

Effect of in-line drinking water chlorination at the point of collection on child diarrhoea in urban Bangladesh: a double-blind, cluster-randomised controlled trial



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Summary

Background Previous blinded trials of household water treatment interventions in low-income settings have failed to detect a reduction in child diarrhoea. Technological advances have enabled the development of automated in-line chlorine dosers that can disinfect drinking water without electricity, while also allowing users to continue their typical water collection practices. We aimed to evaluate the effect of installing novel passive chlorination devices at shared water points on child diarrhoea prevalence in low-income, densely populated communities in urban Bangladesh.

Methods In this double-blind cluster-randomised controlled trial, 100 shared water points (clusters) in two low-income urban communities in Bangladesh were randomly assigned (1:1) to have their drinking water automatically chlorinated at the point of collection by a solid tablet chlorine doser (intervention group) or to be treated by a visually identical doser that supplied vitamin C (active control group). The trial followed an open cohort design; all children younger than 5 years residing in households accessing enrolled water points were measured every 2–3 months during a 14-month follow-up period (children could migrate into or out of the cluster). The primary outcome was caregiver-reported child diarrhoea (≥ 3 loose or watery stools in a 24-h period [WHO criteria]) with a 1-week recall, including all available childhood observations in the analyses. This trial is registered with ClinicalTrials.gov, number NCT02606981, and is completed.

Findings Between July 5, 2015, and Nov 11, 2015, 100 water points with 920 eligible households were enrolled into the study and randomly assigned to the treatment (50 water points; 517 children at baseline; 2073 child observations included in the primary analysis) or control groups (50; 519; 2154). Children in the treatment group had less WHO-defined diarrhoea than did children in the control group (control 216 [10.0%] of 2154; treatment 156 [7.5%] of 2073; prevalence ratio 0.77, 95% CI 0.65–0.91). Drinking water at the point of collection at treatment taps had detectable free chlorine residual 83% (mean 0.37 ppm) of the time compared with 0% at control taps (0.00 ppm).

Interpretation Passive chlorination at the point of collection could be an effective and scalable strategy in low-income urban settings for reducing child diarrhoea and for achieving global progress towards Sustainable Development Goal 6.1 to attain universal access to safe and affordable drinking water. Targeting a low chlorine residual (< 0.5 ppm) in treated water can increase taste acceptability of chlorinated drinking water while still reducing the risk of diarrhoea.

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Introduction

With the number of people living in urban areas expected to reach more than 6 billion by 2050, control of infectious disease in rapidly growing cities in low-income countries is increasingly difficult.¹ Historically, the first major declines in urban mortality rates were attributed to improvements in city water supply, waste management, and personal hygiene. In the USA, the introduction of urban water disinfection systems explains half of the reduction in child mortality during the 20th century.² Few utilities in cities in low-income countries are able to maintain fully pressurised systems that consistently deliver water 24 h per day. Instead, many provide an intermittent supply of water, constrained by factors such as water scarcity and limited

electricity for pumping. Water in these intermittently supplied systems is at high risk of contamination during distribution; water that is safe at the source is often contaminated by the time it arrives at the point of collection.³ Whereas most urban residents in low-income countries have access to piped water sources, many are still at risk of waterborne illness. Roughly 1 billion people accessing improved water sources receive water that does not meet international standards for safety.⁴ Considering the increasing trends in urban population growth and the already unsustainable demands on groundwater supplies in Asian mega-cities,⁵ evidence suggests that intermittent supply, and its associated risks, will continue to be the norm for many low-income urban residents.

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Research in context

Evidence before this study

Most previous water treatment trials in low-income countries have evaluated point-of-use water treatment technologies used at the household level, potentially because of a previous absence of reliable technologies appropriate to treat water at the community level in low-resource settings. A meta-analysis published in 2018 estimated that point-of-use chlorination reduces diarrhoea prevalence by 24%; however, the effect was diminished and non-significant when adjusted for bias from non-blinding. The few published blinded trials assessing the effect of water treatment interventions in low-income countries have failed to detect an effect on diarrhoea. A Cochrane review published at the start of our trial in 2015 by Clasen and others concluded that further studies were needed to evaluate the effect of chlorination at the point of collection (ie, at community level) on diarrhoea.

Added value of this study

Our results contribute new evidence to the literature in several ways. First, whereas previous blinded trials have failed to detect health effects, our trial estimated a significant reduction in child diarrhoea in a low-income setting. In addition, whereas many previous water intervention trials have focused on

household-level water treatment, our findings show that a low-cost automatic point-of-collection (community-level) water treatment intervention can achieve high uptake and reduce diarrhoea in a densely populated setting. Finally, our results suggest that targeting a low chlorine residual dose (0.3–0.5 ppm) in an effort to increase taste acceptability of chlorinated water can still improve water quality and reduce the risk of diarrhoea.

Implications of all the available evidence

Together with previous evidence, our findings suggest that chlorination is an effective strategy to treat water and reduce the risk of child diarrhoea. Our blinded trial provides unbiased evidence that chlorination at the point of collection can improve household stored drinking water quality and reduce child diarrhoea in an urban low-income setting. Chlorination is one of the lowest cost and most widely available methods to make drinking water safe, but low taste and odour acceptability is an important barrier to adoption. Passive (automated) dosing resulting in a chlorine residual concentration below the taste detection threshold has the potential to be transformative by ensuring high adoption rates and contributing to global progress towards Sustainable Development Goal 6.1 for universal access to safe and affordable drinking water.

To address the problem of low-quality water supplies, in-home disinfection technologies, such as chlorine products and filters, have been developed and widely promoted to empower households to treat their own water at the point of use. Although point of use technologies appear to reduce waterborne illness when used correctly and on a consistent basis,⁶ estimates of the health effects of household water treatment might be biased owing to the fact that diarrhoea is self-reported.⁷ A meta-analysis found that adjusting estimates for absence of blinding in trials might significantly attenuate the effects of point of use interventions.⁸ Furthermore, modelling studies have indicated that a very high amount of adherence is required to realise the benefits of point of use treatment.⁹ However, it has proven difficult to motivate low-income households to adopt such technologies and maintain use over time. One study reported that less than 30% of households in Dhaka, Bangladesh, used point of use products when they were provided free of cost.¹⁰ To date, point of use promotion programmes have been unable to provide microbiologically safe water consistently to a high proportion of those households whose children are at greatest risk of death from waterborne disease.

Although point of use methods have several shortcomings, there has been little effort to explore intermediate, community-level options in urban settings (eg, automated treatment at shared water points), in part because appropriate technologies have been unavailable. A Cochrane review of interventions designed to improve

water quality and reduce diarrhoea concluded that further studies on the effects of chlorination at the point of delivery or collection were needed.¹¹ Solutions to improve water in low-income settings have traditionally been framed as a choice between household-level and municipal-level water treatment. Community-based chlorination interventions, which treat water automatically at the point of collection rather than at the source or point of use, provide an alternative with a lower behavioural and economic cost than existing interventions. To establish proof of concept for the community-based water treatment approach, our research team implemented two pilot studies evaluating novel low-cost water treatment products that automatically chlorinate water in Dhaka, Bangladesh. These studies indicated that passive chlorination effectively disinfected water supplies in low-income densely populated communities, required minimal behaviour change for users, and suggested high potential for these types of technologies to increase sustained and consistent access to clean water.^{12,13} The primary aim of this study was to evaluate the effect of installing novel passive chlorination devices at shared water points on child diarrhoea prevalence in low-income, densely populated communities in urban Bangladesh.

Methods

Study design and participants

We did a double-blinded cluster-randomised controlled trial in urban Bangladesh to evaluate the effect of an automated chlorination device on water quality and child

health. The device used in this study, the Aquatabs Flo (Medentech, Inc, Wexford, Ireland), automatically doses chlorine into water as it flows through the device into a water storage tank. The study was done in two study sites: a low-income community within Dhaka city and a low-income community, known as Tongi, on the outskirts of the city. The study was designed to include baseline data collection, followed by randomisation and intervention delivery, and up to 14 months of follow-up data collection (with a measurement frequency of 2–3 months). We planned for a minimum of five and up to seven data collection rounds, contingent on budget availability (as stated in the trial registry). The study protocol was approved by the International Centre for Diarrhoeal Diseases Research, Bangladesh (icddr,b) scientific and ethical review committees (protocol number 14022) and the human subjects institutional review board at Stanford University (protocol number 30456). Field staff obtained informed written consent from the owner (ie, compound landlord) of each water point enrolled and all study participants.

Water points in the study area were eligible for inclusion if they contained a water storage tank compatible with the dosing device (approximately two-thirds of water points were excluded because they were not connected to a water storage tank). Clusters included all compounds (ie, clusters of households that share water, sanitation, and kitchen facilities) with one or more children younger than 5 years of age who used the enrolled water point as their primary drinking-water source. Owing to high urban migration rates, we designed the trial to be an open cohort trial. In each follow-up round, the field team identified and enrolled new children in compounds who used the enrolled water point as their primary water source. These included children born into already-enrolled households and new households that had recently migrated into the study area. Children enrolled at baseline were measured at each follow-up until they become older than 5 years of age or until they migrated out of the study area.

Randomisation and masking

Randomisation was pair-matched by water point and stratified by study site. One investigator (AJP) sorted water points in descending order in each site by the number of children younger than 5 years of age residing and using the enrolled water point as their primary source of drinking water. Water points were then paired in descending order and, within pairs, assigned on a 1:1 allocation ratio to treatment or control status by means of a random number generator.

We masked study participants and outcome assessors to treatment status. After enrolment and baseline data collection, each water point in the treatment clusters received a chlorination device that was maintained and refilled regularly with chlorine by study staff throughout the study. The Aquatabs Flo disinfects drinking water without the need for electricity by using gravity flow to

funnel water past solid tablets of trichloroisocyanurate housed in a plastic cartridge (appendix p 3). We selected the Aquatabs Flo because it performed the best out of all devices we had piloted in the study area. The device doses at the inlet of water storage tanks; our piloting activities had identified that water storage tanks were common in low-income communities in Dhaka (one in four water points were connected to a storage tank in a survey of 45 low-income communities systematically selected from a census). In Dhaka, the dosers were installed in overhead storage tanks connected to taps or in underground storage tanks outfitted with manual handpumps to extract the water. Tongi had submersible pumps; each pump was connected to a tank system that provided water intermittently to households. In Tongi, the dosers were installed at the inlet of overhead water storage tanks that supplied shared taps.

Each control water point received a device that dosed vitamin C into the water supply. Vitamin C was selected in consultation with local ethics experts owing to its potential to provide a benefit to control households, while also being unlikely to affect diarrhoea rates or water quality in low doses. Chlorine and vitamin dosers were identical in appearance and were both manufactured by Medentech. All participants and study staff who collected outcome data not related to water quality were masked to treatment status. A separate field team maintained the dosing devices, refilled them, and collected water samples for chlorine residual and microbial analysis. Control group vitamin C dosing devices were paired with a treatment chlorine doser nearby for maintenance and refilling at the same frequency.

The maintenance field team adjusted the chlorine dosing devices to target a low chlorine residual concentration throughout the study (0.2–0.5 ppm). We chose this range of free chlorine residual to optimise both a safe and effective chlorine residual and to mask study participants to which study group they had been assigned. Before the study, we did a free chlorine residual taste detection experiment among Dhaka residents and found that the median detection threshold for free chlorine was 0.7 ppm, while the median acceptability threshold was 1.2 ppm.¹⁴ In addition, we initially set the chlorine dosers to deliver between 0.1 ppm and 0.2 ppm total chlorine residual in the first 1–2 months of operation to allow for users to become accustomed to the taste.

A field team separate from the outcome assessment and device maintenance teams held promotion sessions with all available members of households accessing enrolled water points. The messaging focused on how water can be contaminated even if it looks clear, the financial burden of waterborne illnesses, and chlorination as an effective method for water treatment. The promotional team was masked to household intervention status and promotional materials and messaging were identical in both treatment and control households. Promoters also held individual promotion sessions with

See Online for appendix

For the study protocol see <https://osf.io/9dh7k/>

enrolled households with children under 5 years of age before installation of the dosers, approximately 1 week after installation, and approximately 2 months after installation. All households were encouraged to continue their typical water treatment and storage practices.

Procedures

Follow-up data collection occurred approximately every 2 months for a total of 14 months to measure health outcomes and water quality. Field staff did up to three revisits per household to complete a survey during each data collection round. Seven data collection rounds in Dhaka and six rounds in Tongi were feasible before chlorine and vitamin C refills were depleted. Field staff did surveys with the primary caregivers of children younger than 5 years of age residing in all enrolled households to measure outcomes. Additional information on demographics, education, employment, dwellings, and assets were also collected from all enrolled households. All survey data were collected on electronic tablets by SurveyCTO (Dobility, Cambridge, MA, USA) and securely uploaded to an online server. During household visits occurring between 6 and 14 months post-device installation, blinding effectiveness was measured by asking respondents if they knew whether their primary water point had a chlorine or vitamin C doser. Even if they did not know, they were asked to make a guess. Pairs of trained anthropometrists measured the weight of all children younger than 5 years of age at baseline and in

each follow-up round. Child height-for-age was only measured at baseline and at the conclusion of the study owing to budget constraints; therefore, the study was not adequately powered to detect changes in child height. See appendix for further details on anthropometric measurements.

To monitor the effectiveness of the chlorine dosing devices, we measured free and total chlorine residual at the point of collection and in household stored water in both study groups. We also measured concentrations of the faecal indicator bacteria, *Escherichia coli* and total coliform, in a subset of tap and household stored water samples (appendix).

Outcomes

Our primary outcome was caregiver-reported diarrhoea, defined as three or more loose or watery stools in a 24-h period, among children younger than 5 years. This definition is recommended by WHO and is a standard definition used in health effect evaluations.¹⁵ We used a recall period of 7 days to maximise power (capture diarrhoea events from a full week), while minimising recall bias.¹⁶ Prespecified additional outcomes in the trial included caregiver-defined diarrhoea, child weight-for-age Z score, child height-for-age Z score, acute respiratory illness (cough or difficulty breathing), illness-related health-care expenditures, microbial water quality, and chlorine residual in household stored drinking water. Before asking about specific gastrointestinal symptoms, the field researcher recorded caregiver-defined diarrhoea by asking the caregiver if the child had diarrhoea by using the local Bengali term (patla paykana). We also used a stool consistency chart (based on the Bristol stool chart) as an alternative measure of the occurrence of loose or watery stool (appendix).¹⁷ Health-care expenditures included total taka (83 taka=US\$1) spent on illness-related treatment in the past 2 months including money spent on provider fees, medicine, diagnostic tests, and transportation to seek treatment. The 2-month recall period for illness-related treatment was selected considering that the field team planned to visit each household every 2 months (the respondent could mark the 2-month period by referencing the last household visit by the study team). Finally, we report the following negative control health outcomes: caregiver reported rash and bruising within the past 7 days.¹⁸

Statistical analyses

We powered the study to detect a 25% reduction in the WHO case definition of diarrhoea; our sample size calculations assumed, on the basis of previous work, that diarrhoea prevalence would be 10% among children aged younger than 5 years in the study area. We did the power calculations using a cluster-level means approach (comparing the mean diarrhoea prevalence by cluster-time-point between groups) because we did not have a good estimate for the

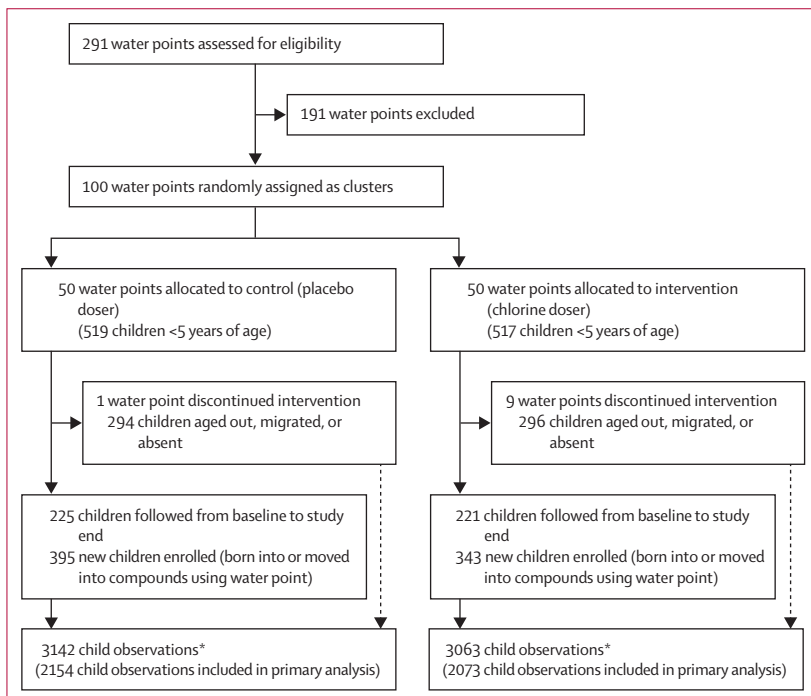


Figure 1: Trial profile

Clusters included all compounds with children younger than 5 years that reported collecting drinking water from enrolled water points. *Each child observation represents one diarrhoea measurement with a 1-week recall period.

| | Control (vitamin) | | Treatment with chlorine | | Dhaka | | Tongi | |
|----------------------------------|-------------------|-----------------|-------------------------|---------------|----------------|-----------------|----------------|---------------|
| | Data available | Mean (SD) | Data available | Mean (SD) | Data available | Mean (SD) | Data available | Mean (SD) |
| Household characteristics | | | | | | | | |
| People in household | 469 | 4.6 (1.8) | 451 | 4.7 (1.7) | 427 | 4.1 (1.4) | 493 | 5.2 (1.9) |
| Single household compound | 469 | 0.18 (0.39) | 451 | 0.21 (0.41) | 427 | 0.00 | 493 | 0.36 (0.48) |
| Own home | 463 | 0.39 (0.49) | 442 | 0.45 (0.50) | 417 | 0.01 (0.08) | 488 | 0.77 (0.42) |
| Household has >1 room | 469 | 0.31 (0.46) | 451 | 0.35 (0.48) | 427 | 0.11 (0.31) | 493 | 0.52 (0.50) |
| Years lived in compound | 469 | 7.4 (10.3) | 451 | 7.1 (9.7) | 427 | 1.7 (2.2) | 493 | 12.0 (11.6) |
| No formal schooling | 469 | 0.10 (0.30) | 451 | 0.14 (0.34) | 427 | 0.07 (0.26) | 493 | 0.16 (0.36) |
| Completed primary school* | 469 | 0.49 (0.50) | 451 | 0.56 (0.50) | 427 | 0.47 (0.50) | 493 | 0.57 (0.49) |
| Income (BDT) | 469 | 17 080 (15 763) | 451 | 16 620 (9397) | 427 | 17 648 (15 933) | 493 | 16 168 (9818) |
| Owns land | 466 | 0.28 (0.45) | 445 | 0.20 (0.40) | 425 | 0.33 (0.47) | 486 | 0.17 (0.37) |
| Owns TV | 469 | 0.82 (0.39) | 451 | 0.83 (0.37) | 427 | 0.81 (0.39) | 493 | 0.84 (0.37) |
| Owns mobile phone | 469 | 0.96 (0.21) | 451 | 0.94 (0.25) | 427 | 0.95 (0.22) | 493 | 0.94 (0.24) |
| Owns wardrobe | 469 | 0.57 (0.50) | 451 | 0.56 (0.50) | 427 | 0.49 (0.50) | 493 | 0.63 (0.48) |
| Owns fridge | 469 | 0.35 (0.48) | 451 | 0.37 (0.48) | 427 | 0.37 (0.48) | 493 | 0.36 (0.48) |
| Water tap in compound or home | 469 | 0.84 (0.36) | 451 | 0.72 (0.45) | 427 | 1.00 (0.05) | 493 | 0.60 (0.49) |
| Perceives water to be unsafe | 466 | 0.52 (0.50) | 448 | 0.52 (0.50) | 426 | 0.79 (0.41) | 488 | 0.29 (0.45) |
| Regularly treats drinking water | 469 | 0.34 (0.47) | 450 | 0.30 (0.46) | 426 | 0.66 (0.47) | 493 | 0.02 (0.15) |
| Tap water has <i>E coli</i> | 53 | 0.70 (0.46) | 48 | 0.85 (0.36) | 75 | 0.87 (0.34) | 26 | 0.50 (0.51) |
| Stored water has <i>E coli</i> | 55 | 0.71 (0.46) | 50 | 0.64 (0.48) | 42 | 0.64 (0.48) | 63 | 0.70 (0.46) |
| Child health | | | | | | | | |
| Age of child (months) | 517 | 29.3 (16.7) | 519 | 29.9 (17.0) | 480 | 29.9 (17.2) | 556 | 29.3 (16.6) |
| Exclusively breastfeeding | 517 | 0.074 (0.261) | 519 | 0.096 (0.295) | 480 | 0.073 (0.260) | 556 | 0.095 (0.294) |
| Caregiver-defined diarrhoea† | 517 | 0.039 (0.193) | 519 | 0.067 (0.251) | 480 | 0.075 (0.264) | 556 | 0.034 (0.182) |
| Loose or watery stool* | 517 | 0.048 (0.215) | 519 | 0.056 (0.230) | 480 | 0.063 (0.242) | 556 | 0.043 (0.203) |
| Blood in stool* | 517 | 0.008 (0.088) | 519 | 0.010 (0.098) | 480 | 0.008 (0.091) | 556 | 0.009 (0.094) |
| Height-for-age Z score | 494 | -1.42 (1.14) | 498 | -1.48 (1.14) | 463 | -1.41 (1.12) | 529 | -1.48 (1.15) |
| Weight-for-age Z score | 513 | -1.29 (1.13) | 515 | -1.44 (1.03) | 478 | -1.39 (1.04) | 550 | -1.35 (1.12) |

E coli=*Escherichia coli*. BDT=Bangladesh taka. *Some respondents started primary school but did not finish. †1-week recall.

Table 1: Baseline household characteristics and child health by treatment assignment and study site

intraclass correlation coefficient for diarrhoea by water point. This approach treats repeated measures at one point in time the same as repeated measures over time. Using this approach, we calculated that we would have 96% power with the study design (50 clusters per arm, with an average of ten children per cluster). We designed the study to be robust to uncertainty in implementing a novel technology in a low-resource setting, budget constraints, and potential variation in intervention effects across seasons.

Our statistical analysis plan is available on Open Science Framework. The primary analysis was independently replicated by two co-authors (AJP, YC). Our primary analysis was intention-to-treat using data from all data collection rounds combined. Poisson regression was used to model binary outcomes and linear regression for continuous outcomes. We also did the following subgroup analyses: each study site (Dhaka and Tongi), children present at baseline, and respondents who thought that there was a vitamin doser installed at their water point (those who assumed they were in the control group). We

also did a prespecified treatment on the treated analysis by classifying all children in the treatment group accessing taps with a chlorine residual into a treated group with children in the control group as the reference. All models included fixed effects for randomisation pair and month of data collection, and we report robust standard errors to account for clustering at the water point level. Blinding was assessed by means of the James' and Bang's indices.^{19,20} Analysis was done in STATA version 14.1. We considered p values below 0.05 significant. We did not correct p values for multiple outcomes because the trial had a single primary outcome and a single intervention arm.^{21,22} This trial is registered with ClinicalTrials.gov, number NCT02606981, and is completed.

Role of the funding source

The funder approved the study design, but had no role in data collection, data analysis, data interpretation, or writing of this report. The corresponding author had full access to all of the data and had final responsibility for the decision to submit for publication.

For the statistical analysis plan see <https://osf.io/9dh7k/>

| | Control | | Treatment with chlorine | | Prevalence ratio (95% CI) | p value |
|--|----------------|---------------|-------------------------|---------------|------------------------------------|---------|
| | Data available | Data | Data available | Data | | |
| Diarrhoea (WHO defined; primary outcome)* | 2154 | 216 (10.0%) | 2073 | 156 (7.5%) | 0.77 (0.65 to 0.91) | 0.0020 |
| Diarrhoea (caregiver-defined)* | 3142 | 244 (7.8%) | 3063 | 184 (6.0%) | 0.77 (0.66 to 0.90) | 0.0009 |
| Diarrhoea (chart defined)* | 2086 | 197 (9.4%) | 2011 | 148 (7.4%) | 0.80 (0.69 to 0.93) | 0.0044 |
| Loose or watery stool* | 3142 | 321 (10.2%) | 3063 | 247 (8.1%) | 0.80 (0.69 to 0.93) | 0.0045 |
| ≥3 defecations in 24 h period* | 2154 | 387 (18.0%) | 2073 | 313 (15.1%) | 0.86 (0.78 to 0.95) | 0.0030 |
| Blood in stool* | 3142 | 29 (0.9%) | 3063 | 29 (0.9%) | 1.03 (0.66 to 1.60) | 0.89 |
| Acute respiratory illness* | 3142 | 416 (13.2%) | 3063 | 395 (12.9%) | 0.99 (0.87 to 1.14) | 0.93 |
| Runny nose† | 3115 | 1209 (38.8%) | 3035 | 1161 (38.3%) | 1.02 (0.95 to 1.10) | 0.56 |
| Rash* | 3142 | 296 (9.4%) | 3063 | 254 (8.3%) | 0.89 (0.69 to 1.14) | 0.36 |
| Bruise* | 3142 | 365 (11.6%) | 3063 | 363 (11.9%) | 1.06 (0.82 to 1.37) | 0.67 |
| Intravenous hydration during illness‡ | 3140 | 36 (1.1%) | 3062 | 25 (0.8%) | 0.78 (0.57 to 1.05) | 0.10 |
| Sought treatment for illness‡ | 3142 | 2202 (70.1%) | 3063 | 2014 (65.8%) | 0.96 (0.93 to 0.99) | 0.0093 |
| Sought treatment for gastrointestinal illness‡ | 3142 | 382 (12.2%) | 3063 | 260 (8.5%) | 0.70 (0.61 to 0.80) | <0.001 |
| Visited hospital for gastrointestinal illness‡ | 2679 | 108 (4.0%) | 2644 | 97 (3.7%) | 0.99 (0.80 to 1.21) | 0.90 |
| Used antibiotics‡ | 2086 | 921 (44.2%) | 2011 | 797 (39.6%) | 0.93 (0.88 to 0.98) | 0.0038 |
| Weight-for-age Z score | 3084 | -1.21 (1.01) | 3014 | -1.25 (1.02) | Difference -0.03 (-0.10 to 0.05) | 0.51 |
| Height-for-age Z score | 414 | -1.36 (1.05) | 385 | -1.33 (1.08) | Difference 0.07 (-0.07 to 0.22) | 0.30 |
| BDT spent on treatment‡ | 3142 | 373.0 (993.0) | 3063 | 333.0 (858.0) | Difference -0.08§ (-0.15 to -0.02) | 0.016 |

Data are n (%) or mean (SD), unless otherwise stated. Prevalence ratios estimated by Poisson regression for binary outcomes and mean differences estimated by linear regression for continuous outcomes. All models include fixed effects for randomisation pair and month of data collection, as well as robust standard errors at the cluster (water point) level. BDT=Bangladesh taka. *1-week recall. †Observed at time of interview. ‡2-month recall. §log10-transformed difference.

Table 2: Effect of the intervention on child diarrhoea and related illness outcomes over all follow-up survey rounds

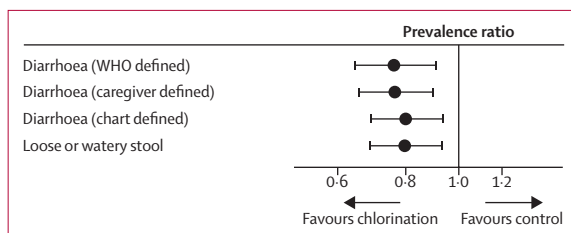


Figure 2: Effect of the intervention on child diarrhoea indicators (1-week recall period)
Including WHO defined diarrhoea (≥3 loose or watery stools in a 24-h period), caregiver defined diarrhoea, diarrhoea defined by an image of liquid stool on a stool consistency chart (chart defined), and any loose or watery stool. Prevalence ratio estimated by Poisson regression with robust standard errors at the cluster level and fixed effects for randomisation block; error bars show 95% CIs.

Results

Enrolment and baseline data collection occurred from July 5, 2015, to Nov 11, 2015. We enrolled 920 eligible households with a total of 1036 children younger than 5 years at baseline (figure 1). The treatment and control groups were well balanced across a range of socioeconomic and child health variables (table 1). Mothers in the treatment group were slightly more likely than those in the control group to have completed primary schooling. The mean weight-for-age Z score among children under 5 years of age in the treatment group was slightly lower than the mean Z score in the

control group. Diarrhoea was slightly higher in the treatment group at baseline (table 1). Although the two study sites did not appear to differ substantially in income levels, households in Tongi were less likely to rent their home, to live in a multifamily compound, to report treating their drinking water, to consider their water source unsafe, and to use a private tap compared with households in Dhaka. Tap microbial water quality was also poorer in Dhaka than in Tongi (table 1).

We collected a total of 3142 child diarrhoea measurements in the control group and 3063 diarrhoea measurements in the treatment group. We had fewer observations for WHO-defined diarrhoea (2154 in the control group and 2073 in the treatment group, intraclass correlation coefficient over all measurements: 0.025) owing to missing data in the first data collection round, as well as fewer observations for chart-defined diarrhoea (2086 in the control group; 2011 in the treatment group) because this indicator was added in data collection round two. Approximately 20% of all baseline children were out of the eligible age range of the study population (aged >5 years). Attrition of baseline children was very similar between the control (294 [57%] of 519 lost to follow-up) and the treatment group (296 [57%] of 517; figure 1).

Children in the treatment group had less WHO-defined diarrhoea than did children in the control group (prevalence ratio [PR] 0.77, 95% CI 0.65–0.91). Similar

| | Control | | Treatment with chlorine | | Difference (95% CI) | p value |
|-------------------------------------|----------------|-------------|-------------------------|--------------|------------------------|---------|
| | Data available | Mean (SD) | Data available | Mean (SD) | | |
| Tap water quality | | | | | | |
| Detectable total Cl (proportion) | 2337 | 0.00 (0.04) | 2009 | 0.83 (0.38) | 0.81 (0.73 to 0.89) | <0.0001 |
| Detectable free Cl (proportion) | 2335 | 0.00 (0.04) | 2003 | 0.80 (0.40) | 0.78 (0.71 to 0.86) | <0.0001 |
| Mean total Cl (ppm) | 2337 | 0.00 (0.01) | 2335 | 0.37 (0.32) | 0.35 (0.21 to 0.40) | <0.0001 |
| Mean free Cl (ppm) | 2335 | 0.00 (0.01) | 2003 | 0.33 (0.28) | 0.31 (0.28 to 0.35) | <0.0001 |
| <i>E coli</i> present (proportion) | 163 | 0.64 (0.48) | 163 | 0.15 (0.36) | -0.47 (-0.56 to -0.39) | <0.0001 |
| Total coliform present (proportion) | 163 | 0.93 (0.25) | 163 | 0.61 (0.49) | -0.33 (-0.40 to -0.26) | <0.0001 |
| <i>E coli</i> log (cfu/100 mL) | 163 | 0.74 (1.01) | 163 | -0.12 (0.55) | -0.84 (-1.02 to -0.66) | <0.0001 |
| Total coliform log (cfu/100 mL) | 163 | 1.63 (0.83) | 163 | 0.71 (1.04) | -0.91 (-1.08 to -0.75) | <0.0001 |
| Stored water quality | | | | | | |
| Detectable total Cl (proportion) | 3199 | 0.00 (0.05) | 3082 | 0.45 (0.50) | 0.45 (0.39 to 0.51) | <0.0001 |
| Detectable free Cl (proportion) | 3198 | 0.00 (0.05) | 3077 | 0.39 (0.49) | 0.39 (0.33 to 0.44) | <0.0001 |
| Mean total Cl (ppm) | 3199 | 0.00 (0.02) | 3082 | 0.17 (0.26) | 0.17 (0.21 to 0.40) | <0.0001 |
| Mean free Cl (ppm) | 3198 | 0.00 (0.01) | 3077 | 0.14 (0.22) | 0.14 (0.28 to 0.35) | <0.0001 |
| <i>E coli</i> present (proportion) | 377 | 0.63 (0.48) | 369 | 0.36 (0.48) | -0.28 (-0.36 to -0.21) | <0.0001 |
| Total coliform present (proportion) | 377 | 0.98 (0.15) | 369 | 0.78 (0.41) | -0.20 (-0.24 to -0.15) | <0.0001 |
| <i>E coli</i> log (cfu/100 mL) | 377 | 0.62 (0.92) | 369 | 0.19 (0.80) | -0.44 (-0.56 to -0.32) | <0.0001 |
| Total coliform log (cfu/100 mL) | 377 | 2.01 (0.56) | 369 | 1.27 (1.03) | -0.76 (-0.92 to -0.61) | <0.0001 |
| Water characteristics | | | | | | |
| Reports good taste (proportion) | 2885 | 0.97 (0.16) | 2732 | 0.72 (0.45) | PR 0.73 (0.69 to 0.77) | <0.0001 |
| Treats drinking water (proportion) | 2885 | 0.25 (0.43) | 2732 | 0.20 (0.40) | PR 0.70 (0.59 to 0.84) | <0.0001 |
| Boils drinking water (proportion) | 2885 | 0.21 (0.41) | 2732 | 0.17 (0.38) | PR 0.72 (0.59 to 0.88) | 0.0017 |
| Filters drinking water (proportion) | 2884 | 0.04 (0.18) | 2728 | 0.02 (0.15) | PR 0.59 (0.37 to 0.94) | 0.027 |

Water treatment practices and taste perceptions also shown by treatment status. Differences and 95% CI estimated by linear regression and prevalence ratios with Poisson regression; all models include cluster robust standard errors and fixed effects for randomisation pair and survey round. n=number of water samples (tap and stored water quality) or number of respondents (water characteristics). *E coli*=*Escherichia coli*. cfu=colony forming units. PR=prevalence ratio.

Table 3: Water quality at the point-of-collection (shared taps) and in household stored drinking water, by treatment status, over all follow-up survey rounds

reductions were estimated for caregiver-defined diarrhoea (0.78, 95% CI 0.66–0.90), and chart-defined diarrhoea (0.80, 95% CI 0.69–0.93; table 2, figure 2). Caregivers in the treatment group were significantly less likely to report seeking illness-related treatment for their child, particularly gastrointestinal-related illnesses (table 2). Reported illness-related expenditures in the past 2 months per child were significantly lower in the treatment group than in the control group; the mean difference per child between groups was 40 taka (approximately US\$0.50; table 2). Caregivers in the treatment group were also less likely to report that their child had consumed antibiotics in the past 2 months (table 2). Respiratory illness and negative control outcomes were very similar between groups, and there were no significant differences between groups in weight-for-age, height-for-age Z scores, or blood in stool (table 2).

Chlorine and vitamin dosers were installed from Sept 14, 2015, to Dec 31, 2015. Study staff maintained the dosers until the conclusion of the study on Dec 22, 2016. The maintenance field team had to uninstall dosers from nine of the 50 chlorine doser sites, and one of the 50 vitamin doser sites before the study conclusion owing

to requests from water point owners or community leaders (figure 1). Uninstallation dates were distributed throughout the follow-up period and included the following dates: Oct 21, 2015; April 20, 2016; June 8, 2016; June 16, 2016; July 13, 2016; Aug 14, 2016; Aug 21, 2016; Sept 1, 2016; Oct 27, 2016; Dec 6, 2016 (appendix p 3). In most instances, community leaders or water point owners complained of the smell and taste of chlorinated water as the reason for requesting uninstallation. All data collection activities continued after uninstallation events (including water quality analysis and child health measurement) in accordance with our intention-to-treat analysis plan.

We detected total chlorine residual at the point of collection (shared taps) 83% of the time in the treatment group compared with 0% in the control group ($p<0.001$; table 3). The mean amount of total chlorine residual at taps in the treatment group was 0.37 ppm (SD 0.32). We detected *E coli* contamination in the treatment group in 15% of tap samples compared with 64% of control tapwater samples ($p<0.0001$). Concentrations of *E coli* in tap samples were an average of 0.84 log-colony forming units per 100 mL lower in the treatment group compared

with the control group ($p < 0.0001$). Field staff succeeded in keeping chlorine dosing low during the first 1–2 months of installation (appendix p 4).

We also detected significant improvements in stored household drinking water in the treatment group compared with the control group (table 3). We detected total chlorine residual in 45% of household stored water samples from the treatment group, compared with 0% in control households ($p < 0.0001$). *E coli* contamination was detected in 36% of household stored drinking water samples in the treatment group, compared with 63% in the control group ($p < 0.0001$). A substantial proportion of households in both treatment (17%) and control groups (21%) reported that they had boiled their stored drinking water at the time of sampling (boiling evaporates chlorine residual from water; table 3). Across all survey rounds, less than 4% of households reported using an additional water source.

When asked if they knew what the device installed at their water point was dosing, 255 (14.0%) of 1808 of respondents in the treatment group and 287 (15.0%) of 1917 of respondent surveys in the control group responded affirmatively (combining data across survey rounds 3–7). Regardless of the answer to this question, respondents were then asked to guess what the device was dosing into their water. 2811 (75.5%) of 3725 respondents thought the device was dosing vitamins. Slightly more respondents in the treatment group thought the device was dosing chlorine (540 [29.9%] of 1808) compared with the control group (374 [19.5%] of 1917). The James' Method blinding index was 0.90 (95% CI 0.89–0.90); values above 0.5 are considered successful blinding.²⁰ The Bang's blinding index value for the treatment group was 0.03 (95% CI 0.01–0.04) and 0.10 for the control group (95% CI 0.08–0.11); the Bang index ranges from –1 to 1, in which 1 indicates complete lack of blinding, 0 perfect blinding, and –1 indicates opposite guessing.¹⁹ A subgroup analysis, including only respondents who reported that they thought the device was dosing vitamins, estimated a prevalence ratio of 0.66 (95% CI 0.51–0.86) in the WHO-defined case definition of diarrhoea in the treatment group compared with the control group.

Compared with the effect size for the full study population, the intervention had a larger effect on diarrhoea prevalence among children living in the Dhaka study site (PR 0.64, 95% CI 0.54–0.77, $n=1838$). By contrast, the intervention did not appear to have a significant effect on diarrhoea among children in Tongi (PR 0.93, 95% CI 0.73–1.18, $n=2389$). Analysing follow-up data from only those children enrolled at baseline, the PR for WHO-defined diarrhoea was 0.82 (95% CI 0.66–1.02, $n=2371$) and caregiver-defined diarrhoea was 0.80 (95% CI 0.67–0.95, $n=3785$); we note that this subgroup consists of older children than included in the primary analysis (appendix p 5). Children accessing taps with a detectable chlorine residual (treatment on the treated analysis) were also less likely to have WHO-defined diarrhoea (PR 0.63,

95% CI 0.55–0.74) and less likely to have caregiver-defined diarrhoea (0.70, 0.58–0.86) compared with children accessing taps without chlorination.

Discussion

Our findings indicate that a passive point of collection chlorination intervention in urban Bangladesh significantly reduced child diarrhoea. The intervention appeared to have a larger effect on diarrhoea among children in the study site located in Dhaka, and connected to the municipal water supply network, compared with the Tongi study site. Although both study sites had intermittently supplied water, the water points in Dhaka received water that had a much longer residence time travelling through unpressurised pipes. Notably, water quality in Dhaka was poorer at baseline than in Tongi; 87% of taps sampled in Dhaka were contaminated with *E coli*, compared with 50% of taps in Tongi. Another potential explanation for the variation in effect across study sites is differential diarrhoeal pathogen profiles; chlorination is not effective against protozoa such as cryptosporidium.²³ Randomised, controlled trials have excellent internal validity but poor external validity. The differentiation in effect size between study sites suggests that the intervention might have the largest health benefits in settings where users are accessing water points connected to large piped water networks supplying water intermittently. Field trials of inline chlorination in additional settings would further clarify where this intervention should be implemented to maximise health benefits.

Previous blinded trials have failed to detect an effect of household water treatment interventions on child diarrhoea in rural and urban India,²⁴ in rural Democratic Republic of Congo (DRC),²⁵ in rural Brazil,²⁶ and in peri-urban Ghana.²⁷ Notably, the India trial had low uptake of the intervention, the Ghana trial measured very low prevalence of diarrhoea in the control group (<3%), and a placebo filter in the DRC trial actually improved water quality. However, these null results raise concerns about the role of reporting bias in self-reported diarrhoea results from unblinded water treatment interventions. Blinding in our trial was largely effective; a subgroup analysis of only respondents who thought they were in the control group estimated a similar effect of the intervention on diarrhoea (34% relative reduction). The potential for social desirability to bias effect estimates upwards is a known issue with interpreting the large literature base evaluating the effect of water treatment on self-reported diarrhoea rates.⁸ Our findings from a blinded trial are similar to estimates from unblinded trials that household water treatment can reduce diarrhoea by 13–42% in low-income settings.⁶ It is possible that effect estimates are similar owing to the combination of higher uptake with lower reporting bias in our trial compared with previous trials.

Observed intervention effects on other gastrointestinal-illness-related indicators lend credibility to the estimated reduction in diarrhoea. For example, households in the intervention group spent less on illness-related treatment costs, were less likely to seek treatment for child gastrointestinal illness, and reported lower consumption of antibiotics in children younger than 5 years. Although lower consumption of antibiotics is consistent with less gastrointestinal illness among children in the treatment group, it is also a valuable outcome in itself given the rise of antibiotic resistant bacterial infections in settings with poor sanitation infrastructure and unregulated antibiotic usage.²⁸ In contrast to the effects we measured on indicators of acute illness, we did not detect an intervention effect on child weight-for-age Z scores. This finding is consistent with randomised, controlled trials of point of use water chlorination in rural Bangladesh and Kenya that reported no improvement in child weight or linear growth.^{29,30} Although child weight-for-age has been hypothesised to be a useful objective indicator of child diarrhoea,³¹ the strength of correlation with diarrhoea episodes can be highly variable.

Our study has several limitations. We had to stop data collection earlier than desired in one of the study sites (Tongi) because of a shortage of chlorine refills (delayed shipment); however, the trial had been designed to allow for flexibility in data collection rounds subject to budget constraints and the follow-up data collection loss was minimal (approximately 7%). An important limitation of our study is that our primary outcome was self-reported. However, a subgroup analysis of participants who believed that they were in the control group gave similar estimates to the primary analysis. In addition, we were unable to estimate 7-day prevalence of WHO-defined diarrhoea at baseline and during early survey rounds owing to the use of a different recall period. However, we were able to measure alternative indicators of diarrhoea during these survey rounds (ie, caregiver-defined diarrhoea), and modelling the effect of the intervention on these other indicators gave similar estimates. Finally, we do not know the extent to which study participants drank water from oppositely randomised water points or other unchlorinated water sources; however, the prevalence of respondents reporting an additional drinking water source was very low (<4%).

The water treatment intervention evaluated in this trial is distinct from previous health effect evaluations in low-income settings in two ways. First, we targeted a low chlorine residual dose to preserve blinding and increase acceptability of chlorinated water in the study population. The mean chlorine residual at the point of collection in the treatment group was 0·4 ppm. *E coli* contamination at the point of collection was reduced from a prevalence of 64% down to 15%. Many household water treatment products deliver a chlorine dose greater than 2 ppm, yet our intervention delivered a mean of 0·14 ppm free chlorine

residual at the point of use. We selected our target dose on the basis of previous work in Dhaka that identified a median chlorine residual taste detection threshold of 0·7 ppm.¹⁴ The installed chlorine dosers were able to consistently and precisely dose chlorine throughout the trial (table 3). Our results suggest that reducing the target dose of both in-line as well as household-level chlorination water treatment devices could increase acceptability while still effectively reducing the risk of waterborne illness. Given that turbidity in our study site was low, additional trials would be valuable to determine optimal dosing amounts in additional contexts.

A second distinctive feature of our water intervention is that although most previous studies have focused on evaluating household-level water treatment products that disinfect water at the point of use, we implemented a novel chlorination technology that automatically disinfected water at the point of collection. Manual chlorine dispensers for disinfecting water in rural settings at the point of collection exist;³² however, a recent randomised controlled trial in rural Kenya of an intervention that included installation of community manual chlorine dispensers and bottled chlorine delivery did not detect an effect on child diarrhoea.²⁹ The Aquatabs Flo chlorine doser does not require electricity to operate, requires minimal behaviour change for the user, and is compatible with intermittent flow systems that utilise water storage tanks. Although the Aquatabs Flo is currently only compatible with water points connected to storage tanks (appendix), additional automated chlorination technologies for disinfecting water at the point of collection have emerged that are low cost and compatible with additional types of water infrastructure, expanding the potential for scale up in low-income settings.^{12,13,33}

Our double-blinded trial provides unbiased evidence that in-line chlorination can improve household stored drinking water quality and reduce child diarrhoea in low-income urban settings with intermittent water supply. Chlorination is widely used for drinking-water disinfection, but taste acceptability is often cited as an important barrier to adoption. Accurate and automated chlorine dosing below the taste detection threshold has the potential to ensure high adoption rates. Our results suggest that this decentralised approach to water treatment could be a transformative strategy for reducing gastrointestinal disease burden in low-income urban communities.

Contributors

AJP and SPL designed the study; AJP, YC, SSu, JS, FG, SAI, SSu contributed to data collection; AJP, YC, JS, and RA contributed to data cleaning and analysis; AJP wrote the first draft; all authors contributed to writing and editing the manuscript.

Declaration of interests

AJP, SSu, SAI, and SPL received salary support from the World Bank during the study.

Data sharing

Study data, including deidentified individual participant data and codebook, are publicly available at the following link with no access

For study data see <https://osf.io/9dh7k/>

restrictions. The statistical analysis plan and study protocol are available at the same location.

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