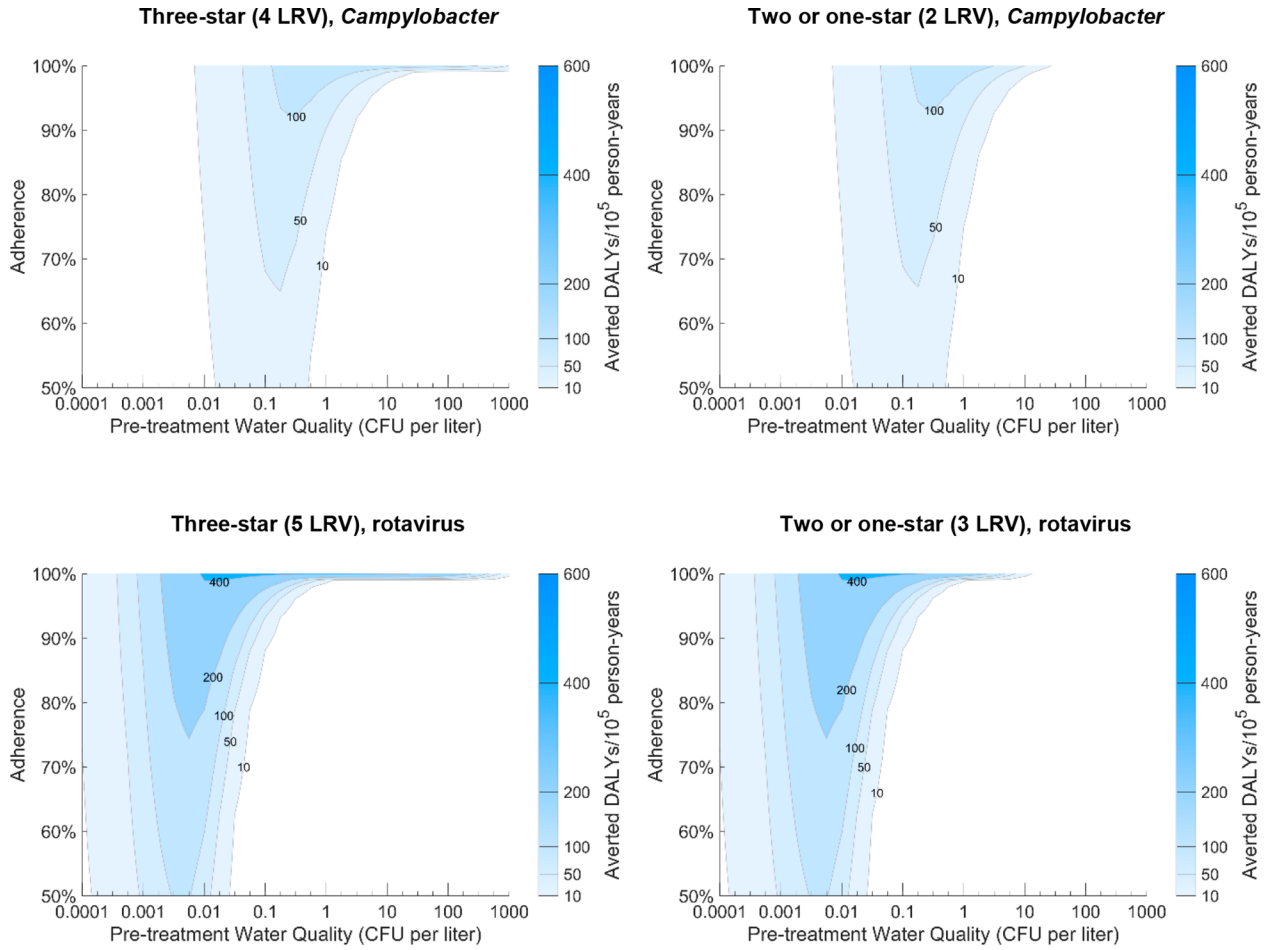

Figure 1. Mean averted DALY contours as estimated via Monte Carlo simulation for two reference pathogens: *Campylobacter* with three-star HWT (4 LRV), upper left; *Campylobacter* with two- or one-star HWT (2 LRV), upper right; rotavirus with three-star HWT (5 LRV), lower left; rotavirus with two- or one-star HWT (3 LRV), lower right. The results for *Cryptosporidium* are shown in Figure S4.

RESULTS

Contours depicting the mean averted DALYs for both *Campylobacter* and rotavirus at three-star and two- or one-star LRVs are shown in Figure 1. These graphs are read like topographic maps with model output, in this case mean averted DALYs, read from the contour (z-axis) given an HWT application scenario characterized by pretreatment water quality (x-axis) and adherence level (y-axis). Contours depicting the mean dose reduction and risk reduction are shown in Figures S1 (*Campylobacter*, Medema dose–response), S2 (*Campylobacter*, Teunis dose–response), and S3 (rotavirus). All output contours for *Cryptosporidium* are shown in Figure S4. Figure 2 displays graphs of mean averted DALYs as a function of pretreatment microbial counts (x-axis) at several combinations of treatment efficacy and adherence value for each reference pathogen. These graphs are analogous to cross sections cut through the averted DALY surfaces in Figure 1 at the adherence level indicated.

For each reference pathogen, health gains are maximized at the combination of highest tier performance (★★★) and 100% adherence. Maximum averted DALYs for *Campylobacter*, *Cryptosporidium*, and rotavirus were 137, 102, and 432 averted DALYs per 10^5 py. Even when pretreatment water quality is significantly degraded, with more than 100 of each reference pathogen per liter, this performance tier results in non-negligible health gains at 100% adherence. As adherence decreases to 90%, however, estimated mean health gains for each reference pathogen are drastically reduced and are realized only if pretreatment water quality is less than 10 reference pathogens per liter. The lower right panel of Figure 2 highlights the reduction in averted DALYs associated with *Campylobacter* as adherence decreases even for HWT in the highest tier of performance. This pattern is consistent for *Cryptosporidium* and rotavirus.

For the middle tier treatment technology (★★), estimated maximum achievable health gains at 100% adherence are 129 averted DALYs/10^5 py for *Campylobacter*, 96 averted DALYs/10^5 py for *Cryptosporidium*, and 428 averted DALYs/10^5 py for rotavirus. These gains are similar in magnitude to technologies in the highest tier. However, unlike the highest tier, the gains rapidly decline with increasing counts of reference pathogens in pretreatment water. At adherence levels less than 99%, technologies in the middle tier achieve almost identical health gains to technologies in the highest tier across all reference pathogen counts (Figure 2).

At the lowest performance tier (★), treatment technologies consist of a combination of LRVs for each reference pathogen such that the two-star criteria are met for two classes of reference pathogen. Therefore, the patterns observed in the middle-tier of treatment are also representative of the lowest performance tier.

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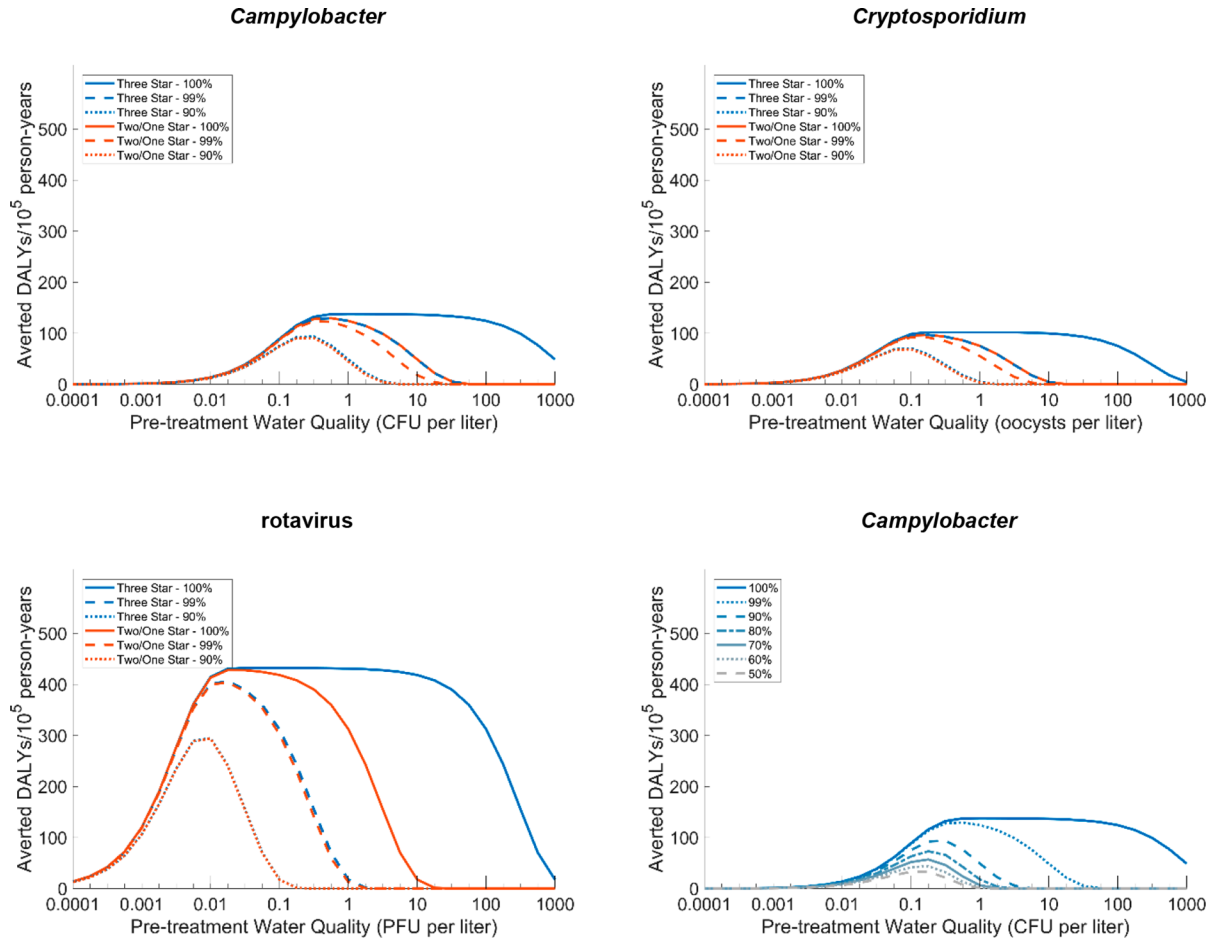

Figure 2. Mean averted DALYs as estimated via Monte Carlo simulation for each reference pathogen across a range of pretreatment water qualities at noted adherence levels for three-star and one- or two-star HWT: *Campylobacter*, upper left; *Cryptosporidium*, upper right; rotavirus, lower left. In the lower right, mean averted DALYs for three-star HWT for *Campylobacter* at adherence levels from 100% to 50% are shown.

Importantly, the end points in our analysis are differences in risk and disease burden, and therefore, the risk reduction and averted DALY contour shapes are similar between the Medema (Figures 1 and S1) and Teunis (Figure S2) *Campylobacter* dose−response models despite the much greater infectivity of *Campylobacter* at low doses in the Teunis model. A recent analysis of dose−response models for *Cryptosporidium*[28] found that oocysts may be up to 10 times more infective at low doses than previous models found, but again, because this analysis considers relative risks and disease burden, this would not significantly change the results found for *Cryptosporidium*.

Results of the sensitivity analysis for each end point and each reference pathogen are summarized in Table 2, averted DALYs, and Tables S2, S3, and S4, dose reduction and risk reduction. Our analyses indicate that estimated mean averted DALYs are most sensitive to pretreatment water quality (Spearman's correlations of −0.60 to −0.85) and adherence (Spearman's correlations of 0.18 to 0.26) over the range of conditions tested. Pretreatment water quality is negatively correlated with averted DALYs because, as can be seen in Figure 2, with increasing reference pathogen counts in pretreated water, the diarrheal disease burden prevented by a given treatment efficacy decreases as the risk of infection associated with consuming untreated water increases. Noticeably, mean averted DALYs were not as sensitive to the log reduction performance (Spearman's correlations of around 0.03).

The sensitivity of the model output to the pretreatment water quality and adherence was consistent across all reference pathogens for both the risk reduction and averted DALY end points. For all reference pathogens, the dose reduction end point was extremely sensitive to the pretreatment water quality. As the sampling range of the input variables was increased from the 20th to 80th percentiles to the 10th to 90th percentiles and finally up to the 1st to 99th percentiles during the one-at-a-time analysis, the risk reduction and averted DALY end points became increasingly more sensitive to adherence (data not shown). These results underscore the central role adherence, as a design variable, plays compared to log reduction value in determining whether a water treatment technology is likely to reduce waterborne disease.

Overall, our results suggest that, when pretreatment water is of poorer quality (≥1 reference microbes/liter), adherence is more important than efficacy for averted DALYs. When pretreatment water is of moderate quality (0.1 to 1 reference microbes/liter), a reduction from the highest tier to the middle tier results in a relatively minor difference in maximum health gains, holding all other variables constant. However, at the highest tier of performance and in the range of pretreatment water quality from 1 to 10 reference microbes/liter, a decrease from 100% adherence to 90% reduces estimated averted

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Table 2. Overview of Model Input Used To Estimate Averted DALYs, Dose Reduction, and Risk Reduction Attributable to Household Water Treatment Technologies in Various Application Contexts

input variable	explained variation (%)	Spearman correlation
Campylobacter, Averted DALYs		
pretreatment water quality (C_R, $\log_{10}$), (−4 to 3)	11.9	−0.60
adherence (A, %), (0 to 100)	85.6	0.26
Campylobacter LRV (LRV, $\log_{10}$), (0 to 7)	0.5	0.04
drinking water consumption (V, liters/day), (1 to 2)	1.9	−0.03
Rotavirus, Averted DALYs		
pretreatment water quality (C_R, $\log_{10}$), (−4 to 3)	100.0	−0.85
adherence (A, %), (0 to 100)	0.0	0.18
drinking water consumption (V, liters/day), (1 to 2)	0.0	−0.03
rotavirus LRV (LRV, $\log_{10}$), (0 to 7)	0.0	0.03
susceptible population (S, %), (1 to 6)	0.0	0.00
rotavirus per-case DALY weight (DW, DALYs/case), (1.4×10^{-2} to 4.8×10^{-1})	0.00	0.00
Cryptosporidium, Averted DALYs		
pretreatment water quality (C_R, $\log_{10}$), (−4 to 3)	29.6	−0.73
adherence (A, %), (0 to 100)	70.1	0.23
drinking water consumption (V, liters/day), (1 to 2)	0.3	−0.03
Cryptosporidium LRV (LRV, $\log_{10}$), (0 to 7)	0.0	0.03

DALYs by approximately 30% across all reference pathogens. At lower levels of reference pathogens in pretreatment water, both the potential health gains from treatment performance and the sensitivity to adherence are reduced, suggesting that the importance of treatment efficacy and high adherence are elevated for treatment of poorer quality waters and reduced for higher quality waters. These results highlight that even a single consumption event of a small untreated water volume bypasses the log reduction of HWT, eliminates any resulting health benefit from treatment, and drives annualized infection risks and subsequent diarrheal disease burden. While the use of a three-star technology does dramatically decrease the risk of infection for treated water, the exposure of a user to the infection risks associated with even as little as 10% untreated water volume quickly overcomes any potential protective effects associated with superior efficacy. Therefore, predicted health gains associated with a three-star technology are comparable to that of the two-star technology when decreasing adherence is considered.

DISCUSSION

The potential health impact estimates we report here should be interpreted in light of the uncertainty of the assumptions and necessary simplifications used to produce them.[29] Pretreatment water quality, for example, is likely to be highly variable in any given setting, with implications for LRV targets associated with treatment technologies to protect public health. Dose−response models for reference pathogens have been derived from few studies, mostly using data from healthy adults in high-income countries;[27] they may not accurately represent risk of disease in the settings where HWT is most prevalent, given that asymptomatic enteric infections are widely prevalent.[30] As an approach to estimating health risk, QMRA incorporates a number of assumptions whose values and ranges are uncertain. Where possible, we have attempted to use realistic ranges of pretreatment water quality, adherence, treatment effectiveness in reducing microbes, and other key variables. When confronted with assumptions, we used inputs that would tend to result in conservative estimates of risk reduction and prevented disease. QMRA is a quickly evolving approach, and models like the one we have used will benefit from further refinement of methods and assumptions.[31]

Despite these limitations, several insights are possible from this analysis, with important implications for interpretation of the new WHO Scheme. First, our analysis suggests that the middle tier of efficacy, ★★, is likely to yield comparable health gains to the highest tier of performance under actual implementation conditions. The exception is when pretreatment water is of very poor quality (≥10 reference microbes/liter) and treatment is exclusive (100% adherence). This scenario may be realistic during waterborne disease outbreaks, where risks are high and consumers may reasonably be expected to use the technology exclusively due to heightened awareness of exposure risks via drinking water, though this may not always hold true.[32] Second, the model output suggests that technologies at the lowest tier of performance (★) may yield health gains similar to the middle tier (★★) under certain conditions (Figure 1). An important caveat is that the causative disease agent and limitations of the technology must be known: for example, during a cholera outbreak, sodium hypochlorite solution as a standalone treatment option, due to lack of efficacy against *Cryptosporidium*, may be warranted if there is certainty of the outbreak etiology and the treatment is known to be highly effective against the pathogen of interest in this context. Because microbial risks are generally uncharacterized before recommendation of treatment technologies, the lowest tier should be reserved for these specialized cases. Third, adherence must be near 100% (exclusive use) to realize maximum health gains across all tiers of performance, and adherence is especially important where waterborne disease risk is high. Therefore, the likelihood that a given water treatment technology is used consistently, correctly, and over long periods (i.e., high adherence) is the central factor in treatment technology selection once the "comprehensive protection" performance tier has been met. Our findings on adherence are consistent with previous analyses, suggesting decreasing marginal health gains with increasing log-levels of microbial reduction.[9,11,33] Unfortunately, high adherence may not be achieved in practice in many settings: previous studies of HWT suggest that high adherence is the exception rather than the rule.[34−37]

Implications for HWT Technology Selection and Recommendation. It is commonly assumed that greater microbiological efficacy for water treatment options, generally measured by LRVs across pathogen classes, should yield proportionally greater health gains among users, though, to our knowledge, this has never been measured directly in controlled health impact trials comparing multiple water treatment technologies across ranges of performance. Alternatively, our analysis suggests that technologies that have been shown to meet basic efficacy criteria and are likely to be used exclusively, or nearly so, are likely to be more effective in preventing waterborne infections and subsequent disease and that technology selection and recommendation should move beyond efficacy measures only to incorporate water treatment behaviors and associated drivers to be leveraged in HWT

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programming. Explicitly incorporating adherence is unlikely to be simple as social behavioral drivers of adherence are many, including user preferences,[35] the extent to which a technology requires changes to existing household behaviors or increased effort in terms of water management,[34] taste and aesthetics,[36] perception of risk,[38] reliability of the technology,[39] and whether a user has invested in the technology.[40] Given the potential for trade-offs between treatment efficacy, cost, and adherence, particularly in technologies designed to be used by nonexperts in underserved settings, our results suggest that, once a technology has demonstrated microbial efficacy consistent with the "comprehensive protection" (★★) tier in the WHO Scheme, promoting adherence is more critical in delivering health gains than increasing microbiological performance. For most settings, achieving consistent, correct, and sustained use, focusing on human behavior, is critical to delivering on the public health promise of HWT.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.est.8b05682.

Figure S1: *Campylobacter* associated end points from Monte Carlo simulations using the Medema et al.[22] dose−response function; Figure S2: *Campylobacter* associated end points from Monte Carlo simulations using the Teunis et al.[23] dose−response function; Figure S3: Rotavirus associated end points from Monte Carlo simulations; Figure S4: *Cryptosporidium* associated enpoints from Monte Carlo simulations; Table S1: Sensitivity of *Campylobacter* end point estimates to Monte Carlo simulation input; Table S2: Sensitivity of rotavirus end point estimates to Monte Carlo simulation input; Table S3: Sensitivity of *Cryptosporidium* end point estimates to Monte Carlo simulation input (PDF)

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