SUPPORTING INFORMATION: Adherence to point-of-use water treatment over short-term implementation: parallel crossover trials of flocculation-disinfection sachets in Pakistan and Zambia

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Product use

As flocculant-disinfectant sachets intended for batch treatment of water, the two products we tested are similar, but with a few key differences in terms of the specific steps and amount of time for use. Here is an overview:

Instructions to users: PoW and Pureit

Product aspects	**PoW**	**Pureit**
Volume of water treated / sachet	10L	10L
Stirring time	5 min	2 min
Contact time	25 min	20 min
Order of waiting	Stir, filter and then wait	Stir, wait, and then filter

PoW and Pureit use steps

PuR: Add product to 10 l water ➔ stir 5 min ➔ let stand 5 min ➔ filter through cloth into container ➔ let stand 20 min ➔ consume

Pureit: Add product to 10 l water ➔ stir 2 min ➔ let stand 20 min ➔ filter through cloth into container ➔ consume

Sample size

We conducted a literature review to inform the detectable difference to assess between the two products as well as the overall level of adherence to expect. Among the most relevant studies was a two-month longitudinal POU usage trial by Albert and colleagues in Kenya[1]. Adherence (defined as the fraction of treated water with *E.coli* concentrations <1 colony forming unit/100mL) was highest in the first week of the study (at 60%), and dropped to 40% within the first month (a 33% reduction), where it remained relatively stable through the second month. Albert and colleagues (2010) assessed three products (a filter, liquid chlorine, and a flocculant-disinfectant), finding flocculant-disinfectant usage to be the lowest[1].

The first step to our calculation was based on the methods outlined by Diggle et al (2002), and Leon (2004) to analyse binary outcomes with repeated observations[2, 3]. Equation 3.1 was used to calculate the required number of participants for a two arm trial over four repeat observations. In light of our study using two flocculant-disinfectants, and in order to remain conservative, an initial adherence level of 50% was set, powered to detect a 20% difference between products, and an intraclass correlation coefficient (ICC) of 0.1. This calculation yielded 126 households required per arm (252 households in total), observed over four visits per household.

<u>Equation S1: Sample size equation based on Diggle et al. (2002) and Leon (2004) to analyse binary outcomes with repeated observations:</u>

$$m = \frac{\left(z_{\frac{\alpha}{2}}\sqrt{2\bar{p}\bar{q}} + z_{\beta}\sqrt{p_A q_A + p_B q_B}\right)^2 (1 + (n-1)\rho)}{nd^2}$$

Where:

$Z_{\alpha/2}$= Z value at α= 0.05
Z_{β}= Z value at (1-β)= 0.8
p_A= response rate for group A
p_B= response rate for group B
q_A= 1-p_A
q_B=1-p_B
p(bar)= (p_A+p_B)2
q (bar)= 1-p(bar)
n= number of observations
ρ= intraclass correlation coefficient
d= smallest meaningful difference to be detected

The second step was to bring the crossover design into consideration. Several studies note that crossover designs can substantially increase the statistical efficiency of effects estimates, consequently reducing the required sample size. Though no conclusive estimates of power reduction were identified, it was estimated to be as high as 50%[4, 5]. For this study, a more conservative reduction estimate of 25% was made to the initial assessment of 126 households per arm, leading to 100 households per exposure arm, and 200 households in each country study. As the primary comparison in a crossover design is within the same unit of measurement (i.e., usage in households exposed to PoW and Pureit), the two arms referred to in this calculation actually refer to the different exposures (products) given to the same households at different times (i.e., one month each). Our sample size calculation is thus primarily for 100 households to be followed for four repeat measures, and subsequently exposed to the alternative product, as the second "arm". However, in order to account for order effects, 100 households were exposed to Pureit before PoW (AB), and a further 100 to PoW before Pureit (BA). It is an advantage of this design that different groups of households could also be compared to each other, including: Pureit vs PoW users in crossover period 1 or 2, respectively, and the total sachet usage of all households to Pureit and PoW (both periods). Finally, in order to account for a 10% potential loss to follow-up and issues with data integrity, at least 220 households were recruited in each site.

Used sachets were not employed in the sample size calculation as the evidence from studies focusing on flocculant-disinfectant usage varied widely and did not have sufficiently reported details. A number of studies have assessed flocculant-disinfectants[6-9], and though sachets were counted in all of them, only one reported on longitudinal sachet adherence over time[6]. Chiller and colleagues[2] found weekly household usage to rise steadily from 5 to 10 sachets per week over 13 weeks. On the other hand, Luby and colleagues[9] found average usage to be as high as 21 sachets per week in a 9 month study in Karachi[10]. Reller and colleagues (2003) conducted a one year study in Guatemala, finding an average of 6 sachets used per household per week[11]. Crump and colleagues 20-week study found over 85% of users to have detectable chlorine during weekly scheduled visits, but only 44% during unannounced visits[8].

Further product details

Pureit contains the same coagulant (ferric sulfate) and chlorine-based disinfectant (calcium hypochlorite) as PoW. Its most significant departure from PoW is the presence of a chlorine-quenching agent, the details of which are proprietary. Pureit is intended to release a high initial dose of chlorine to induce maximum microbial removal, followed by the delayed action of a chlorine-quenching agent to reduce the free chlorine concentration with the intention of improving taste acceptability. Pureit's developers approximated initial free chorine concentration to be between 2 - 4 mg/L, dropping to 0.5 mg/L between 2 - 5 hours post-treatment due to the chlorine quenching agent. While specifying that concentrations were subject to different source water conditions, water was intended to be safe to consume for 48 hours if safely stored (R. Venkataraghavan, Hindustan Unilever, personal communication). Each 2.5 g sachet is capable of treating 10 L of water.

PoW was developed by Procter & Gamble (P&G) in collaboration with the US Centers for Disease Control and Prevention (CDC). It uses calcium hypochlorite for disinfection, ferric sulfate for coagulation, and also contains a buffer made from clay and a polymer to help control the reaction of the chlorine disinfectant in water. The product comes in a 4 gram sachet that treats 10L of water.

Product distribution and implementation

After obtaining their consent, participating households were given tokens and a time and location to receive product training and project supplies. Distribution was conducted in batches, and was assisted by community mobilizers. The central training point in Zambia was a local church that was active in the target zone in community work and education. In Pakistan, trainings took place in every neighborhood, as the community was fully covered, and clearly divided by neighborhood, which were divided along lines of caste. Implementation was designed to broadly replicate the protocol for short-term point-of-use water interventions used by Oxfam and their partner NGOs (*N.Bazezew, L.Katsi, S.Baloch Oxfam GB, personal communication*). Training did not go beyond group explanations of product usage, and did not include strong messaging to increase potential behavior change. Households were given thorough explanations on product use, specifically differentiating the two products and all safety information. Households had the freedom to use the products as much or as little as they wished.

A list of all households was compiled after recruitment, and used to randomly allocate households to the first product in such a way as to have two equal arms. All households were also given complementary items to use the product with, as per Oxfam protocol, and in order to ensure comparability of results across households and sites. Supply distribution and data collection took place at the household level, defined as a family unit that shares daily drinking water and live together on a regular basis. This was relatively simple in Zambia where households were physically separate and participants were randomly selected over a wider area. The community selected in Pakistan was fully covered.

Supplies

Participating households were given:

- 1 x 10L bucket
- 1 x 1m^2 cotton cloth
- 1 x 10-12L safe storage container, with a tap for drinking-water and a lid to protect it
- 1 x stirring spoon (wooden or metallic)
- 1 x brochure with pictorial explanations of the given product
- Sufficient sachets of either PoW or Pureit to last one month.

Each household was given one month's set of the allocated product, at the beginning of each four-week usage phase. Households in Zambia were given 93 sachets per phase (based on 3 sachets/household/day for 31 days). After observing usage in Zambia, households in Pakistan were given 62 sachets per phase (2 sachets/household/day for 31 days). Households were asked to retain all used and unused sachets in containers provided for this purpose, and informed that they would be provided more if they ran out.

Table S1: Somer's D p-values for univariate and bivariate hypothesis tests for three outcomes (per capita consumption, observed weekly sachet usage, and presence of detectable chlorine) across products, visits, and crossover period

Country study: Zambia						
Independent variables:	**Per capita consumption (% adherence to Sphere)**		**Observed weekly used sachets**		**Total chlorine presence/absence**	
		Interpretation		**Interpretation**		**Interpretation**
PRODUCT (univariate level)	0.91	**Not different across products**	0.67	**Not different across products**	0.006	**Different across products**
Stratified by: Crossover period 1	0.34	No further difference within periods	0.45	No further difference within periods	0.009	Only different in crossover period 1
Stratified by: Crossover period 2	0.39		0.36		0.32	
CROSSOVER PERIOD (univariate level)	<0.001	**Different across crossover periods**	<0.001	**Different across crossover periods**	0.049	**Different across crossover periods**
Stratified by: Product 1 (Pureit)	0.043	Also different within products	0.001	Also different within products	0.56	Borderline difference product 2
Stratified by: Product 1 (Purifier of water)	<0.001		<0.001		0.056	
VISIT 1 - 8 (univariate level)	<0.001	**Different over all visits**	<0.001	**Different over all visits**	0.13	**No difference over visits**
Stratified by: Crossover period 1	0.029	Only different in period 1	0.14	Only different in crossover period 1	0.29	Only different in crossover period 2
Stratified by: Crossover period 2	0.36		<0.001		0.046	

Country study: Pakistan						
Independent variables:	**Per capita consumption (% adherence to Sphere)**		**Observed weekly used sachets**		**Total chlorine presence/absence**	
		Interpretation		**Interpretation**		**Interpretation**
PRODUCT (univariate level)	0.36	**Not different across products**	0.14	**Not different across products**	0.99	**Not different across products**
Stratified by: Crossover period 1	0.87	No further difference within periods	0.76	No further difference within periods	0.98	No further difference within periods
Stratified by: Crossover period 2	0.47		0.22		0.85	
CROSSOVER PERIOD (univariate level)	<0.001	**Different across crossover periods**	<0.001	**Different across crossover periods**	0.038	**Different across crossover periods**
Stratified by: Product 1 (Pureit)	<0.001	Also different within products	<0.001	Also different within products	0.12	No difference after stratifying by product

Stratified by: Product 1 (Purifier of water)	<0.001		<0.001		0.23	
VISIT 1 - 8 (univariate level)	<0.001	**Different over all visits**	<0.001	**Different over all visits**	0.53	**No difference over all visits**
Stratified by: Crossover period 1	0.26	Only different in period 2	0.99	No difference after stratifying by period	0.013	Only different in crossover period 1
Stratified by: Crossover period 2	0.001		0.33		0.85	

Table S2: Negative binomial regression (Zambia) and zero-inflated negative binomial regression (Pakistan) models testing differences in observed sachet counts per household over crossover period, product, untreated water consumption status and household size.

Country study: Zambia (n=204)					Country study: Pakistan (n=233)					
COVARIATE	**Predictor categories (% distribution)**	**Outcome: Rate of average usage per week**			**COVARIATE**	**Predictor categories (% distribution)**	**Outcome: Rate of average weekly usage per week (non-zero values) and odds of 0 sachets used per week (for 0 values)**			
		EFFECT SIZE (IRR*)	**95% CI**	**P-VALUE**			**EFFECT SIZE***		**95% CI**	**SIGNIFICANCE (p-value**)**
Crossover period	1 (50%)	1			Crossover period	baseline: 1 (50%)	IRR	0.85	0.8-0.91	<0.0001
	2 (50%)	0.7	0.64-0.77	<0.001		2 (50%)	OR	8.6	4.5-16	
Product	Pureit (50%)	1			Product	baseline: Pureit (51%)	IRR	1.04	0.98-1.1	0.37
	Purifier of Water (50%)	1.02	0.93-1.1	0.71		Purifier of Water (49%)	OR	0.98	0.67-1.4	
Untreated water consumption	no (45%)	1			Untreated water consumption	baseline: no (69%)	IRR	0.87	0.8-0.94	<0.0001
	yes (55%)	0.93	0.84-1.04	0.21		yes (31%)	OR	1.7	1.2-2.4	
Household size		1.02	1-1.04	0.05	Household size		IRR	1.02	1-1.04	0.038
							OR	0.98	0.9-1.07	

** Every outcome for a given independent variable in the zero-inflated negative binomial models is associated with two components: IRRs for all positive integers (i.e sachet counts ≥1), and odds ratios (ORs) comparing the odds of 0 sachets to ≥1 sachets (i.e. representing the odds of no sachets being used, reported as "non-usage" in this manuscript).*

*** Wald's p-values including both components of the zero-inflated model (IRR and ORR)*

Table S3: Summary of observed and self-reported consumption (daily frequency averaged across each visit) and households with reportedly treated water at all visits

	ZAMBIA		PAKISTAN	
Observed	**N (HH visits)**	**%**	**N (HH visits)**	**%**
0	105	7	222	13
<1	850	54	547	31
1+	615	39	981	56
Total	1570	100	1750	100
Stated				
0	5	0.5	0	0.5
<1	395	24.5	113	6
1+	1196	75	1676	93.5
Total	1596	100	1789	100

	N (total households)	**%**	**N (total households)**	**%**
Percentage households reporting water during all of their visits	185	4%	232	19%

Table S4: Median adherence measures per weekly visit (observed weekly sachets, observed daily sachet usage rate, adherence to Sphere guidelines, and comparison of observed and self-reported daily usage rates)

ZAMBIA	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range
Weekly usage per visit	6	0-47	6	0-52	5	0-64	6	0-51	3	0-23	4	0-26	5	0-48	4	0-28
Daily per capita per visit	0.75	0-5.9	0.85	0-8.5	0.86	0-10.7	1	0-8.5	0.6	0-4.4	0.6	0-6.5	0.63	0-5.8	0.57	0-4
Adherence percentage to SPHERE per visit	52	0-500%	57	0-1133%	57	0-1066%	70	0-800%	40	0-420%	46	0-400%	44	0-581%	44	0-414%
Percentage of household visits with water with detectable chlorine per visit	29	-	34	-	29	-	23	-	44	-	25	-	23	-	18	-
stated 1 or more	74	-	78	-	77	-	70	-	66	-	70	-	78	-	86	-
observed 1 or more	36	-	44	-	46	-	53	-	29	-	37	-	35	-	34	-
liters per capita	1.3	0-13	1.4	0-28	1.4	0-27	1.7	0-20	1	0-10	1.1	0-10	1.1	0-15	1.1	0-10

	Visit 1		Visit 2		Visit 3		Visit 4		Visit 5		Visit 6		Visit 7		Visit 8	
PAKISTAN	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median	Range
Weekly used sachets/household/visit	10	0-50	8	0-40	8.5	0-37	9	0-34	6	0-50	5	0-46	4	0-38	6	0-44
Daily used sachets/household/visit	1.4	0-7	1.2	0-5	1.2	0-5.2	1.3	0-4.3	0.65	0-5.2	0.75	0-6.3	0.71	0-5.4	0.85	0-6.7
% adherence to SPHERE consumption guidelines	105%	0-857%	100%	0-960%	95%	0-529%	100%	0-850%	44%	0-485%	57%	0-700%	57%	0-1085%	70%	0-1333%

% households with detectable chlorine	78%	-	65%	-	71%	-	64%	-	43%	-	48%	-	47%	-	56%	-
% Stated adherence ≥1 sachet/capita/day	97%	-	97%	-	95%	-	98%	-	97%	-	87%	-	89%	-	89%	-
% Observed adherence ≥1 sachet/capita/day	76%	-	71%	-	65%	-	67%	-	39%	-	40%	-	42%	-	47%	-
Median treated water consumed (L/person/day)	2.60	0-21	2.50	0-24	2.30	0-13	2.50	0-21	1.10	0-12	1.40	0-18	1.40	0-27	1.70	0-33

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