BMJ Open

WASH Upgrades for Health in Amhara (WUHA): study protocol for a cluster-randomised trial in Ethiopia

D M _ r ,[1] Ar .[2] _ r ,[3] J M ,[1] Kr A
1,10

To cite: Wittberg DM, Aragie S, Tadesse W, . WASH Upgrades for Health in Amhara (WUHA): study protocol for a cluster-randomised trial in Ethiopia. *BMJ 0* 2021;**11**:e039529. doi:10.1136/bmjopen-2020-039529

3 Prepublication history and additional materials for this aper is available online. To w these les, please visit urnal online (http://dx.doi. 1136/bmjopen-2020-

ril 2020
ber 2020
2021

ABSTRACT

Introduction Facial hygiene promotion and environmental improvements are central components of the global trachoma elimination strategy despite a lack of experimental evidence supporting the effectiveness of water, sanitation and hygiene (WASH) measures for reducing trachoma transmission. The objective of the WUHA (WASH Upgrades for Health in Amhara) trial is to evaluate if a comprehensive water improvement and hygiene education programme reduces the prevalence of ocular chlamydia infection in rural Africa.

For numbered af liations see end of article.

Correspondence to
Dr Jeremy D Keenan;
jeremy.keenan@ucsf.edu

sufficient for elimination in areas with hyperendemic trachoma.[3–10]

Facial hygiene promotion and environmental improvements (ie, the 'F' and 'E' components of SAFE) are thought to be important for trachoma elimination.[11 12] However, evidence supporting the efficacy of non-antibiotic measures for preventing transmission of ocular chlamydia comes primarily from observational studies, with no confirmatory randomised trials to date.[13–16] Moreover, very few studies have implemented a comprehensive water, sanitation and hygiene (WASH) package with a trachoma endpoint, even though many believe that only the full SAFE strategy will be effective to prevent transmission of trachoma.[17 18]

WASH Upgrades for Health in Amhara (WUHA) is an ongoing cluster-randomised trial sponsored by the National Eye Institute to test the efficacy of a comprehensive WASH intervention for trachoma. The trial's ultimate goal is to support evidence-based decision-making for trachoma programme managers.

Objectives

This study aims to determine the efficacy of a comprehensive WASH package for reducing ocular chlamydia infection and trachoma.

METHODS AND ANALYSIS

Trial design

WUHA is a parallel-group, cluster-randomised trial in which 20 clusters receive a comprehensive WASH package and 20 control clusters do not receive a WASH intervention until the conclusion of the trial. Mass antibiotics are

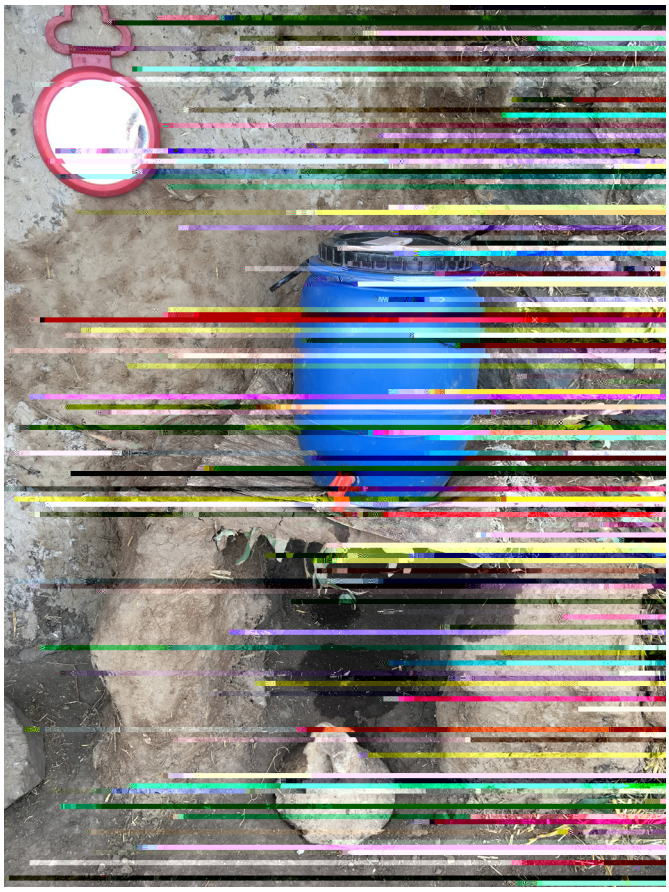

Figure 1 H

starting after the month 36 visit (ie, WUHA II), allowing a comparison of antibiotics plus WASH versus antibiotics alone. All individuals enumerated on the 36-, 48-, 60- and 72-month censuses receive a single oral dose of azithromycin (20 mg / kg for children using height-based approximation; 1 g for adults), except children under 6 months, pregnant women and those allergic to macrolides, who are offered a 6-week course of ophthalmic tetracycline two times a day instead.[21]

Community-based interventions

These aspects of the intervention are available for anyone in the community, regardless of whether they are enumerated on the census.

C mmu

A geohydrological survey identifies the most promising area to construct a water point in each randomisation unit. The water point (eg, hand-dug well, capped spring or shallow borehole) is constructed during the first year post-randomisation. Each study cluster forms a water committee, and members receive basic training in maintenance after construction of the water point. Water point implementation is conducted by Catholic Relief Services and the local Ethiopian nongovernmental organisation Water Action.

Su m m

Annual hygiene trainings are performed for government-appointed health extension workers, women's health development army members and local priests to help facilitate hygiene messages. A kick-off event is held at the unveiling of the water point to review the hygiene messages and gain community buy-in.

School-based interventions

Primary schools are targeted for hygiene education because children are the main transmitters of ocular chlamydia.[22 23] Efforts are made to encourage children to disseminate their hygiene knowledge to other members of their households.

Cu.. u um

A primary school hygiene curriculum designed by the investigators specifically for the study consists of five to six age-appropriate lesson plans per year for grades 1 through 4. Lesson plans cover a wide array of topics, including face-washing, hand-washing and latrine use (online supplemental file 3). Curriculum development was iterative, with several rounds of feedback from teachers and health officials as well as thorough pilot-testing with teachers and students in the study area. Teachers are trained in the curriculum before each school year.

ASH u

Primary schools in this region of Ethiopia offer extracurricular clubs moderated by teachers, including WASH clubs. We provide training materials for WASH activities (eg, songs, dances, dramas, community engagement activities) to existing WASH club leaders and work with principals of schools to ensure that WASH clubs are formed if they do not already exist.

WASH process indicators: intervention clusters

The RE-AIM framework (Reach, Efficacy, Adoption, Implementation and Maintenance) is used to assess whether the WASH interventions are being implemented as planned.[24 25] Intervention uptake is summarised for each community, results are reviewed with hygiene coordinators and HPWs, and specific actions taken in communities with deficiencies.

H - -

The study's hygiene coordinator conducts biannual spot-checks in each intervention cluster throughout the duration of the intervention. Spot-checks are designed to determine uptake of the school hygiene curriculum, usability of the study water point, presence and functionality of household latrines and wash stations, and practice of the targeted hygiene behaviours. A random sample of eight households with pre-school children per cluster is visited at each spot-check to document the presence of a wash station and its functionality (eg, presence of water in the container and soap), the presence of a latrine and its functionality (eg, whether walls and a roof are present),

a Samsung Galaxy NX camera equipped with a 60 mm *f* / 2.8 macro lens (Seoul, South Korea), with camera settings set automatically by the mobile application (ISO 400, native flash engaged, automatic white balance, aperture priority, *f* / 11 for face, *f* / 32 for conjunctiva). Photographs are uploaded to a secure server (Salesforce.com, San Francisco, CA) and eventually graded at a grading centre at the University of Gondar (Gondar, Ethiopia). Photo-graders masked to treatment allocation, study visit and participant identifier assign clinical trachoma grades to each eye using a modification of previously described grading systems.[26 27] Photographs from baseline and the final visit are also presented side-by-side to photo-graders masked to treatment allocation and study visit, and the more severe clinical presentation is noted.

B m

Blood from a finger stick is applied to five of six ears of a TropBio filter paper disk (Cellabs, Sydney, Australia), allowed to air dry and then placed in plastic bags with desiccant packets. Dried blood spots are stored at −20°C until shipped to the US Centers for Disease Control and Prevention (Atlanta, GA) for serologic testing, including for the chlamydial antibodies pgp3 and CT694.[28]

S m

A container with a plastic bag liner is given to participants or their caregiver with instructions to provide a stool sample. Participants unable to produce stool take the materials home and are instructed to collect a stool sample the following morning, which is retrieved by study personnel later that day. Fresh stool samples are divided into two specimen containers in the field, with 1 g transferred to a tube with 10 mL sodium acetate–acetic acid–formalin (SAF) and 500 mg transferred to an empty tube subsequently filled with 500 mL 5% potassium dichromate. Stool samples are stored and transported similarly to conjunctival swabs; the samples stored in SAF are processed at the Amhara Public Health Institute for ova and parasites and the samples stored in potassium dichromate are processed at Smith College (Northampton, MA) with a PCR assay for soil-transmitted helminths.[29]

N m

A FLOQSwab (COPAN Diagnostics, Murrieta, CA) is inserted approximately 10 mm through the right nostril, then twisted at the posterior aspect of the nasopharynx. The swab is stored in a tube with skim milk–tryptone–glucose–glycerine (STGG) media. Tube storage and transport is similar to conjunctival swabs. Nasopharyngeal swabs are processed at the Amhara Public Health Institute; standard microbiological methods are used to isolate *Streptococcus pneumoniae* and then a disk diffusion assay used to determine antimicrobial resistance to penicillin, azithromycin, tetracycline, and clindamycin.

A m

A wooden stadiometer (Schorr Productions, Olney, MD, USA) is used to measure standing height for children who can stand or recumbent length for those who cannot. A Seca 874 floor scale (Seca, Hamburg, Germany) is used for weight measurements. Both height and weight are taken in triplicate, with the median value used for analyses.

Data collection, management and analysis

Data collection

Census and examination data are collected on mobile devices using a custom-designed software application (Conexus, Los Gatos, CA) and then uploaded to a relational database on Salesforce.com (Salesforce, San Francisco, CA). The data can be monitored in real time via customisable dashboards on the Salesforce website. Data from spot-checks are collected with a Research Electronic Data Capture (REDCap) mobile application and uploaded to a database stored at the University of California, San Francisco. Structured observation data are collected on paper and entered into a REDCap database.

Statistical methods

Sample size

Power calculations are based on a cluster-level two-sample t-test and assume a SD of 10% in the community-specific prevalence of ocular chlamydia based on a prior trial in Ethiopia, a significance level of 5% and no clusters lost to follow-up.[14] Under these assumptions, 22 communities per arm would be required to achieve 80% power to detect an 8% difference in ocular chlamydia between the two arms. However, due to a severe drought in the study area at the beginning of the trial, only 40 potential water points could be identified. The sample size was thus reduced to 20 per arm, providing 79% power (ie, 3% less power than the originally planned sample size) to detect an 8% effect size.

Primary analysis

Post-baseline cluster-specific prevalences of ocular chlamydia are modelled in a mixed-effects linear regression model that includes treatment allocation, time since baseline in months and baseline chlamydia prevalence as fixed effects, and a random intercept for cluster. The treatment by time interaction term is included only if it is statistically significant, in which case statistical significance will be determined from the deviance statistic contrasting the model with all terms versus the model without the treatment and treatment-by-time interaction terms. More details are available in the statistical analysis plan (online supplemental file 5).

Secondary analyses

Secondary outcomes will be analysed at the cluster level with a similar approach to the primary outcome. Chlamydial load and helminth density will be analysed as a cluster-specific index. Worsening of clinical trachoma will be assessed in an individual-level analysis of the cohort of children aged 0–5 years at baseline using a mixed-effects logistic regression model with a random intercept for the cluster term. Anthropometric outcomes will also be assessed in the cohort of children 0–5 years old

at baseline, and modelled in an individual-level analysis using a mixed-effects linear regression with a random intercept and slope for children nested in cluster.

Signi□cance testing

Monte Carlo permutation at the cluster level will be implemented, with a two-sided alpha level of 0.05 for each phase of the study (ie, WUHA I and WUHA II).

Cost analysis

The costs of all aspects of the intervention will be tabulated during the study for use in cost-effectiveness analyses.

Monitoring

2 M P, P R, R . : G E 2020 (GE 2020). *Am J Trop Med Hyg* 2003;69:33 5.
3 B RL, A P, HC, *et al*. R . *Lancet* 1993;342:453 6.
4 J, K, M D, *et al*. A . *Lancet* 1999;354:630 5.
5 H JI, A B, P C, *et al*. A : . *Lancet* 2009;373:1111 8.
6 A, H MJ, A NDE, *et al*. M . *N Engl J Med* 2004;351:1962 71.
7 C JD, A , M M, *et al*. E