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The joint effects of efficacy and compliance: A study of household water treatment effectiveness against childhood diarrhea

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ABSTRACT

The effectiveness of household water treatment (HWT) at reducing diarrheal disease is related to the efficacy of the HWT method at removing pathogens, how people comply with HWT, and the relative contributions of other pathogen exposure routes. We define compliance with HWT as the proportion of drinking water treated by a community. Although many HWT methods are efficacious at removing or inactivating pathogens, their effectiveness within actual communities is decreased by imperfect compliance. However, the quantitative relationship between compliance and effectiveness is poorly understood. To assess the effectiveness of HWT on childhood diarrhea incidence via drinking water for three pathogen types (bacterial, viral, and protozoan), we developed a quantitative microbial risk assessment (QMRA) model. We examined the relationship between $\log_{10}$ removal values (LRVs) and compliance with HWT for scenarios varying by: baseline incidence of diarrhea; etiologic fraction of diarrhea by pathogen type; pattern of compliance within a community; and size of contamination spikes in source water. Benefits from increasing LRVs strongly depend on compliance. For perfect compliance, diarrheal incidence decreases as LRVs increase. However, if compliance is incomplete, there are diminishing returns from increasing LRVs in most of the scenarios we considered. Higher LRVs are more beneficial if: contamination spikes are large; contamination levels are generally high; or some people comply perfectly. The effectiveness of HWT interventions at the community level may be limited by imperfect compliance, such that the benefits of high LRVs are not realized. Compliance with HWT should be carefully measured during HWT field studies and HWT dissemination programs. Studies of pathogen concentrations in a variety of developing-country source waters are also needed. Guidelines are needed for measuring and promoting compliance with HWT.

1. Introduction

An effective intervention can be defined as one that reduces disease (i.e., is efficacious) and one that people use (i.e., they comply). For example, a drug or vaccine must be protective and people must take the drug or receive the vaccine; contaminated water must be correctly treated and people must drink the treated water. Both efficacy and compliance

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must be evaluated when assessing the ability of an intervention to reduce illness; both are dynamic factors that can vary over time. Household water treatment (HWT) interventions are an interesting example that illustrates these two factors, where pathogen removal characterizes efficacy and behavior characterizes compliance. In this manuscript we examine the joint effects of 1) pathogen removal by a HWT device, and 2) the degree to which communities use the device. We focus on the protective effects of HWT against childhood diarrhea in developing countries, a leading cause of morbidity and mortality (Kosek et al., 2003).

Household water treatment (HWT) is a common strategy for reducing diarrhea in developing countries. HWT technologies most often used include chlorination, filtration, solar disinfection (SODIS), and boiling. Systematic reviews of field trials suggest that HWT is generally effective in preventing some diarrhea (Arnold and Colford, 2007; Clasen et al., 2009). However, lack of blinding and publication bias are important issues in the HWT literature that may exaggerate effectiveness (Hunter, 2009; Schmidt and Cairncross, 2009; Waddington et al., 2009).

Antimicrobial effectiveness of HWT is commonly measured by $\log_{10}$ reduction values (LRVs) from laboratory testing. Such tests use indicator organisms to represent the three main classes of waterborne pathogens: viruses, bacteria, and protozoan cysts. LRVs are a common metric for assessing different HWT methods (Sobsey et al., 2008; Sobsey and Brown, 2011). The United States standard for HWT "microbiological water purifiers" is LRVs of 6 for bacteria (99.9999% inactivation or removal), 4 for viruses, and 3 for protozoa (USEPA, 1987). The World Health Organization (WHO) recommends that "highly protective" devices have LRVs of 4 for bacteria, 5 for viruses, and 4 for protozoa (Sobsey and Brown, 2011). The WHO recommendations come from a quantitative microbial risk assessment (QMRA) assuming perfect compliance and an acceptable risk level of 10^{-6} disability-adjusted life-years (DALYs) for diarrheal disease from each pathogen type (Sobsey and Brown, 2011).

In contrast, compliance, the extent to which persons (or a population) use a HWT method, is often poorly defined and poorly measured. Compliance (sometimes referred to as adherence) has many dimensions. Individuals might reject a HWT method because of cost, difficulty using HWT, or taste of treated water. Well-established theory regarding adoption of new technologies indicates that 10%–20% of a community will not use the new technology, even after acceptance by most of the community (Rogers, 2003). Furthermore, preventive practices (such as HWT) have difficulty spreading because the benefit (e.g., cases of diarrhea averted) is a 'non-event'; therefore, the benefit gained is not obvious to the user (Rogers, 2003). HWT devices might simultaneously be used frequently and inconsistently. For example, someone might drink treated water at home, but untreated water while working. During a HWT field trial in rural Congo, nearly all households sometimes drank untreated water (Boisson et al., 2010).

Although the variable and incomplete nature of compliance is widely recognized, it is mostly unmeasured or incompletely measured by field trials. A review of 30 field trials of water quality interventions found that 7 did not report compliance, and 9 measured compliance by "occasional observation" only (Clasen et al., 2009). Furthermore, consumption of treated water was never directly measured (Clasen et al., 2009). Studies that report compliance find that communities rarely use HWT devices 100% of the time. For example, a meta-analysis of HWT chlorination studies indicated a median of 78% of samples having detectable free chlorine (range 36–100% over 12 studies) (Arnold and Colford, 2007).

Compliance is difficult to measure and is subject to various biases. Participants might be more likely to comply by virtue of knowing that they are part of a study (Hawthorne effect) (McCarney et al., 2007). Participants in a study might also report that they use an intervention more frequently than they actually do (Dharod et al., 2007). Compliance might increase during a trial because study personnel remind people to use HWT (deliberately or not). Field trials over longer periods show lower HWT effectiveness against diarrhea; decreasing compliance over time is one explanation (Hunter, 2009). It is particularly difficult to determine the amount of untreated water that HWT users consume outside the home.

Despite not being well measured, compliance clearly influences the ability of HWT to prevent diarrhea, because HWT can only be effective if people use it (Duflo et al., 2007). Field measurements of LRVs tend to be lower than laboratory-measured LRVs for many reasons, such as differing water quality or suboptimal maintenance of HWT devices (Sobsey et al., 2008). Nonetheless, the benefits from HWT might be eroded by slight noncompliance. For example, a risk assessment of diarrheal infection from intermittent treatment by a Ugandan water treatment plant estimated that water treatment failure for 1 day per year increased the annual probability of enterotoxigenic *Escherichia coli* (ETEC) infection via drinking water from 0.001 to 0.1 (Hunter, 2009).

The relationship between compliance and LRVs (which measure efficacy) can be illustrated with a simple mathematical example:

$$d = u(1-c) + uc10^{-L} \quad (1)$$

where d is the dose of pathogens consumed, u is pathogens per liter of untreated water, c is compliance (the proportion of drinking water treated), and L is the LRV of the HWT method. Assuming that source water contains 10,000 pathogens per liter, 5 LRVs of pathogens are inactivated, and 1% of drinking water is untreated, then 100 pathogens are ingested for each liter of water ingested. For LRVs of 4, 3, 2, and 1, the numbers of pathogens consumed are, respectively: 101, 110, 199, and 1090. The dose (and therefore the infection risk) is very similar for LRVs of 3 or higher, and the largest incremental benefit is from LRVs of 1 and 2; we therefore hypothesize that incomplete compliance results in marginal reductions in diarrheal disease as LRVs increase. If this hypothesis is true, then the current WHO recommendations for LRVs from HWT must be considered in the context of compliance. In this manuscript we test this hypothesis in more detail, using a quantitative microbial risk assessment (QMRA) model to examine the joint effects between device efficacy (measured by LRVs) and compliance (measured by how often the device is used). In doing so, we provide a more complete framework for evaluating the effectiveness of HWT interventions.

2. Material and methods

Our QMRA model simulates waterborne transmission of diarrheal infection (bacteria, viruses, and protozoa, represented by diarrheagenic *E. coli*, rotavirus, and *Giardia*, respectively) in children aged < 5 years. It is based on a similar model (Enger et al., 2012) that was used to simulate a randomized controlled trial of the LifeStraw® Family device (a HWT filter) in rural Congo (Boisson et al., 2010). Briefly, the model simulates repeated daily exposure of children to three types of diarrheal pathogens. The children do not age and are identical to one another. Susceptible children may develop infection when ingesting contaminated water. The dose of pathogens ingested is determined by the pathogen concentrations (modeled by gamma distributions whose mean values come from Figure S2 (in the Supplementary materials); the variance is from an analysis of thermotolerant coliform data from Boisson et al., 2010) and by the amount of water ingested daily. Based on this dose, the probability of infection is estimated using published dose response functions (Table 2). The durations of infections are randomly distributed according to pathogen-specific distributions (Table 2). Infected children also have pathogen-specific probabilities of developing diarrhea (morbidity ratios; Table 2). Infected children become susceptible again 7 days after their infection has resolved. Complete long-term immunity to infection is not explicitly included in the model; however, the morbidity ratios, based on observational studies of children in developing countries, account for partial protection from disease (Gilman et al., 1988; Cravioto et al., 1990; Valentiner-Branth et al., 2003; Havelaar et al., 2009). The model only considers diarrhea transmitted by drinking water, omitting other transmission routes (e.g., contaminated food or hands). The model is programmed in MATLAB 7.12 and Octave 3.2; results were analyzed with R 2.11. Further details regarding the model have been described previously (Enger et al., 2012) or are provided in the Supplementary Material to this paper. Parameter values that were fixed during all model runs are described in Table 2.

Four important concepts in this model are: compliance, baseline incidence, etiologic fractions, and short-term contamination spikes. Parameters describing these concepts were varied in order to use the model to describe different scenarios.

Table 1 – Criteria for the calibration step of the quantitative microbial risk assessment (QMRA) model.

Description	Midpoint and range of etiologic fractions for childhood diarrhea		
	Bacteria	Protozoa	Viruses
Pathogen mixture A. High bacteria, medium protozoa, low viruses	55% 47.5–62.5%	30% 22.5–37.5%	15% 7.5–22.5%
Pathogen mixture B. High bacteria, medium viruses, low protozoa	55% 47.5–62.5%	15% 7.5–22.5%	30% 22.5–37.5%
Pathogen mixture C. Bacteria slightly predominating over protozoa and viruses	40% 32.5–47.5%	30% 22.5–37.5%	30% 22.5–37.5%

The incidence ranges were: low, 0–2 episodes per child-year; medium, >2–6 episodes per child-year; and high, >6–12 episodes per child-year.

2.1. Compliance

Compliance with HWT within a community is modeled considering three groups of children: 1) children who exclusively consume treated water ("perfect compliance"); 2) children who never consume treated water ("no compliance"); and 3) children who consume fixed proportions of treated and untreated drinking water ("partial compliance"). Overall compliance (c) is calculated as follows:

$$c = (1 - (a + n))p + a \quad (2)$$

where a is the proportion of children who always use HWT, n is the proportion of children who never use HWT, and p is the proportion of water treated by partial compliers. For a given value of c, we define three types of compliance at the community level: α) c children with perfect compliance and the remainder with no compliance; β) $c/2$ children with perfect compliance, $(1 - c)/2$ children with no compliance, and the remainder partially comply, treating a fraction c of their daily water intake (see Supplementary Material, Table S1); γ) all children partially comply by treating a fraction c of their water. If $c = 1$ or 0, only compliance type α is possible.

2.2. Baseline incidence and etiologic fraction

To further generalize our results, we considered differences in the baseline incidence of diarrhea and the relative contributions of viruses, bacteria, and protozoa to diarrheal incidence (etiologic fractions). The average incidence categories are: 0–2 (low); 2–6 (medium); and 6–12 (high) episodes per child-year (Kosek et al., 2003). We used three sets of etiologic fractions based on reviews of etiologic studies of childhood diarrhea (Lanata and Mendoza, 2002; Ramani and Kang, 2009). For a summary, see Table 1; for details, see Supplementary Material, section B.

2.3. Short-term contamination spikes

Measurements from surface waters indicate that concentrations of indicator organisms are highly variable (Boehm, 2007; Levy et al., 2009). Furthermore, large spikes of contamination occasionally occur due to rainfall or other events (Hunter, 2003); however, the size and frequency of these spikes are highly variable. We assume that this variability also applies to pathogens. We simulated spikes of pathogen concentrations that occur on random days. We assumed that each spike lasts exactly one day, there are n spikes per year, and the spike height is x fold higher than the mean baseline concentration on days lacking a spike. Due to uncertainty regarding the magnitudes of these spikes, for this analysis we assume a range of spike magnitudes from $x = 1$ (no spikes), 10, 10^3, or

Table 2 – Fixed parameter values used in the quantitative microbial risk assessment (QMRA) model.

Description	Value	Reference
Shape parameter for all gamma distributions of pathogen type concentrations[a]	1.85	(Boisson et al., 2010; Enger et al., 2012)
Water ingestion	1.178 L/day	(Akpata, 2004)
Dose response function parameters		(QMRAwiki, 2012)
E. coli (enteroinvasive); beta-Poisson parameters	$\alpha = 0.155$ $N_{50} = 2.11 \times 10^6$	(DuPont et al., 1971)
Rotavirus; beta-Poisson parameters	$\alpha = 0.2531$ $N_{50} = 6.171$	(Ward et al., 1986; Haas et al., 1993)
Giardia; exponential k parameter	0.0198	(Rendtorff, 1954; Rose et al., 1991)
Duration of infection		
E. coli (gamma distribution, mean 3 days)	Shape = 1.775 Scale = 1.690	(Estrada-Garcia et al., 2009)
Giardia (gamma distribution, mean 11 days)	Shape = 3.206 Scale = 3.431	(Kent et al., 1988)
Rotavirus (uniform distribution; mean 2.5 days)	Range: 1–4 days	(Kapikian et al., 1983)
Morbidity ratios (proportion of infected who are symptomatic)		
E. coli	0.214	(Vergara et al., 1996)
Giardia	0.590	(Peréz Cordón et al., 2008)
Rotavirus	0.397	(Fischer et al., 2002)
Period of immunity for all pathogens	7 days	

a The scale parameters for the gamma distributions of pathogen types are determined by the mean concentrations of pathogen types, which are randomly sampled from a uniform distribution during calibration.

10^5. We also assume that the number of spikes per year is $n = 5$. Our goal in this analysis was to compare the impact of exposures with differing levels of aggregation over time, independent of the overall exposure magnitude. To aid comparison between spike scenarios, therefore, we define the mean number of pathogens in t daily 1-L samples of source water to be equal regardless of spike height: b_0 is the mean baseline concentration in a scenario without spikes, and b_s is the mean baseline concentration in a scenario with spikes. Solving for b_s gives the appropriate mean baseline concentration during spike scenarios:

$$b_0 t = b_s(t - n) + nxb_s \rightarrow b_s = b_0 t/(nx + t - n) \quad (3)$$

2.4. Calibration step and estimation step

The simulation was implemented in two steps: calibration and estimation. The calibration step simulates transmission of diarrheal infection by drinking water in the absence of HWT. It estimates concentrations of bacteria, viruses, and protozoa that are consistent with: 1) assumptions of low, medium, or high incidence of diarrhea; and 2) assumptions about the relative importance of these pathogen types to diarrheal etiology (Table 1). The estimation step uses these pathogen concentrations to estimate the risk of diarrhea under various HWT scenarios, defined by different LRVs and different levels of compliance.

The calibration step models waterborne diarrheal infection and disease in a simulated community prior to the introduction of an HWT intervention. The calibration step is run 12 times (3 incidence levels × 4 spike heights) and each of these yields 3 sets of pathogen concentrations (since there are 3 sets of etiologic fractions), for a total of 36 calibration scenarios. Each calibration step consists of 100,000 model runs. Each model run begins by randomly selecting a mean pathogen concentration for each of the three marker pathogens independently. These pathogen concentrations are used to determine the scale parameters of gamma distributions whose shape parameter was obtained by fitting the distribution of thermotolerant coliforms measured in source water from a rural area of the Congo (Boisson et al., 2010; Enger et al., 2012). The central 95% of that distribution spans 1.4 $\log_{10}$. Therefore, concentrations can vary 25 fold, even in the absence of spikes. See Supplementary Material (section B) for more detail regarding the calibration process.

Each calibration run follows 100 simulated children over 1 year with no HWT use. The output of each run yields a community incidence of diarrheal disease and etiologic fractions for the three pathogen types. The mean pathogen concentrations used by a calibration run are retained for use in the estimation step if: 1) the incidence of diarrhea estimated from the model run falls into the appropriate range (Fig. 1a); and 2) the proportions of diarrhea episodes attributable to bacteria, protozoa, or viruses falls into one of the three sets of etiologic fractions (Fig. 1b; see also Table 1 and Supplementary Material, Fig. S1).

The estimation step models waterborne diarrheal infection and disease in a simulated community after a HWT intervention is introduced. Each estimation scenario uses marker pathogen concentrations from one of the 36 calibration scenarios, for 5000 simulated children over 50 years. Estimation scenarios are defined by the treatment efficacy of the device and the level of compliance. Specifically, we use a combination of three factors: 1) LRV of the HWT device against all three pathogen types (see Supplementary Material, section E, Fig. S8 for LRVs corresponding to WHO and USEPA recommendations); 2) overall compliance by the community; 3) type of compliance by the community (α, β, or γ). For each of the 36 sets of pathogen concentrations from calibration, an estimation step was run once for every possible combination of three factors: 1) LRVs for bacteria, protozoa, and viruses (1, 2, 3, 4, or 5); 2) overall compliance (c = 1, 0.99, 0.95, 0.80, or 0); and 3) compliance type (α, β, or γ). Each estimation step for a given scenario had 70 to 150 model runs. If the appropriate calibration step supplied more than 150 sets of pathogen concentrations, 150 sets were randomly sampled for use in the estimation step. Incidences and incidence ratios (IRs) were determined for various combinations of compliance and device effectiveness; IRs were relative to scenarios in which no HWT was used.

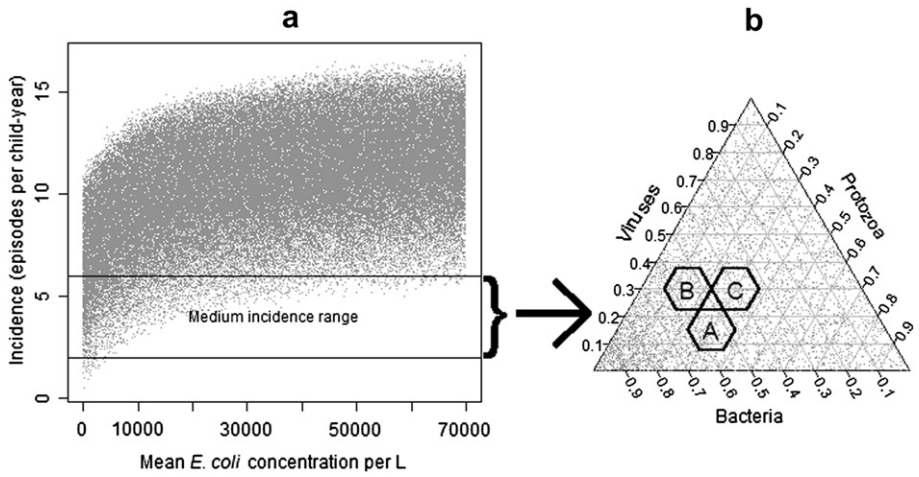

Fig. 1 – Calibration of a quantitative microbial risk assessment (QMRA) model by: (a) selecting runs whose incidence of diarrhea is within a given range; and then (b) selecting runs with appropriate etiologic fractions (hexagonal regions A, B, or C). Although all three pathogen types (bacteria, viruses, and protozoa) were considered simultaneously, only the scatterplot for bacteria is shown. See Supplementary Material, Fig. S1, for more detail.

2.5. *Replication of the WHO model*

For comparison, we replicated the QMRA model that was used to develop the WHO HWT recommendations (Sobsey and Brown, 2011) in R 2.11. To facilitate comparison with our model, we: 1) modified the replicated model to output incidence instead of DALYs; 2) we eliminated the assumption of 94% immunity to rotavirus, since our model only considers young children; and 3) we used rotavirus-based parameters as a proxy for other diarrhea-causing viral pathogens. To obtain total diarrhea incidence from the WHO model, we summed the bacterial, protozoan, and viral diarrhea incidences from its output.

3. Results

3.1. *Calibration step*

Each calibration step (100,000 runs) yielded 70 to 1164 runs consistent with each of the 36 calibration scenarios. Fig. 1 displays typical calibration output (see Supplementary Material, Fig. S1, for more detail); if a run is consistent with the incidence criterion (Fig. 1a), it is tested for consistency with pathogen mixtures A, B, or C (Fig. 1b; Table 1). The resulting pathogen concentrations (ranging from approximately 10^3 to 10^5 per liter for bacteria; 10^{-1} to 1 per liter for protozoa; 10^{-3} to 10^{-1} per liter for viruses) in untreated drinking water are shown in the Supplementary Material (Fig. S2).

3.2. *Estimation step*

Each estimation step consisted of 70–150 model runs, representing distributions of incidences and incidence ratios (IRs) of diarrheal disease given a particular scenario. Figs. 2–6 (and Supplementary Material, Figs. S5–S8) show medians of the incidence distributions for various scenarios.

Our model and the WHO model (Sobsey and Brown, 2011) produced consistent estimates of diarrhea risk reduction, assuming 100% compliance; the WHO model predicted diarrhea risks that were intermediate between the risks predicted by our model, assuming low or high incidence. (Fig. 2). This occurred despite differing pathogens and parameter values in each model, as well as substantial differences in model structure (our model considers community-level risk; the WHO model considers individual risk). The WHO model

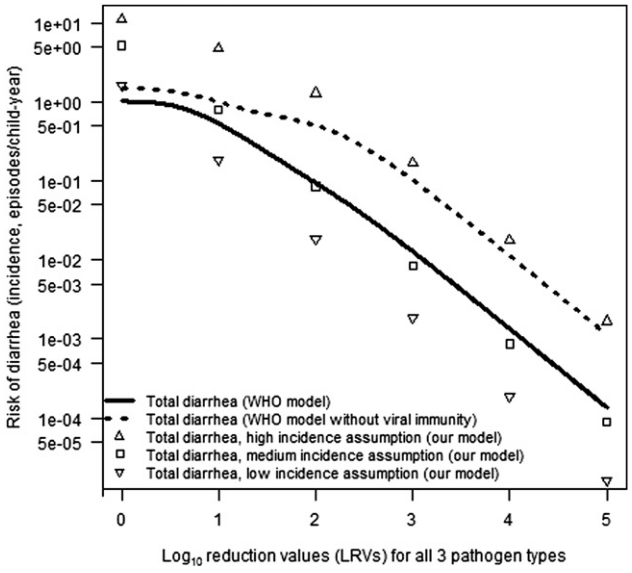

Fig. 2 – Comparison of quantitative microbial risk assessment (QMRA) models of diarrheal risk, assuming perfect compliance with household water treatment. The WHO model (represented in a simplified fashion in this figure) was recently used to determine household water treatment (HWT) performance targets (Sobsey and Brown, 2011). For more detail, see Supplementary Material, Fig. S4.

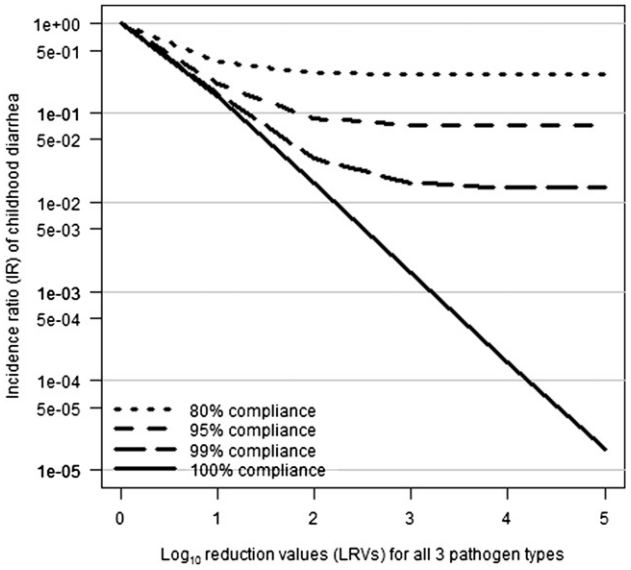

Fig. 3 – Effect of compliance with household water treatment (HWT) on the incidence ratio of childhood diarrhea, by LRV from HWT, assuming medium incidence, compliance type β, no spikes, and pathogen mixture A. See Supplementary Material for more scenarios.

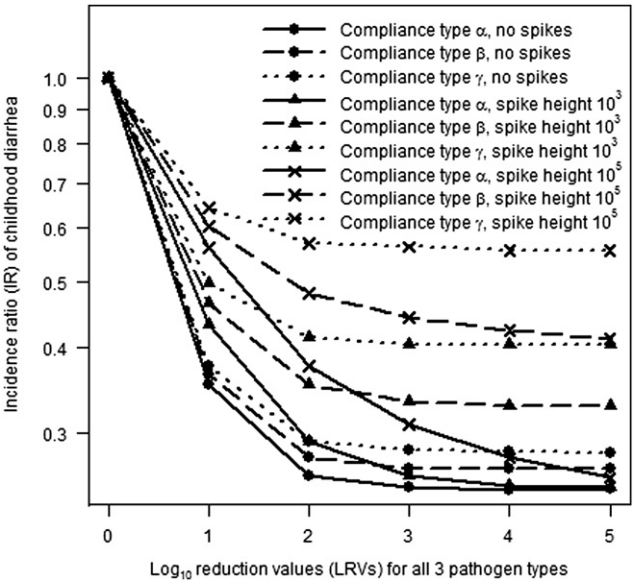

Fig. 5 – Effect of compliance level, compliance type, and spike height on the incidence ratio of childhood diarrhea, by LRV from household water treatment, assuming medium incidence, compliance of 0.8, and pathogen mixture A. See Supplementary Material for more scenarios.

(modified to assume no viral immunity) best resembled our model assuming high incidence. However, the WHO model does not account for repeated episodes of diarrhea in one year, hence its incidence cannot be greater than one episode/child-year for each pathogen type. The WHO model predicts that bacteria cause fewer cases of diarrhea than viruses or protozoa (Supplementary Material, Fig. S4); this may be inaccurate among children in many developing country settings (Lanata and Mendoza, 2002).

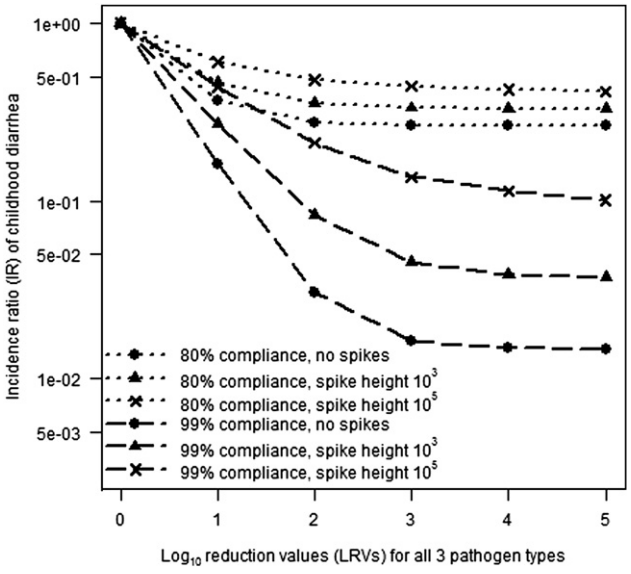

Fig. 4 – Effect of compliance and spike height on the incidence ratio of childhood diarrhea, by LRV from household water treatment, assuming medium incidence, compliance type β, and pathogen mixture A. See Supplementary Material for more scenarios.

If compliance slightly decreases to 99% and there are no pathogen spikes, our model predicts little or no additional benefit from LRVs above 3 in many scenarios (e.g., Fig. 3). If compliance is 80%, there is little benefit from increasing LRVs beyond 2. This behavior is similar regardless of compliance type (α, β, γ), pathogen mixture (A, B, C), or incidence level (low, medium, high) (see Supplementary Material, Figs. S5a, S6a, S7a).

If pathogen spikes are included, the incidence ratio increases as spike height increases, for all LRVs (Fig. 4). This effect is not due to an overall increase in incidence, because the model is calibrated to maintain the same incidence (baseline pathogen concentrations are also reduced to compensate for spike height; Equation (3)). Rather, the increase in IR is due to the nonlinearity of the dose–response function at high doses; during a large spike, reducing dose x-fold might only reduce risk by a factor less than x (see Supplementary Material, section I and Fig. S13). Note that diminishing returns from LRV increases are still seen when spikes are introduced. Spikes 10 times above baseline give similar results as no spikes (Supplementary Material, Figs. S5–S7).

Compliance type changes the relationship between LRVs, IR, and spikes (Fig. 5). If there are no spikes, the results for compliance types α, β, and γ are similar. However, as spike height increases, α has the lowest IRs and γ has the highest IRs. Fig. 5 also shows additional benefit from LRVs 4 and 5 for the highest spike scenario (10^5-fold baseline). The benefits are greatest for compliance type α, in which 80% of the children consume treated water 100% of the time, and 20% of children consume only untreated water. The benefits are smaller but

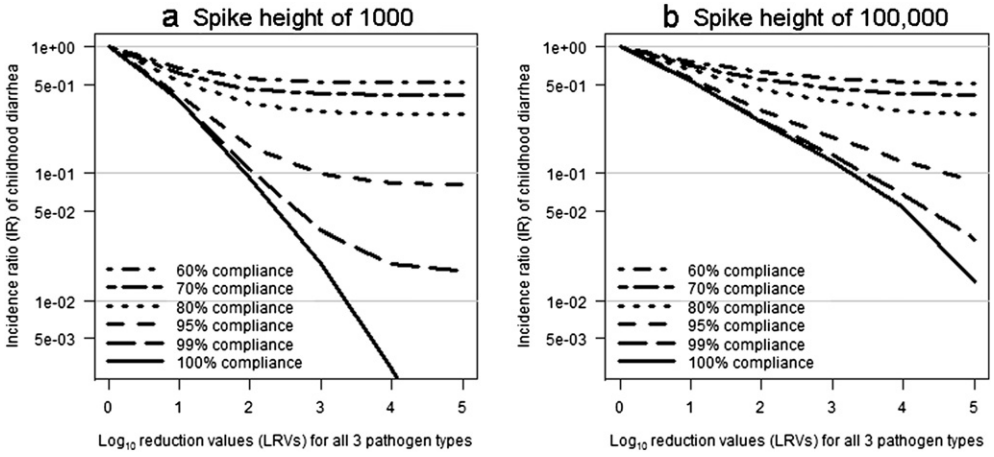

Fig. 6 – Effect of compliance level on the incidence ratio of childhood diarrhea if large spikes sometimes occur, by LRV from household water treatment, assuming medium incidence, compliance type α, and pathogen mixture C. See Supplementary Material for more scenarios.

still evident for β, in which 40% of children consume treated water 100% of the time, 50% of children consume treated water 80% of the time, and 10% of children consume only untreated water (see also Supplementary Material, Table S1). In contrast, under γ every child constantly consumes some untreated water.

Benefit from higher LRVs is more pronounced under conditions of high incidence, large spikes, compliance type α, and high compliance (Fig. 6). The benefits decrease as compliance decreases.

Pathogen mixture C tends to give lower IRs than A or B if incidence is high or spike height is high (see Supplementary Material, Figs. S5–S8). As incidence is increased from low to high, the effect of pathogen mixture (and compliance type) tends to increase.

The effects of differing scenarios on the benefit from increasing LRVs are more fully described in the Supplementary Material (Sections E, F, And G), including significance testing and classification trees.

4. Discussion

Under perfect compliance conditions, the risk of diarrhea decreases linearly with pathogen removal by HWT, a direct consequence of the fact that the dose response relationships used in this analysis are linear in the range of pathogen doses that individuals usually receive. These results are consistent with those reported in the WHO guidelines on health-based targets for HWT devices (Sobsey and Brown, 2011). Although the model used in our analysis uses a similar QMRA approach as the WHO guidelines, there are some important distinctions. For example, the three indicator pathogens that we used were pathogenic *E. coli*, rotavirus, and *Giardia*, whereas the WHO guidelines used *Campylobacter*, rotavirus, and *Cryptosporidium*. We chose pathogenic *E. coli*, rotavirus, and *Giardia* because they appear to be the most common types of bacteria, viruses, and protozoa (respectively) that cause childhood diarrhea (Lanata and Mendoza, 2002). We used time-varying pathogen concentrations that were calibrated to reflect realistic diarrhea incidence levels and etiologic fractions of pathogens based on published work. The WHO guidelines assumed constant concentrations of the pathogens in sewage, and that drinking water is contaminated with 0.01% sewage. Most importantly, we relaxed the assumption of perfect compliance, examining the joint effects of compliance and LRVs. Assuming imperfect compliance, our results differed greatly from the WHO model, particularly for higher LRVs.

For many of our scenarios with imperfect compliance, we observed diminishing health improvements from increasing LRVs; similar conclusions from a differently structured QMRA model were published recently (Brown and Clasen, 2012). Specifically, when the variation in pathogen concentration is limited to 25 fold (i.e., no spikes) and compliance is 99%, little additional diarrhea is prevented for LRVs above 3 (Fig. 3). Assuming 80% compliance, LRVs above 2 prevent little additional diarrhea. If spikes occurred and some of the population complied perfectly (compliance types α or β), LRVs above 3 sometimes prevented additional episodes of diarrhea.

These results indicate the importance of including compliance in risk estimations and in policy development, and also emphasize the importance of understanding the different dimensions of compliance. For example, some people may never comply, others may comply when they are home but not when they are away from home, and yet others may comply only during periods of perceived high risk. Our simulations suggest that, given a particular compliance level within a community, HWT scenarios that include more perfectly complying individuals prevent more diarrhea. Although the implications of these different dimensions of compliance is not well understood, it is clearly difficult to obtain long-term, high compliance with household antidiarrheal interventions in developing countries (Makutsa et al., 2001; Arnold et al., 2009; Luby et al., 2009).

Difficulty in achieving high compliance with intervention strategies also extends to sanitation and hygiene interventions. Handwashing compliance is incomplete in both industrialized (Bischoff et al., 2000) and developing countries,

especially with soap (Curtis and Cairncross, 2003). Despite the obvious importance of sanitation in removing pathogens from the environment and breaking the fecal–oral cycle of transmission, approximately half the population of southern Asia and sub-Saharan Africa openly defecates or has an unimproved latrine (World Health Organization and UNICEF, 2010). Even if latrines are available, they might not be used (Banda et al., 2007; Arnold et al., 2010; Montgomery et al., 2010).

Although many of the scenarios we examined had diminishing health improvements beyond 3 LRVs (and sometimes beyond 2 LRVs), we also identified scenarios where LRVs above 3 are beneficial (Figs. 5 and 6, and Supplementary Material, Figs. S5, S6, S7, sections E and F). Understanding which scenarios are most realistic requires a better characterization of the variability in contamination levels, the pathogen mixture in the contaminated water, and the extent to which these pathogens are also transmitted through other environmental pathways. We further discuss these issues below.

Little information is available on the variability of pathogen concentrations in source water. Even point measurements of pathogen concentrations are scarce (Enger et al., 2012), and it is unclear what reasonable spike concentrations would be. However, contamination spikes are plausible due to various mechanisms, including stormwater runoff, defecation directly into source waters, or washing of contaminated items like diapers. Although we have some guidance regarding temporal variation of contamination levels from indicator data, in, for example, rural Congo (Boisson et al., 2010) and rural Ecuador (Levy et al., 2009), in our simulations we examined sensitivity to different spike magnitudes (see Figs. 4–6). More detailed measurements of pathogen concentrations in source waters over time are needed to better characterize the variation of pathogen concentrations over time.

The contribution of different pathogens to diarrheal disease is also uncertain and depends upon ecology, sociology, and infrastructure. Published etiologic fractions include diarrhea from all transmission routes, not only drinking water; pathogen profiles for different routes, for example food versus water, will differ. In addition, the true distribution of etiologies may differ from the distribution of reported etiologies. For example, certain bacteria may be more frequently identified because they are easier to culture. For this analysis, we chose three broad mixtures of etiologic fractions, based on the most comprehensive information available. Future research, particularly from the Global Enterics Multicenter Study (University of Maryland, 2012), will further clarify diarrheal etiology.

Finally, our model only accounts for infection via drinking water. Additional routes of transmission (e.g., contaminated hands, objects, or food) operate in underdeveloped communities. Considering these routes would decrease the apparent effectiveness of a HWT device, since these routes would affect users and nonusers of HWT alike. Our model also does not account for infection transmission between individuals. Effective HWT would reduce the number of infected people, thus reducing pathogen shedding and indirectly preventing infection in people not using HWT. This would increase the apparent effectiveness of HWT, assuming imperfect compliance (Halloran et al., 1991). Although examining effectiveness in the context of multiple transmission pathways is important, we do not believe it would affect our general conclusions about the joint effects of compliance and LRVs on the effectiveness of HWT interventions.

5. Conclusions

Recent WHO guidelines (Sobsey and Brown, 2011) provide an important framework for evaluating the health benefits of HWT devices resulting from their ability to remove pathogens. Our simulation results indicate that these health benefits are limited by compliance. Thus, the classification system in the WHO guidelines incompletely informs HWT users and promoters regarding effectiveness of devices. More research is necessary to understand the full complexities of compliance, to explicitly measure compliance in intervention trials, and to incorporate compliance in development policy. We provide a modeling framework that examines the impact of compliance on the effectiveness of interventions as an initial step toward more complete consideration of compliance by researchers, policymakers, and development workers.

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Appendix A. Supplementary material

Supplementary material associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.watres.2012.11.034.

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