BMJ Open

Effectiveness of hygiene kit distribution to reduce cholera transmission in Kasaï-Oriental, Democratic Republic of Congo, 2018: a prospective cohort study

Lauren D'Mello-Guyett ,[1,2] Oliver Cumming,[1] Sharla Bonneville,[3] Rob D'hondt,[2] Maria Mashako,[3] Brunette Nakoka,[3] Alexandre Gorski,[3] Dorien Verheyen,[2] Rafael Van den Bergh,[2] Placide Okitayemba Welo,[4] Peter Maes,[5] Francesco Checchi[1]

To cite: D'Mello-Guyett L, Cumming O, Bonneville S, *et al*. Effectiveness of hygiene kit distribution to reduce cholera transmission in Kasaï-Oriental, Democratic Republic of Congo, 2018: a prospective cohort study. *BMJ Open* 2021;**11**:e050943. doi:10.1136/bmjopen-2021-050943

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-050943).

Received 04 March 2021
Accepted 24 September 2021

[1]London School of Hygiene & Tropical Medicine, London, UK
[2]Médecins Sans Frontières, Brussels, Belgium
[3]Médecins Sans Frontières, Kinshasa, Congo
[4]Ministry of Health, Kinshasa, Congo
[5]UNICEF, Kinshasa, Congo

Correspondence to
Ms Lauren D'Mello-Guyett; lauren.dmello-guyett@lshtm.ac.uk

ABSTRACT

Introduction Household contacts of cholera cases are at a greater risk of *Vibrio cholerae* infection than the general population. There is currently no agreed standard of care for household contacts, despite their high risk of infection, in cholera response strategies. In 2018, hygiene kit distribution and health promotion was recommended by Médecins Sans Frontières for admitted patients and accompanying household members on admission to a cholera treatment unit in the Democratic Republic of Congo.

Methods To investigate the effectiveness of the intervention and risk factors for cholera infection, we conducted a prospective cohort study and followed household contacts for 7 days after patient admission. Clinical surveillance among household contacts was based on self-reported symptoms of cholera and diarrhoea, and environmental surveillance through the collection and analysis of food and water samples.

Results From 94 eligible households, 469 household contacts were enrolled and 444 completed follow-up. Multivariate analysis suggested evidence of a dose-response relationship with increased kit use associated with decreased relative risk of suspected cholera: household contacts in the high kit-use group had a 66% lower incidence of suspected cholera (adjusted risk ratio (aRR) 0.34, 95% CI 0.11 to 1.03, p=0.055), the mid-use group had a 53% lower incidence (aRR 0.47, 95% CI 0.17 to 1.29, p=1.44) and low-use group had 22% lower incidence (aRR 0.78, 95% CI 0.24 to 2.53, p=0.684), compared with household contacts without a kit. Drinking water contamination was significantly reduced among households in receipt of a kit. There was no significant effect on self-reported diarrhoea or food contamination.

Conclusion The integration of a hygiene kit intervention to case-households may be effective in reducing cholera transmission among household contacts and environmental contamination within the household. Further work is required to evaluate whether other proactive localised distribution among patients and case-households or to households surrounding cholera cases can be used in future cholera response programmes in emergency contexts.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study is one of few published evaluations on the effectiveness of water, sanitation and hygiene interventions for cholera control from an emergency context, and within the confines of a rapid response to an outbreak.
⇒ This study was conducted outside of controlled study conditions and among challenges of an ongoing humanitarian crisis and reflects potential study designs that can be used in complex settings.
⇒ Randomisation was not logistically feasible in this setting and the acute phase of an emergency response and our study thus relies on a comparison group who did not receive the intervention due to implementation failures rather than deliberate study design.
⇒ Unfortunately, we had originally aimed to enrol 250 cholera cases and their households, expected to be at least 985 household contacts, but due to political tensions in the region less than half (n=94) were enrolled and only 444 household contacts had complete data.
⇒ Information on developing cholera or diarrhoea was self-reported and may have resulted in recall bias. Additionally, the ascertainment of our primary outcome by self-report may lead to misclassification of our outcomes.

INTRODUCTION

Annually, there are an estimated 1.3–4.0 million cases of cholera worldwide resulting in between 21 000 and 143 000 deaths.[1] The Democratic Republic of Congo (DRC) accounts for 5%–14% of the global cholera burden annually,[2] with >56 000 cholera cases and 1190 deaths in 2017 alone.[3] DRC has been experiencing outbreaks of cholera annually since the 1970s[2] while also experiencing multiple humanitarian crises across the country that in turn exacerbate the risk of cholera epidemics.[2 4–7]

Risk factors for infection with *Vibrio cholerae* include the consumption of contaminated water and food, not washing hands with soap prior to eating and living in the same household as a cholera case.[8] Several studies have found that household contacts of cholera cases are at 100 times higher risk of becoming infected than the general population,[9–11] particularly during the first 7–10 days after a cholera case becomes symptomatic and seeks care at a healthcare facility (HCF).[9 10 12] This is due to the prolific shedding of *V. cholerae* by symptomatic and asymptomatic cases which can last up to 14 days after onset of symptoms.[13–15] Up to 80% of *V. cholerae* transmission can occur within households,[16 17] and cases have been observed to cluster within 200m of case-households during the first 5 days after the case becomes symptomatic.[18–20] These high secondary transmission rates suggest an important role for human-to-human transmission at the household level via contamination of shared stored drinking water and/or food, and inadequate hygiene practices such as handwashing with soap.[8 21]

For patients with suspected cholera admitted to HCFs, the standard package of care includes case management with oral rehydration solution (ORS) or intravenous fluids and infection prevention and control (IPC) to prevent transmission from the patient to staff or within the cholera treatment unit (CTU) or centre (CTC).[13 22–26] Guidelines to limit cholera transmission have historically directed attention to community-wide interventions rather than being targeted to case-areas or case-households.[22–30] While work has sought to either define packages of care for household contacts[31 32] or to calculate the speed or area at which interventions should be delivered, that is, through case-area targeted interventions (CATI),[19 33–38] there is currently no agreed standard of care for household contacts or households surrounding case-households, despite their high risk of infection.

Since 2017, hygiene kit distribution combined with health promotion has been recommended in guidelines by the international non-governmental organisation (NGO), Médecins Sans Frontières (MSF), as a rapid and localised intervention for patients and their accompanying household members on admission to a CTU/CTC.[22] The hygiene kit is intended to be used at the household-level and typically includes a container (eg, 10– L) for water collection and storage, bars or bags of soap, point of use (POU) water treatment product/s (eg, chlorine, filters and/or flocculant disinfectants) and a handwashing device (eg, a 10 L bucket with tap).[22] Health promotion and contact with the patient and their accompanying household member when seeking treatment in the HCF provides an opportunity for intervention delivery, particularly as the perceived severity of disease and the perceived benefits of the intervention are likely to be highest.[39–42] Hygiene kit distribution combined with health promotion has been part of MSF's response strategy and accompanies case management, community-wide health promotion, support to the healthcare system and enhanced surveillance for the duration of the outbreak.[43]

The CHOBI7 RCT in Dhaka, Bangladesh, which demonstrated a 50% reduction in symptomatic and asymptomatic cholera infection among household contacts from a similar yet more intensive intervention strategy,[31] and other work in Haiti[35] and Yemen,[44] has supported this change to the MSF guidelines and concentration on CATI or CATI-like responses in emergencies. In addition, there are a few other published studies on water, sanitation and hygiene (WASH) interventions to support guidelines and practice, but while the studies did report reductions in cholera incidence between 25% and 75%, they are of variable study quality and predominantly community-wide interventions.[45–50] To date, which WASH interventions to include for cholera control as part of CATI or targeted to case-households in other response formats have not been extensively evaluated in humanitarian settings or outside of controlled study conditions.[32 34 45 51–54]

METHODS

Study design

In this prospective cohort study, we investigated the effectiveness of hygiene kit distribution combined with health promotion to reduce suspected cholera and self-reported diarrhoea among household contacts of patients with suspected cholera admitted to MSF-supported CTUs in Kasaï-Oriental province, DRC. Patient-household sets were enrolled consecutively during the study period irrespective of whether they received the MSF hygiene kit. This was an observational study and the intervention was not allocated to particular groups. Households were revisited after 7 days, and data were analysed for the association between hygiene kit use and disease outcomes as well as the evolution of water and food contamination from enrolment to 7-day follow-up. We have separately published a process evaluation conducted in parallel to this study which evaluates the implementation and population response to the distribution of hygiene kits during an emergency response to a cholera outbreak in DRC.[43]

Study site and period

The Programme National d'Elimination du Choléra et de lutte contre les autres Maladies Diarrhéiques (PNECHOL-MD) issued a country-wide alert of a laboratory confirmed cholera case in Kasansa district, Kasaï-Oriental province, DRC, on 9 August 2018 (Epidemiological Week 28 (W28)).[55] A second alert and call for assistance came from the PNECHOL-MD on 22 August 2018 (W34).[56–58] The cholera response in Kasansa was led by the Ministry of Health (MoH) and supported by MSF over a 5-week period between 22 October and 23 November 2018 (W43–47). Between W28 and W42, there were 443 suspected cholera cases and 29 deaths across Kasansa. A further 224 suspected cholera cases and 3 deaths occurred during the MSF response between W43 and W47. The overall case fatality ratio (CFR) was 5% and

the attack rate (AR) of suspected symptomatic cases in the population was 0.28% between W28 and W47.[55 57–64]

During the outbreak, MSF supported seven government HCFs, two CTUs and five Oral Rehydration Points (ORPs) with case management, essential medicine supply, enhanced surveillance, community-level health promotion and infrastructure improvements. A total of 196 suspected cholera cases (75% of total reported suspected cases) were treated across all seven MSF-supported HCFs (121 in CTUs and 75 in ORPs) between W43 and W47. This study was conducted in the only two HCFs in the district, both of which were supported by MSF. Data were collected for this study between 22 October and 4 December 2018 (W43 and W49).

Study intervention

In this cholera response, the MSF hygiene kits distributed included a 20 L container for water collection and storage, 1 kg of bar soap, a 2-month supply of POU water treatment products (Aquatabs disinfectant and/or P&G Purifier of Water combined flocculant/disinfectant) and a 10 L bucket with tap as a handwashing device. One hygiene kit per household, accompanied by standard WASH-related health promotion messages, was delivered by community health workers (CHWs) to the household contacts of patients on the day of the patient's admission at either of the two MSF-supported CTUs. The WASH-related health promotion messages included the following components: cholera transmission (e.g., F-diagram); encouraging case-seeking behaviours at HCFs; treatment at MSF facilities is free of charge; increase in water stored in the household (by using the water container provided to you); boil or treat drinking water; limit open defecation; practice safe corpse preparation; wash hands at key times (before eating, before food preparation, after toilet, after changing a baby's nappy, after caring for the ill/ contact with a cholera case).[43] The hygiene kit was intended to be delivered to the households of all patients, regardless of their participation in the study. However, due to implementation challenges described in a parallel process evaluation published elsewhere,[43] there were delays in receiving the hygiene kits to the project site and the initial households seeking care and later enrolled into the study had not received a hygiene kit or health promotion at the HCF. Only accompanying household contacts of the admitted patient received the health promotion messages.

Study participants

All suspected cholera cases, defined as patients admitted with acute watery diarrhoea (three or more loose stools over a 24-hour period) and/or moderate to severe dehydration, using the WHO definitions,[22 30] were eligible for enrolment into the study. Patients were not selected randomly and were enrolled through a convenience sample as they were admitted to the CTU. We excluded any patients aged <2 years old and/or who had a household contact previously or currently enrolled in the study. All patients were tested for the presence of *V. cholerae* on rectal swab samples using the SD Bioline Rapid Diagnostic Test (RDT).[65 66] All rectal swab samples were transferred to Cary-Blair media and enriched in alkaline peptone water (APW) for 24 hours at room temperature (approximately 25–27°C)[67–69] prior to testing by RDT. Patients and patient-household sets were retained in the study regardless of their RDT result.

Household contacts were defined as individuals sleeping under the same roof and sharing a cooking pot with the suspected cholera case during at least the previous 5 days. Eligible household contacts present at the CTU at the time of patient enrolment were invited to participate in the study, and a household visit was made within 48 hours of patient enrolment to recruit the remaining household contacts. To be eligible for the study, household contacts had to plan to reside in the house for the following 2 weeks. Follow-up visits were conducted at households 7 days after the case presented at the CTUs.

Data collection

Exposure to the intervention

Measures of intervention compliance within households which received a hygiene kit were prespecified, based on standard WHO or WHO/UNICEF Joint Monitoring Programme indicators[70 71] and included: availability of a 20 L drinking water container distributed as part of the intervention; presence of water in the 20 L container; presence of Aquatabs or P&G Purifier of Water, specifically distributed as part of the intervention; a recommended cut-off value of 0.5 mg/L free residual chlorine (FRC) for household drinking water;[71 72] availability of soap, specifically distributed as part of the intervention; presence of soap within 2 m of the toilet; presence of soap within 1 m of the kitchen area and availability of the 10 L handwashing bucket with tap including the presence of water and soap.

To assess the association between presence of the intervention, intervention compliance and our outcomes of interest, we established four subgroups: no kit, low use of kit, medium use of kit and high use of kit. Receipt of the kit by the household was confirmed at the CTU and verified by observation at the household. All groups came from the same study population. Households in the no kit group were not randomly allocated at the CTU and the reason they did not receive a kit was due to delayed implementation.[43] For the other three subgroups, intervention compliance was not random but based on assessing by first estimating the percentage of physical kit components used by the household and then categorising households and the individuals residing in the house as high (71%–100%), medium (31%–70%) or low (0%–30%) users. These equally sized categories were selected owing to the limited evidence on the relative effect of individual kit components.[53]

Clinical outcomes

The occurrence during the ensuing 7-day follow-up period of syndromes consistent with cholera (hereafter referred to as 'suspected cholera') as well as self-reported diarrhoea, were ascertained among household contacts based on verbal report. A 7-day follow-up period was selected based on the 7–10-day high risk period for transmission following admission to a HCF, as noted in other work,[9 10 12] and feasibility for follow-up. Each household contact reported their own symptom history, with caregivers reporting disease for children. Suspected cholera was defined as diarrhoea (three or more loose stools over a 24-hour period), vomiting and/or attending a HCF with suspected cholera in the past 5 days.[13 22] Self-reported diarrhoea was defined as three or more loose stools over a 24 hours period, with or without the presence of blood, in the past 5 days.[73] We were unable to confirm cholera through RDT or by culture among household contacts during this study.

Environmental outcomes

Stored water samples were collected at enrolment and 7-day follow-up whereas source water was collected only at enrolment. Food samples were collected when prepared food was available at both visits. Environmental samples were collected in 100 mL Whirl-Pak bags (Nasco, Fort Atkinson, Wisconsin, USA) and transported with ice packs in cooler bags to the purpose-built laboratory at the CTU.

Water samples were tested for the presence of *Enterococcus* spp (coliform forming units per 100 mL (CFU/100 mL)),a thermotolerant faecal indicator bacteria,[74–76] by culture on *Enterococcus* indoxyl-β-D-glucoside (mEI) selective medium through standard membrane filtration techniques.[77] FRC concentrations (mg/L) were measured with using a pool tester. The recommended thresholds for chemical and physical characteristics of water samples included 1.0 mg/L FRC for water sources 0.5 mg/L FRC for stored drinking water and 5 NTU for both source and stored water.[72]

Enterococci were also enumerated in food samples, of which a 5 g aliquot was diluted in 50 mL of sterile water, homogenised by shaking and allowed to settle. The 5 mL volumes of supernatant were filtered through sterile membranes with 50 mL of sterile water.

All environmental samples were processed for incubation at 41°C for 24 hours in a Wagtech Potatest 2 incubator (Palintest, Tyne & Wear, UK) within 6 hours of collection. Method blanks and positive controls were analysed in each batch of samples. The number of CFU/100 mL was counted and microbiological contamination of water and food samples was defined as >10 CFU/100 mL of detectable *Enterococcus* spp according to previously published work.[22 72 74–76]

Data collection procedures

Household data were collected through structured questionnaires written in English, translated to French and then back translated to confirm wording. The French translations were required for training of the enumerators and while the study site was still being determined as it was dependent on where the next cholera outbreak would be in DRC. Once the study site was confirmed as the Tshiluba-speaking Kasaï-Oriental, Tshiluba translations of the questions were checked during training of the local enumerators and all enumerators were asked to come to consensus on how to ask particular questions. Questionnaires were administered in the local language (Tshiluba) by two-person teams of Congolese enumerators speaking French and Tshiluba. Survey data were entered directly onto tablets through KOBO Toolbox platform (Harvard Humanitarian Initiative, Cambridge, Massachusetts, USA). Questionnaires were administered to all available household contacts at enrolment and 7-day follow-up. Individual and household characteristics that may have confounded the association between the intervention and the outcomes of interest were measured. A separate questionnaire administered to the head of each household was used to assess access to, and use of, WASH interventions, in accordance to global standard definitions by the WHO/UNICEF Joint Monitoring Programme.[70] The individual and household questionnaires can be found in online supplemental file 1.

Sample size

We wished to detect a reduction of at least 50% (relative risk ≤0.5) in suspected cholera risk among household contacts with high kit use, compared with those with no use of the hygiene kit, with 5% significance and 80% power. We assumed a 20% risk of suspected cholera in the unexposed (no use of the kit) group,[11 21] yielding a sample size of 197 people per group. Further assuming that the high-use and no use kit groups were each ≥20% of the study population, a total of 985 individual household contacts were needed. Assuming a mean household size of five people (average household sizes are 5.3 across DRC[78]) for each case, and a loss to follow-up of 25%, we aimed to enrol 250 cholera cases and their households in the study.

Due to ongoing political instability in the country[4] and upcoming elections in December 2018,[79] the study was stopped mid-way and did not reach the intended sample size.

Statistical analysis

All statistical analyses were conducted in Stata V.16 (Stata, College Station, Texas, USA).

For clinical outcomes, log generalised linear models (GLM) with a binomial distributional assumption were fitted to estimate the relative risk (risk ratio, RR) of household contacts developing suspected cholera and self-reported diarrhoea between enrolment and 7-day follow-up, with robust standard errors to account for household clustering. The association of exposure to the intervention, no kit, low-use, mid-use and high-use, with the outcomes was tested univariately and adjusted for potential confounders or effect modifiers, including

socioeconomic status (SES), environmental conditions (water source, sanitation type), handwashing and water and food storage practices, selected based on an *a priori* causal framework (online supplemental file 2) and Theory of Change previously published for this intervention.[43] All variables were converted to categorical variables according to appropriate thresholds. Variables with a *p* value of 0.1 in univariate analysis, as well as those variables that were related to the outcome in our causal framework, were considered for inclusion in the multivariable model. Each such variable was included into the model in turn, and likelihood ratio tests (LRT) were used to compare the base model with each new model. This process was repeated until no variables left improved model fit. Variables included in the final multivariable model were also checked for interaction and collinearity.

For environmental outcomes, censored tobit linear regression models (selected because of right-censoring in the outcomes: CFU levels were only quantified up to 1000/100 mL) were used to assess the change in coliform density counts of *Enterococcus* spp (CFU/100 mL) in water and food samples between enrolment and 7-day follow-up. As data were longitudinal, we treated households as a random effect. Because of low sample size for this analysis, we considered receipt of the kit as the exposure, irrespective of use. Exposure to the intervention and risk factors were tested in univariate models with a *p* value of 0.1. The multivariable model was built forward iteratively comparing the new model to the base model where the LRT and Akaike Information Criterion (AIC) statistic were included in the same model and minimised. Regression diagnostic plots of the residuals were visualised to test linear regression assumptions such as normality, linearity and homogeneity of variance.

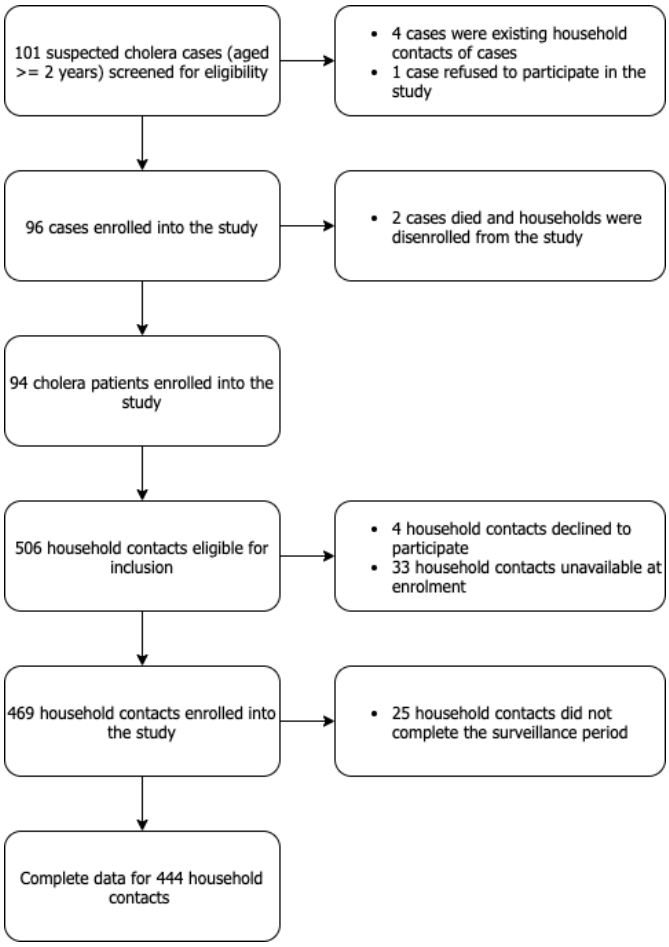

Figure 1 Flowchart of study participation in a prospective cohort study of hygiene kit distribution to patients with suspected cholera, Kasaï-Oriental, DRC, October–December 2018.

Patient and public involvement

Research questions and outcome measures were developed and informed by the lack of an agreed standard of care for patient-households and the patient experience in cholera outbreaks, and the global research agendas for cholera prevention and control[80] and emergency WASH interventions.[81] Patients and the public were first involved in the research at the point of enrolment when admitted to the CTU and were recruited to the study during admission to the HCF. Patients and the public were not involved in the design of the study. All participants were informed about the study objectives and time required to participate in the research. Results of the study have been provisionally shared with all research partners nationally and internationally and will be further disseminated to district level partners and the population through community meetings and a lay summary report of the findings.

RESULTS

Description of patients with suspected cholera

Of the 101 suspected cholera cases screened for eligibility before the study was stopped, four were excluded as household contacts of enrolled cases, one person declined to participate and two cases died during treatment and these households were disenrolled on request by the households (figure 1). There were no cases <2 years of age. A total of 94 suspected cholera cases were therefore enrolled and defined as patients with cholera, based on syndromic diagnosis, of which 52.1% (n=49) tested positive for *V. cholerae* by SD Bioline RDT. The average age of admitted patients with cholera was 30.6 years with an even gender ratio. Prior to, or during the study, 36.1% of patients had taken antibiotics in the past 5 days. Most patients had no to moderate dehydration (table 1).

Description of household contacts

All identified household contacts of enrolled patients were invited to participate in the study. Of the 506 eligible household contacts, four declined to participate and 33 were unavailable at the time of the enrolment visit. Of the 469 enrolled household contacts, 25 (5.3%) did not complete 7-day follow-up (figure 1). Of the 444 who completed 7-day follow-up, the mean age was 19.0 years and approximately half were female (51.1%). Most participants had received primary level or above

Table 1 Characteristics of the enrolled patients with suspected cholera in Kasaï-Oriental, DRC, 2018

	% (n)
Number of patients with suspected cholera	94
Age of patient with suspected cholera, mean (x)±SD (min–max)	30.6±18.3 (2–81)
2–5 years	9.6 (9)
5–15 years	14.9 (14)
>15 years	75.5 (71)
Gender of patient with suspected cholera	
Female	51.1 (48)
Male	48.9 (46)
Individual taken antibiotics in the last 5 days	36.1 (34)
No vaccination with OCV	100 (94)
Cholera treatment plan of patient with suspected cholera	
Plan A (no dehydration)	39.4 (37)
Plan B (some dehydration)	39.4 (37)
Plan C (severe dehydration)	21.3 (20)
Cholera diagnosis of suspected patient confirmed by RDT	52.1 (49)

OCV, oral cholera vaccine; RDT, rapid diagnostic test.

education and the majority were employed. No patient or household contact had received oral cholera vaccination (OCV). Some (18.7%) household contacts reported caring responsibilities for patients with cholera, while most contacts only reported sharing food and water with patients. During the surveillance period, 91.4% reported eating or drinking outside of the household and 35.8% had contact with another suspected cholera case outside of the household (table 2). All household contacts confirmed that they had resided in the household for the entirety of the 7-day follow-up period.

Description of households

Household sizes averaged 8.4 persons, which was greater than the average reported by recent surveys,[78] and 73.4% of households were categorised in the lowest category of SES based on principal component analysis (PCA) weightings.[82 83] The small sample size dictated that we reduce the typical five SES categories to a binary variable. Unimproved sources or surface water were used by 86.2% of households, and average time to walk to and back from water sources was 66.3±56.0 min. The average volume of water stored at the time of visit was 50.3±36.4 L. Water source samples were collected for all households and >10 CFU/100 mL *Enterococcus* spp was found in 42.6% of source water samples and chlorine concentrations were all <1.0 mg/L FRC. Unimproved sanitation, as defined by the WHO/UNICEF JMP,[70] was found in 84.0% of households, and a further 4.3% of households practiced open defecation (table 3).

Effect of the intervention on suspected cholera risk

At enrolment of household contacts, a total of 175 (39.4%) household contacts reported suspected cholera in the previous 5 days. At 7-day follow-up, 25 (5.6%) household contacts reported suspected cholera in the previous 5 days. Univariate associations are shown in online supplemental table 1. Multivariate analysis suggested evidence of a dose-response relationship with increased kit use associated with decreased risk of suspected cholera: household contacts in the high kit-use group had a 66% lower incidence of suspected cholera (adjusted risk ratio (aRR) 0.34, 95% CI0.11 to 1.03, p=0.055), the mid-use group had a 53% lower incidence (aRR 0.47, 95% CI 0.17 to 1.29, p=1.44) and low-use group had 22% lower incidence (aRR 0.78, 95% CI 0.24 to 2.53, p=0.684), compared with household contacts who had not received a hygiene kit (table 4). Overall, there was a 56% lower incidence of suspected cholera among household contacts with a hygiene kit than those without (aRR 0.44, 95% CI 0.20 to 0.99, p=0.046). aRR associations were adjusted for confounders including age, gender, education, employment, types of contact with index cases and sanitation coverage (online supplemental table 2). There were no systematic differences between the hygiene kit user groups noted in our analysis.

Effect of the intervention on self-reported diarrhoea risk

At enrolment, a total of 155 (34.9%) household contacts had self-reported diarrhoea in the previous 5 days. At 7-day follow-up, 16 (3.6%) household contacts had self-reported diarrhoea in the previous 5 days. Univariate associations are shown in online supplemental table 3. A similar dose-response relationship was observed between increased kit use and decreased risk of self-reported diarrhoea; the high kit-use group had a 45% lower incidence of self-reported diarrhoea (aRR 0.55, 95% CI0.15 to 2.00, p=0.366), the mid-use group had a 35% lower incidence (aRR 0.65, 95% CI 0.18 to 2.21, p=0.487) and low-use group had 20% lower incidence (aRR 0.80, 95% CI 0.16 to 4.00, p=0.786), compared with household contacts who had not received a hygiene kit. Overall, there was a 45% lower incidence in self-reported diarrhoea among household contacts with a hygiene kit than those without (aRR 0.55, 95% CI 0.18 to 1.69, p=0.296). However, there results were not statistically significant (table 5). aRR associations were adjusted for confounders including age, types of contact with index case and cholera treatment plan (online supplemental table 4).

Effect of the intervention on contamination of drinking water and food

At enrolment, 46.8% of stored drinking water samples were contaminated (>10 *Enterococcus* spp CFU/100 mL)

Table 2 Sociodemographic characteristics of enrolled household contacts and clinical surveillance in Kasaï-Oriental, DRC, 2018

	Total	Enrolment % (n)	7-day follow-up % (n)
Number of household contacts	444		
Age of household contact, mean (x)±SD (min–max)		19.0±16.7 (2–81)	
2–5 years		17.3 (77)	
5–15 years		39.6 (176)	
>15 years		43.0 (191)	
Gender of household contact			
Male	444	47.3 (210)	
Female	444	52.7 (234)	
Education			
None	444	27.5 (122)	
Any education	444	72.5 (322)	
Ability to read	444	31.1 (139)	
Ability to write	444	30.9 (137)	
Currently employed	444	78.4 (348)	
No vaccination with Oral Cholera Vaccine (OCV)	444	100 (444)	
Types of contact with patient with suspected cholera in the last 5 days			
Shared food, water and caring responsibilities	444	18.7 (83)	
Shared food and water	444	81.3 (361)	
Individuals reported eating or drinking outside of the household during the surveillance period	444	91.4 (406)	
Individuals reported contact with another suspected cholera case during the surveillance period	444	35.8 (159)	
Clinical surveillance			
Number of household contacts with suspected cholera (any diarrhoea, vomit and cholera) in the last 5 days	444	39.4 (175)	5.6 (25)
Number of household contacts with symptoms of cholera in the last 5 days			
Diarrhoea (three or more loose stools in 24 hours)	444	34.9 (155)	3.6 (16)
Vomiting	444	14.9 (66)	3.4 (15)
Cholera (determined by attendance at a HCF and clinical diagnosis)	444	4.1 (18)	0.9 (4)

HCF, healthcare facility.

and 80.7% of samples reported chlorine concentrations <0.5 mg/L FRC. At 7-day follow-up, 31.9% drinking water samples were contaminated (>10 *Enterococcus* spp CFU/100 mL) and 71.3% of samples reported chlorine concentrations <0.5 mg/L FRC (table 3). Univariate associations are shown in online supplemental table 5. Multivariate analysis showed that there was statistically significant reduction in drinking water contamination observed among all groups receiving the kit (adjusted effect estimates −224.1, 95% CI −365.9 to −82.3, p=0.002) (table 6). Effect estimate adjusted for confounders including SES and availability of a handwashing facility at enrolment (online supplemental table 6).

Of the 77 households with food prepared at enrolment, 53.3% covered the food at the time of visit and 63.6% of food samples collected were contaminated (>10 *Enterococcus* spp CFU/100 mL). At 7-day follow-up, 57.1% of households covered the food and 74.0% of food samples collected were contaminated (>10 *Enterococcus* spp CFU/100 mL) (table 3). Univariate associations are shown in online supplemental table 7. There was no statistically significant reduction in food contamination (adjusted effect estimates −114.4, 95% CI −417.4 to 188.5, p=0.459) (table 7). Effect estimate adjusted for confounders including SES (online supplemental table 8).

Table 3 Sociodemographic and WASH characteristics of households in Kasaï-Oriental, DRC, 2018

	Total	Enrolment % (n)	7-day follow-up % (n)
Number of households	94		
Household size, x±SD (min–max)		8.4±4.1 (2–23)	
Average number of adults, x±SD		3.3±1.8	
Average number of children (5–18 years), x±SD		3.8±2.5	
Average number of infants (0–5 years), x±SD		1.37±1.3	
Socioeconomic status			
Lowest	94	73.4 (69)	
Highest	94	26.6 (25)	
Water source coverage and access			
Improved: basic (improved, <30 min) and limited (improved, >30 min)	94	13.8 (13)	
Unimproved: unimproved and surface water (rivers, unprotected springs)	94	86.2 (81)	
Average time to and back from water source (in minutes), x±SD (min–max)		66.3±56.0 (0–240)	
Volume of water stored in household (L), x±SD (min–max)		50.3±36.4 (1–200)	
Source water with a median chlorine concentration <1.0 mg/L FRC	94	100 (94)	
Source water with >10 *Enterococcus* spp (CFU/100 mL)	94	42.6 (40)	
Sanitation coverage			
Limited (improved, shared >2 households)	94	11.7 (11)	
Unimproved	94	84.0 (79)	
Open defecation	94	4.3 (4)	
Water storage and treatment practices			
Any safe water storage available	94	79.8 (75)	96.8 (91)
Safe water storage distributed to households (20 L container)	94	0 (0)	96.8 (91)
Water present in any safe water storage	94	91.5 (86)	91.5 (86)
Water present in distributed safe water storage (20 L container)	94	0 (0)	86.2 (81)
Decant or drink water from water storage container with glass or cup	94	95.7 (90)	95.7 (90)
Water treatment options available (Aquatabs or P&G Purifier of Water)	94	0 (0)	75.5 (71)
Soap availability			
Any soap available	94	81.9 (77)	73.4 (69)
Soap distributed to households (1 kg of bar soap)	94	0 (0)	73.4 (69)
Soap observed within 1 m of kitchen	94	8.5 (8)	18.1 (17)
Soap observed within 2 m of latrine	94	4.3 (4)	1.1 (1)
Handwashing facility			
Basic facility (facility, water and soap)	94	20.2 (19)	24.5 (23)
Limited facility (facility and water)	94	36.2 (34)	46.8 (44)
No handwashing facility	94	43.6 (41)	28.7 (27)
Food storage practices			
Food covered	77	66.7 (36)	79.3 (42)
Receipt of a hygiene kit during the surveillance period	94	0 (0)	80.8 (76)
Environmental surveillance			
Stored drinking water with median chlorine concentration <0.5 mg/L FRC	94	80.7 (75)	71.3 (67)
Stored drinking water with >10 *Enterococcus* spp (CFU/100 mL)	94	46.8 (44)	31.9 (30)
Food samples with >10 *Enterococcus* spp (CFU/100 mL)	77	63.6 (49)	74.0 (57)

WASH, water, sanitation and hygiene.

Table 4 Multivariate analysis for suspected cholera (diarrhoea, vomiting and/or cholera) during the surveillance period in Kasaï-Oriental, DRC, 2018

	Contacts (n)	Suspected cholera (% (n))	Univariate (RR)	Multivariate (aRR)	Lower 95% CI	Upper 95% CI	P value
Suspected cholera among household contacts	444	5.6 (25)					
Receipt of a hygiene kit during surveillance period							
No (reference)	99	36.0 (9)	(ref.)	(ref.)			
Yes	345	64.0 (16)	0.51	0.44	0.20	0.99	0.046
Receipt of a hygiene kit and intervention compliance during surveillance period							
Did not receive the hygiene kit (reference)	99	36 (9)	(ref.)				
Received a hygiene kit with low use	54	16 (4)	0.81	0.78	0.24	2.53	0.684
Received a hygiene kit with mid-use	149	28 (7)	0.52	0.47	0.17	1.29	0.144
Received a hygiene kit with high use	142	20 (5)	0.39	0.34	0.11	1.03	0.055

Log GLM with a binomial distributional assumption were fitted and aRR associations were adjusted for confounders including age, gender, education, employment, types of contact with index cases and sanitation coverage.
aRR, adjusted risk ratio; GLM, generalised linear models.

DISCUSSION

The distribution of hygiene kits combined with health promotion, by MSF in Kasaï-Oriental, DRC, reduced the incidence of suspected cholera among household contacts of admitted patients with cholera by 22%–66% during the intervention period. This was highest, and statistically significant, among individuals with high use of the hygiene kits compared with households without a kit. A similar relationship was observed in the reduction of self-reported diarrhoea among household contacts; however, this association was not statistically significant. Overall, these findings indicate that the distribution of hygiene kits and health promotion may be effective in reducing suspected cholera and the relative risk of diarrhoeal disease during the high-risk period for household contacts of patients with suspected cholera. Furthermore, these results suggest that the impact of these kits is greatest when compliance is highest. The observed dose-response associations support a causal link between kits and reduced disease risk.

Consistent with these findings, kit receipt was associated with a reduction in drinking water, though not food, contamination. We potentially attribute this success and failure to the components of the hygiene kit and contents of the health promotion messages. The hygiene kit incorporated two components designed to treat or store water safely and seems to have been both effective in making people use the water treatment and safe storage when previously they did not, as previously reported in a parallel process evaluation.[43] However, the kit contained no components to limit food contamination, improve food storage or health promotion for food-related behaviours and thus failed to have any effect on food contamination other than potentially through improving the presence of handwashing facilities. It may also be that the measurement of food contamination in this study was too variable to capture changes which may occur between different times of day, types of food, storage practices or other factors.[76 84 85] Lastly, health promotion messages were only addressed to the accompanying household contacts at the CTU and diffusion of messages to the other household contacts may be limited or ineffectual.

Identified risk factors for suspected cholera and self-reported diarrhoea among household contacts included the type of contact with patients and age of household contacts. Although not statistically significant, we found that individuals without direct caring responsibilities for the patient with cholera had a reduced relative risk of disease outcomes compared with other household contacts. This is consistent with previous studies which have identified caring responsibilities as a risk factor for intrahousehold transmission.[8] However, further analyses

Table 5 Multivariate analysis for self-reported diarrhoea during the surveillance period in Kasaï-Oriental, DRC, 2018

	Contacts (n)	Self-reported diarrhoea (% (n))	Univariate (RR)	Multivariate (aRR)	Lower 95% CI	Upper 95% CI	P value
Self-reported diarrhoea among household contacts	444	3.6 (16)					
Receipt of a hygiene kit during surveillance period							
No (reference)	99	43.8 (7)	(ref.)	(ref.)			
Yes	345	56.2 (9)	0.63	0.55	0.18	1.69	0.296
Receipt of a hygiene kit and intervention compliance during surveillance period							
Did not receive the hygiene kit (reference)	99	31.2 (5)	(ref.)	(ref.)			
Received a hygiene kit with low use	54	12.5 (2)	0.73	0.80	0.16	4.00	0.786
Received a hygiene kit with mid-use	149	31.3 (5)	0.66	0.65	0.18	2.21	0.487
Received a hygiene kit with high use	142	25.0 (4)	0.56	0.55	0.15	2.00	0.366

Log GLM with a binomial distributional assumption were fitted and aRR associations were adjusted for confounders including age, types of contact with index case and cholera treatment plan.
aRR, adjusted risk ratio; GLM, generalised linear models.

would be required to understand the relative difference between those with and without caring responsibilities in the household-high-risk environment. Household contacts >5 years of age had a reduced risk of both suspected cholera and diarrhoea which is consistent with previous studies.[8 86] Key WASH practices, such as individuals practicing open defecation, increased the relative risk of suspected cholera which is consistent with a number of previous studies.[8]

Our findings are broadly consistent with the 25%–75% reductions in cholera incidence reported in previous evaluations of WASH interventions[31 46–50] and echoes the CHOBI7 RCT intervention in Bangladesh, which included distribution of a hygiene kit to patients and their household contacts and both point-of-care and household hygiene promotion, which reported a 50% reduction in symptomatic and asymptomatic incidence of cholera.[31] Thus, our study contributes to a growing body of evidence demonstrating that targeted WASH interventions delivered through CATI or targeted to case-households during cholera outbreaks may be an effective approach to reduce household transmission and to control the epidemic.[19 32–37 44]

The reported reduction in household transmission of cholera may be attributed to three notable factors. First, the intervention was delivered to households at the point-of-care allowing for early adoption of the intervention. Admitted patients with cholera typically attended HCFs within 1 day of the onset of symptoms, and kits were taken to their respective dwellings within 1–3 days of receipt and used within the 7-day high risk period.[43] Second, there was high user acceptance of the intervention reported among households which may have led to increased uptake of the intervention,[43] as found in other

Table 6 Multivariate analysis for change in *Enterococcus* spp coliform density counts in drinking water samples during the surveillance period in Kasaï-Oriental, DRC, 2018

	Households (n)	%	Effect estimate	Lower 95% CI	Upper 95% CI	P value
Receipt of a hygiene kit during surveillance period						
No (reference)	18	19.2	(ref.)			
Yes	76	80.8	−224.1	−365.9	−82.3	0.002

Censored tobit linear regression models were fitted and effect estimates adjusted for confounders including socioeconomic status and availability of a handwashing facility at enrolment.

Table 7 Multivariate analysis for change in *Enterococcus* spp coliform density counts in food samples during the surveillance period in Kasaï-Oriental, DRC, 2018

	Households (n)	%	Effect estimate	Lower 95% CI	Upper 95% CI	P value
Receipt of a hygiene kit during surveillance period						
No (reference)	18	19.2	(ref.)			
Yes	76	80.8	−114.4	−417.4	188.5	0.459

Censored tobit linear regression models were fitted and effect estimates adjusted for confounders including socioeconomic status.

WASH studies.[52 87 88] Third, the uptake of the intervention may have been enhanced due to the severe illness and perceived risk of diarrhoeal disease at the moment of delivery, as observed in other studies of WASH interventions.[39–42]

Nevertheless, and despite the reduction in suspected cholera incidence, a high proportion of household contacts reported symptoms of cholera in the previous 5 days before enrolment: our enrolled patients were thus not necessarily the primary cases in their households, many of whom could have been mild or asymptomatic, and did not require hospitalisation. This implies that much of intrahousehold transmission may have occurred before households received the kit and potentially when the outbreak was already dissipating, meaning that the first generation of intrahousehold transmission may not have been mitigated. Another difference between exposure groups may be at what stage of the outbreak did households receive a kit. This was not explored in this study and may have affected the reported outcomes. The overall potential for impact of the intervention, therefore, may be considerably less than this study's finds. Further, the 16-week delay between outbreak confirmation and intervention delivery would need to be greatly shortened,[33 43] coverage of interventions would need to be greater[89 90] and surveillance would need to be more timely and heightened[33 91 92] if this intervention were to have an impact on early epidemic propagation.

Limitations

Implementing research in the context of an ongoing cholera outbreak is complex and often compounded by the broader instability which characterises settings where cholera outbreaks occur.[93 94] Challenges with implementation, compounded by the ongoing conflict in DRC,[4] led to a delayed response and low coverage of the intervention.[43] Second, there may not have been a clear division between the evaluators and healthcare providers during the outbreak. Both sets of staff were employed and worked wearing MSF-branded clothing and both were present in the community at similar times. There may be challenges in the reflexivity of the evaluators and potential bias introduced to data collected. For example, social desirability bias may have been introduced when households reported symptoms, intervention uptake and use especially as they were in receipt of hygiene kits distributed by MSF. The participants may be more likely to recall a positive health outcome, or forget a negative experience, to the MSF-related evaluators. Third, the enumerators were aware of whether the household had received the intervention and the outcome variables. This brings potential risk to how questions were asked by the study team. Last, this evaluation was not independent of MSF the organisation and although this work contributes to increasing the quantity of operational research evaluations and meaningful partnerships in the humanitarian sector, it brings risk to independence. We hope to have addressed this through being open and transparent throughout the evaluation, and MSF has no say in the decision to publish the results.

Randomisation was not logistically feasible in the acute phase of an emergency response and our study thus relies on a comparison group who did not receive the intervention due to implementation failures rather than deliberate study design.[93 95] The no kit group was not randomly selected, and the observed associations may be subject to residual unobserved confounding due to their plausibly different baseline circumstances (eg, other factors related to poverty or lower access to care, beyond those we adjusted for). Additionally, and as noted earlier in the paper, due to political instability in the country[4] and upcoming elections in December 2018,[79] we did not reach the required sample size for this study and our power to detect an association was reduced. If we had been able to enrol our target sample size, we may have had power to observe associations more precisely.

Another limitation of our study is the use of suspected symptomatic cholera as an outcome measure among household contacts compared with collection of rectal swab samples for case ascertainment, a decision that was made by MSF and outside of the influence or control of the study team. The ascertainment of our primary outcome was therefore based on self-reported symptoms and may lead to misclassification of our outcomes, as other studies have found.[96] It may have also led to an inflation of suspected cholera at enrolment, as the case definition may have been too broad and captured any cause diarrhoea. We were unable to test suspected cholera diagnoses among our study population by RDT or culture. Other studies have been able to test the stool or rectal swab samples of household contacts,[21 31] and this would have strengthened outcome ascertainment. It is unlikely that misclassification would have been differential by hygiene kit use: as such, the most likely effect of this bias is underestimation of effect sizes. Additionally, we used a

5-day recall of diarrhoea rather than 7-day recall, which could lead to reporting of more outcome events and may have further reduced study power.

Our study also only examined faecal indicator bacteria counts for *Enterococcus* spp in food and water. We were unable to conduct microbiological analysis of *V. cholerae* in environmental samples or extend the microbiological analysis to other samples such as hand rinses[97] or surfaces within the household which have been found to be heavily contaminated with *V. cholerae* in other studies.[98] These additional measures would be useful in future studies to understand the effect on overall cholera transmission within the household.

Last, in this study, our measurement of intervention exposure was based on uptake and use of the intervention. We assigned equal weight to each kit component due to lack of evidence to the contrary[53] and also because the intervention was delivered as a package: the study thus does not shed light on which components are more effective, are preferred or should be included in future kit compositions. Due to the arbitrary nature of the thresholds and number of assumptions needed, we also chose not to conduct sensitivity analysis and robust estimates could differ if other cut-off values had been selected. Moreover, our measures serve only as proxies for the use of the intervention. For example, availability of soap anywhere in the dwelling, that is, within 1 m of the kitchen area or 2 m of a latrine, indicates that the intervention is in the household[99] but not whether soap was used consistently. Similarly, soap and water availability at the handwashing device does not necessarily mean that people wash hands.[100] Positive behaviours such as handwashing are often overreported.[101 102]

CONCLUSION

Hygiene kit distribution is a promising intervention for cholera control. The integration of a WASH intervention at the point of admission of suspected cases is new in cholera control efforts, particularly in outbreaks and complex emergencies. This study has shown that the distribution of hygiene kits accompanied by health promotion may be effective in reducing cholera transmission among household contacts and a may be an important component of CATI responses.

Further evaluations of hygiene kit distribution are still warranted, with a more established and rigorous counterfactual or control group, to assess if the intervention may be as effective as this study found. Further, studies should evaluate hygiene kit distribution to hospitalised patients and their households at the HCF and also in a CATI response where there is proactive localised delivery to vulnerable households surrounding a case who are at an increased risk of interhousehold transmission.[18 19 34 35 89 103] Additionally, postdistribution evaluation should extend beyond 1 week to establish the sustainability of intervention compliance and use by the household and other advantages such as the cost-effectiveness of case-centred delivery, should this intervention be adopted and adapted in future responses.

Acknowledgements We are grateful to the support of several colleagues who have engaged in the practical and academic aspects of this study in DRC, Belgium and the UK. Thanks go to our enumerators: Jeannette Luthala, Gaspard Tapo, Denis Lungi, Kalume Kalumwendo, Noel Mufumbele; other members of the team including Rollin Ndombe, Noè Kanyinda, Ali Luyeye, Marisel Méndez Yépez, Hilde Vochten, and the Pool d'Urgence Congo (PUC) from MSF DRC; to Paul Mukendi, Dieu Donne Kashala, Emmanuel Kayembe, Benoit Kabeya and Yvonne Tshibwaya our translators and our fleet of 20 motorcycle drivers in Kasaï-Oriental; to Pierre Pech, Damien Scarlett, Thierry Sakora, Ahmed Abd-Elrahman, Vincent Lambert, Emmanuel Lampaert from MSF Brussels; and to Robert Dreibelbis, Karl Blanchet, Adam Biran and Sandy Cairncross at LSHTM. Last but by no means least, we thank the participants and communities of Kasansa for their support for this study.

Contributors LDG is the guarantor for the study and accepts full responsibility for the finished work and/or the conduct of the study, had access to the data, and controlled the decision to publish. LDG conceived the study and designed the study with input from OC, RD, RVdB, PM and FC. SB contributed to the collection of data during the intervention implementation. BN conducted the microbiological analysis of environmental samples. LDG, SB, AG, DV, POW and MM oversaw all data collection. LDG analysed the data with input from FC and OC. LDG drafted the manuscript and all coauthors contributed revisions to the manuscript. All authors read and approved the final manuscript.

Funding This study was funded by Médecins Sans Frontières.

Disclaimer The funders of the study reviewed the study protocol but had no role in study design, data analysis or decision to publish.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval All study procedures were approved by the Research Ethics Committee of the London School of Hygiene and Tropical Medicine (No. 14425), the Kinshasa School of Public Health at the University of Kinshasa, DRC and the Comité National d'Ethique de la Santé, DRC (No. 67/CNES/BN/PMMF/2018). The international ethics board of Médecins Sans Frontières provided approval of a generic protocol for the study (No. 1805b).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article or uploaded as supplementary information. The original datasets with deidentified participant data are available upon request from the corresponding author. The original datasets with deidentified participant data are available upon request from the corresponding author.

ORCID iD

Lauren D'Mello-Guyett http://orcid.org/0000-0002-8174-1737

REFERENCES

1 Ali M, Nelson AR, Lopez AL, *et al*. Updated global burden of cholera in endemic countries. *PLoS Negl Trop Dis* 2015;9:e0003832.
2 Ingelbeen B, Hendrickx D, Miwanda B, *et al*. Recurrent cholera outbreaks, Democratic Republic of the Congo, 2008-2017. *Emerg Infect Dis* 2019;25:856–64.

3 WHO. Cholera 2017. *Weekly Epidemiological Record* 2018;38:489–500.
4 Zarocostas J. Mega-crisis in DR Congo. *Lancet* 2018;391:297–8.
5 Bompangue Nkoko D, Giraudoux P, Plisnier P-D, *et al*. Dynamics of cholera outbreaks in Great lakes region of Africa, 1978-2008. *Emerg Infect Dis* 2011;17:2026–34.
6 Bompangue D, Giraudoux P, Piarroux M, *et al*. Cholera epidemics, war and disasters around Goma and lake Kivu: an eight-year survey. *PLoS Negl Trop Dis* 2009;3:e436.
7 Talisuna AO, Okiro EA, Yahaya AA, *et al*. Spatial and temporal distribution of infectious disease epidemics, disasters and other potential public health emergencies in the world health organisation Africa region, 2016-2018. *Global Health* 2020;16:9.
8 Richterman A, Sainvilien DR, Eberly L, *et al*. Individual and household risk factors for symptomatic cholera infection: a systematic review and meta-analysis. *J Infect Dis* 2018;218:S154–64.
9 Spira WM, Khan MU, Saeed YA, *et al*. Microbiological surveillance of intra-neighbourhood E1 Tor cholera transmission in rural Bangladesh. *Bull World Health Organ* 1980;58:731–40.
10 Mosley WH, Ahmad S, Benenson AS, *et al*. The relationship of vibriocidal antibody titre to susceptibility to cholera in family contacts of cholera patients. *Bull World Health Organ* 1968;38:777–85.
11 Weil AA, Khan AI, Chowdhury F, *et al*. Clinical outcomes in household contacts of patients with cholera in Bangladesh. *Clin Infect Dis* 2009;49:1473–9.
12 Weil AA, Begum Y, Chowdhury F, *et al*. Bacterial shedding in household contacts of cholera patients in Dhaka, Bangladesh. *Am J Trop Med Hyg* 2014;91:738–42.
13 Harris JB, LaRocque RC, Qadri F, *et al*. Cholera. *Lancet* 2012;379:2466–76.
14 Merrell DS, Butler SM, Qadri F, *et al*. Host-Induced epidemic spread of the cholera bacterium. *Nature* 2002;417:642–5.
15 Hartley DM, Morris JG, Smith DL. Hyperinfectivity: a critical element in the ability of V. cholerae to cause epidemics? *PLoS Med* 2006;3:e7.
16 Domman D, Chowdhury F, Khan AI, *et al*. Defining endemic cholera at three levels of spatiotemporal resolution within Bangladesh. *Nat Genet* 2018;50:951–5.
17 Meszaros VA, Miller-Dickson MD, Baffour-Awuah F, *et al*. Direct transmission via households informs models of disease and intervention dynamics in cholera. *PLoS One* 2020;15:e0229837.
18 Debes AK, Ali M, Azman AS, *et al*. Cholera cases cluster in time and space in Matlab, Bangladesh: implications for targeted preventive interventions. *Int J Epidemiol* 2016;45:dyw267–9.
19 Finger F, Bertuzzo E, Luquero FJ, *et al*. The potential impact of case-area targeted interventions in response to cholera outbreaks: a modeling study. *PLoS Med* 2018;15:e1002509.
20 Bi Q, Azman AS, Satter SM, *et al*. Micro-Scale spatial clustering of cholera risk factors in urban Bangladesh. *PLoS Negl Trop Dis* 2016;10:e0004400.
21 Sugimoto JD, Koepke AA, Kenah EE, *et al*. Household transmission of Vibrio cholerae in Bangladesh. *PLoS Negl Trop Dis* 2014;8:e3314.
22 MSF. *Management of a cholera epidemic. Médecins sans Frontières*, 2017.
23 UNICEF. *Cholera toolkit*. New York, USA: United Nations Children's Fund, 2013.
24 ACF. *Manuel Pratique: Eau, Assainissement, Hygiène dans La Lutte Contre Le Choléra*. Paris, France: Action Contre la Faim, 2013.
25 Oxfam. *Cholera outbreak guidelines: preparedness, prevention and control*. Oxford, UK: Oxfam, 2012.
26 ICDDR'B. *Cots program 2.0*. Dhaka, Bangladesh, 2018.
27 D'Mello-Guyett L, Gallandat K, Van den Bergh R, *et al*. Prevention and control of cholera with household and community water, sanitation and hygiene (wash) interventions: a scoping review of current international guidelines. *PLoS One* 2020;15:e0226549.
28 Global Task Force on Cholera Control. *Cholera outbreak response: field manual (January 2019 Prepress copy*. Geneva, Switzerland: WHO, 2019.
29 Sphere. *The sphere project: humanitarian charter and minimum standards in humanitarian response*. Geneva, Switzerland, 2018.
30 WHO. *Cholera outbreak, assessing the outbreak response and improving preparedness*. Geneva, Switzerland: World Health Organisation, 2004.
31 George CM, Monira S, Sack DA, *et al*. Randomized controlled trial of hospital-based hygiene and water treatment intervention (CHoBI7) to reduce cholera. *Emerg Infect Dis* 2016;22:233–41.
32 Shannon K, Hast M, Azman AS, *et al*. Cholera prevention and control in refugee settings: successes and continued challenges. *PLoS Negl Trop Dis* 2019;13:e0007347.
33 Ratnayake R, Finger F, Edmunds WJ, *et al*. Early detection of cholera epidemics to support control in fragile states: estimation of delays and potential epidemic sizes. *BMC Med* 2020;18:397.
34 Ratnayake R, Finger F, Azman AS, *et al*. Highly targeted spatiotemporal interventions against cholera epidemics, 2000-19: a scoping review. *Lancet Infect Dis* 2021;21:e37–48.
35 Rebaudet S, Bulit G, Gaudart J, *et al*. The case-area targeted rapid response strategy to control cholera in Haiti: a four-year implementation study. *PLoS Negl Trop Dis* 2019;13:e0007263.
36 von Seidlein L, Deen JL. Preventing cholera outbreaks through early targeted interventions. *PLoS Med* 2018;15:e1002510.
37 Roskosky M, Acharya B, Shakya G, *et al*. Feasibility of a comprehensive targeted cholera intervention in the Kathmandu Valley, Nepal. *Am J Trop Med Hyg* 2019;100:1088–97.
38 Bruckner C, Checchi F. Detection of infectious disease outbreaks in twenty-two fragile states, 2000-2010: a systematic review. *Confl Health* 2011;5:13.
39 White S, Thorseth AH, Dreibelbis R, *et al*. The determinants of handwashing behaviour in domestic settings: an integrative systematic review. *Int J Hyg Environ Health* 2020;227:113512.
40 Friedrich MND, Binkert ME, Mosler H-J. Contextual and psychosocial determinants of effective handwashing technique: recommendations for interventions from a case study in Harare, Zimbabwe. *Am J Trop Med Hyg* 2017;96:430–6.
41 Curtis VA, Danquah LO, Aunger RV. Planned, motivated and habitual hygiene behaviour: an eleven country review. *Health Educ Res* 2009;24:655–73.
42 George CM, Biswas S, Jung D, *et al*. Psychosocial factors mediating the effect of the CHoBI7 intervention on handwashing with soap: a randomized controlled trial. *Health Educ Behav* 2017;44:1090198116683141.
43 D'Mello-Guyett L, Greenland K, Bonneville S, *et al*. Distribution of hygiene kits during a cholera outbreak in Kasaï-Oriental, Democratic Republic of Congo: a process evaluation. *Confl Health* 2020;14:51.
44 Spiegel P, Ratnayake R, Hellman N, *et al*. Responding to epidemics in large-scale humanitarian crises: a case study of the cholera response in Yemen, 2016-2018. *BMJ Glob Health* 2019;4:e001709.
45 Yates T, Vujcic JA, Joseph ML, *et al*. Water, sanitation, and hygiene interventions in outbreak response: a synthesis of evidence. *Waterlines* 2018;37:5–30.
46 Azurin JC, Alvero M. Field evaluation of environmental sanitation measures against cholera. *Bull World Health Organ* 1974;51:19–26.
47 Colwell RR, Huq A, Islam MS, *et al*. Reduction of cholera in Bangladeshi villages by simple filtration. *Proc Natl Acad Sci U S A* 2003;100:1051–5.
48 Conroy RM*et al*. Solar disinfection of drinking water protects against cholera in children under 6 years of age. *Arch Dis Child* 2001;85:293–5.
49 Deb BC, Sircar BK, Sengupta PG, *et al*. Studies on interventions to prevent eltor cholera transmission in urban slums. *Bull World Health Organ* 1986;64:127–31.
50 Huq A, Yunus M, Sohel SS, *et al*. Simple sari cloth filtration of water is sustainable and continues to protect villagers from cholera in Matlab, Bangladesh. *MBio* 2010;1.
51 Bompangue D, Moore S, Taty N, *et al*. Description of the targeted water supply and hygiene response strategy implemented during the cholera outbreak of 2017-2018 in Kinshasa, DRC. *BMC Infect Dis* 2020;20:226.
52 Gartley M, Valeh P, de Lange R, *et al*. Uptake of household disinfection kits as an additional measure in response to a cholera outbreak in urban areas of Haiti. *J Water Health* 2013;11:623–8.
53 Taylor DL, Kahawita TM, Cairncross S, *et al*. The impact of water, sanitation and hygiene interventions to control cholera: a systematic review. *PLoS One* 2015;10:e0135676.
54 Lantagne D, Yates T. Household water treatment and cholera control. *J Infect Dis* 2018;218:S147–53.
55 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 28*. Kinshasa, DRC: Ministère de la Santé, 2018.
56 Cholera Platform. *Cholera outbreaks in central and West Africa cholera: 2018 updates week 34*, 2018.
57 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 35*. Kinshasa, DRC: Ministère de la Santé, 2018.
58 WASH Cluster. *Reunion de cluster WASH- Mbuji Mayi, S41. Mbuji Mayi, Kasaï-Oriental*, 2018.
59 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 38*. Kinshasa, DRC: Ministère de la Santé, 2018.
60 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 33*. Kinshasa, DRC: Ministère de la Santé, 2018.
61 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 32*. Kinshasa, DRC: Ministère de la Santé, 2018.

62 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 29*. Kinshasa, DRC: Ministère de la Santé, 2018.
63 PNECHOL-MD. *Situation épidémiologique Du choléra en RDC à La Semaine 30*. Kinshasa, DRC: Ministère de la Santé, 2018.
64 WASH Cluster. *Reunion de cluster WASH- Mbuji Mayi, S46. Mbuji Mayi, Kasaï-Oriental*, 2018.
65 Mwaba J, Ferreras E, Chizema-Kawesa E, *et al*. Evaluation of the SD Bioline cholera rapid diagnostic test during the 2016 cholera outbreak in Lusaka, Zambia. *Trop Med Int Health* 2018;23:834–40.
66 Matias WR, Julceus FE, Abelard C, *et al*. Laboratory evaluation of immunochromatographic rapid diagnostic tests for cholera in Haiti. *PLoS One* 2017;12:e0186710.
67 Bwire G, Orach CG, Abdallah D, *et al*. Alkaline peptone water enrichment with a dipstick test to quickly detect and monitor cholera outbreaks. *BMC Infect Dis* 2017;17:726.
68 George CM, Rashid M-U, Sack DA, *et al*. Evaluation of enrichment method for the detection of Vibrio cholerae O1 using a rapid dipstick test in Bangladesh. *Trop Med Int Health* 2014;19:301–7.
69 Ontweka LN, Deng LO, Rauzier J, *et al*. Cholera rapid test with enrichment step has diagnostic performance equivalent to culture. *PLoS One* 2016;11:e0168257.
70 JMP. WHO/UNICEF joint monitoring programme for water supply, sanitation and hygiene. Available: https://washdata.org/monitoring
71 WHO. *Guidelines for drinking water quality*. 4th edition, 2017: 631.
72 Médecins Sans Frontières. *Public health engineering in precarious situations*. 2nd edn. Paris, France, 2010.
73 WHO. Diarrhoea. Available: https://www.who.int/topics/diarrhoea/en/
74 Pickering AJ, Julian TR, Mamuya S, *et al*. Bacterial hand contamination among Tanzanian mothers varies temporally and following household activities. *Trop Med Int Health* 2011;16:233–9.
75 Pickering AJ, Julian TR, Marks SJ, *et al*. Fecal contamination and diarrheal pathogens on surfaces and in soils among Tanzanian households with and without improved sanitation. *Environ Sci Technol* 2012;46:5736–43.
76 Bick S, Perieres L, D'Mello-Guyett L, *et al*. Risk factors for child food contamination in low-income neighbourhoods of Maputo, Mozambique: an exploratory, cross-sectional study. *Matern Child Nutr* 2020;16:e12991.
77 United States Environmental Protection Agency. Method. *1600: enterococci in water by membrane filtration using membraneEnterococcus Indoxyl-β-D-Glucoside agar (mEI) (EPA-821-R-06-009*, 2002.
78 DHS. StatCompiler: the DHS program. Available: http://www.statcompiler.com/en/
79 Litanga P. What next for the Dr Congo after the disputed election? *ALJAZEERA* 2019.
80 GTFCC. *Cholera roadmap research agenda*. Geneve, Switzerland: World Health Organization, 2020.
81 D'Mello-Guyett L, Yates T, Bastable A, *et al*. Setting priorities for humanitarian water, sanitation and hygiene research: a meeting report. *Confl Health* 2018;12:22.
82 Howe LD, Hargreaves JR, Huttly SRA. Issues in the construction of wealth indices for the measurement of socio-economic position in low-income countries. *Emerg Themes Epidemiol* 2008;5:3.
83 Vyas S, Kumaranayake L. Constructing socio-economic status indices: how to use principal components analysis. *Health Policy Plan* 2006;21:459–68.
84 Tsai K, Simiyu S, Mumma J, *et al*. Enteric pathogen diversity in infant foods in low-income neighborhoods of Kisumu, Kenya. *Int J Environ Res Public Health* 2019;16:506.
85 Doza S, Jabeen Rahman M, Islam MA, *et al*. Prevalence and association of Escherichia coli and diarrheagenic Escherichia coli in stored foods for young children and flies caught in the same households in rural Bangladesh. *Am J Trop Med Hyg* 2018;98:1031–8.
86 Glass RI, Becker S, Huq MI, *et al*. Endemic cholera in rural Bangladesh, 1966-1980. *Am J Epidemiol* 1982;116:959–70.
87 Greenland K, Chipungu J, Chilekwa J, *et al*. Disentangling the effects of a multiple behaviour change intervention for diarrhoea control in Zambia: a theory-based process evaluation. *Global Health* 2017;13:78.
88 George CM, Zohura F, Teman A, *et al*. Formative research for the design of a scalable water, sanitation, and hygiene mobile health program: CHoBI7 mobile health program. *BMC Public Health* 2019;19:1028.
89 Lessler J, Moore SM, Luquero FJ, *et al*. Mapping the burden of cholera in sub-Saharan Africa and implications for control: an analysis of data across geographical scales. *Lancet* 2018;391:1908–15.
90 Lee EC, Azman AS, Kaminsky J, *et al*. The projected impact of geographic targeting of oral cholera vaccination in sub-Saharan Africa: a modeling study. *PLoS Med* 2019;16:e1003003.
91 Ratnayake R, Tammaro M, Tiffany A, *et al*. People-centred surveillance: a narrative review of community-based surveillance among crisis-affected populations. *Lancet Planet Health* 2020;4:e483–95.
92 Azman AS, Moore SM, Lessler J. Surveillance and the global fight against cholera: setting priorities and tracking progress. *Vaccine* 2020;38:A28–30.
93 Ager A, Burnham G, Checchi F, *et al*. Strengthening the evidence base for health programming in humanitarian crises. *Science* 2014;345:1290–2.
94 Blanchet K, Ramesh A, Frison S, *et al*. Evidence on public health interventions in humanitarian crises. *Lancet* 2017;390:2287–96.
95 Falb K, Laird B, Ratnayake R, *et al*. The ethical Contours of research in crisis settings: five practical considerations for academic institutional review boards and researchers. *Disasters* 2019;43:711–26.
96 Wolf J, Hunter PR, Freeman MC, *et al*. Impact of drinking water, sanitation and handwashing with soap on childhood diarrhoeal disease: updated meta-analysis and meta-regression. *Trop Med Int Health* 2018;23:508–25.
97 Ram PK, Jahid I, Halder AK, *et al*. Variability in hand contamination based on serial measurements: implications for assessment of hand-cleansing behavior and disease risk. *Am J Trop Med Hyg* 2011;84:510–6.
98 Gallandat K, Huang A, Rayner J, *et al*. Household spraying in cholera outbreaks: Insights from three exploratory, mixed-methods field effectiveness evaluations. *PLoS Negl Trop Dis* 2020;14:e0008661.
99 Kumar S, Loughnan L, Luyendijk R, *et al*. Handwashing in 51 countries: analysis of proxy measures of handwashing behavior in multiple indicator cluster surveys and demographic and health surveys, 2010–2013. *Am J Trop Med Hyg* 2017;97:447–59.
100 Biran A, Schmidt W-P, Wright R, *et al*. The effect of a soap promotion and hygiene education campaign on handwashing behaviour in rural India: a cluster randomised trial. *Trop Med Int Health* 2009;14:1303–14.
101 Contzen N, De Pasquale S, Mosler H-J. Over-Reporting in handwashing Self-Reports: potential explanatory factors and alternative measurements. *PLoS One* 2015;10:e0136445.
102 Freeman MC, Stocks ME, Cumming O, *et al*. Hygiene and health: systematic review of handwashing practices worldwide and update of health effects. *Trop Med Int Health* 2014;19:906–16.
103 Azman AS, Luquero FJ, Salje H, *et al*. Micro-hotspots of risk in urban cholera epidemics. *J Infect Dis* 2018;218:1164–8.