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Short Report: The Association between Latrine Use and Trachoma: A Secondary Cohort Analysis from a Randomized Clinical Trial

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Abstract. Latrine use has been promoted as a component of an integrated strategy for trachoma control. As part of a randomized trial in Ethiopia, 12 communities received a mass azithromycin distribution followed by a latrine promotion intervention. A random sample of children ages 0–9 years in each community was monitored longitudinally for ocular chlamydia. After latrine construction ended, those communities with a higher proportion of households using latrines were more likely to experience a reduction in the prevalence of ocular chlamydia. Specifically, for each 10% increase in latrine use, there was a 2.0% decrease (95% confidence interval = 0.2–3.9% decrease) in the community prevalence of ocular chlamydia over the subsequent year ($P = 0.04$).

INTRODUCTION

Efforts to eliminate trachoma, the leading infectious cause of blindness, have revolved around a comprehensive approach known as the surgery, antibiotics, facial cleanliness, and environmental improvements (SAFE) strategy.[1] Improvements in sanitation, including latrine construction, have been among the most promoted environmental improvements, because improved sanitation facilities reduce the density of the eye-seeking flies thought to be important for chlamydial transmission.[2–7]

In a previously reported clinical trial, we randomized 12 communities to a latrine promotion intervention and another 12 communities to no latrine promotion.[8] The primary intention-to-treat analysis found no difference in ocular chlamydia between the two groups. However, adoption of latrines was not uniformly high in the communities randomized to latrine promotion. This result prompted us to perform a non–pre-specified secondary analysis to determine whether the prevalence of ocular chlamydia was related to the proportion of households using latrines.

METHODS

The study was conducted in the Amhara region of Ethiopia from May of 2006 to July of 2008; 72 subkebeles (administrative units consisting of approximately 1,500 people) were randomized to one of six study arms: a single mass azithromycin distribution, a single mass azithromycin distribution plus latrine promotion, repeated annual mass azithromycin distributions, repeated biannual mass azithromycin distributions, quarterly azithromycin to children, or delayed treatment.[8–10] We restricted the current analysis to the only study arm that received the latrine promotion intervention to determine whether latrine uptake was associated with subsequent ocular chlamydia. We monitored for ocular *Chlamydia trachomatis* infection and clinically active trachoma in a random sample of children from a randomly chosen sentinel state team (administrative subdivision of the subkebele consisting of approximately 200–400 people) from each of 12 subkebeles in the latrine promotion arm at baseline and 12 and 24 months.

All individuals ≥ 1 year of age were offered a single dose of directly observed oral azithromycin several weeks after the baseline monitoring visit. Subsequently, health extension workers intensified an existing latrine promotion program as described previously.[8] Latrine construction started 6 months after the baseline monitoring visit and continued for 6 months. Participation in the program was voluntary, and there were no financial incentives.

We randomly selected 10 households per sentinel state team for a latrine survey and inspection at 12 months; households were selected regardless of whether they participated in the latrine promotion program.[8] The exposure variable of interest for the current study was recent latrine use, defined as the presence of fresh feces in the latrine pit as observed by a trained survey administrator.

At each monitoring visit, we examined and swabbed the upper right tarsal conjunctiva of 50 randomly selected children ages 0–9 years from each sentinel state team.[8] We defined clinically active trachoma as follicular trachoma (TF) and/or intense inflammatory trachoma (TI) according to the World Health Organization (WHO) simplified grading system; grading was validated as described previously.[11,12] The prevalence of ocular chlamydia in each sentinel state team was estimated from pooled swabs using the AMPLICOR polymerase chain reaction assay (Roche Diagnostics, Branchburg, NJ).[13]

To account for clustering, we performed all analyses at the community (i.e., state team) level. We performed univariate linear regression to assess the association between the proportion of households using a latrine at month 12 and the change in the prevalence of ocular chlamydia in the subsequent year (i.e., from month 12 to 24). Because of the limited sample size, we could not account for all potential confounders in a single model. Therefore, we sequentially added a single confounding variable to the regression model to assess the magnitude of change in the regression coefficient. We performed similar analyses for the secondary outcome of change in TF/TI from month 12 to 24. We used Stata 10 (Statacorp, College Station, TX) for all analyses.

The study was approved by the University of California, San Francisco Committee on Human Research, the Ethiopian

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Science and Technology Commission, and Emory University. Informed consent in Amharic was obtained for all participants.

RESULTS

As reported previously, the median baseline prevalence of ocular chlamydia in children ages 0–9 years in 12 sentinel communities was 39.6% (interquartile range [IQR] = 31.9–57.1%).[8] A mass azithromycin distribution of all community members was conducted several weeks later, with a median antibiotic coverage of 82.9% (IQR = 77.1–87.7%). Latrine promotion activities took place successfully in all 12 subkebeles over the subsequent year. At the 12-month study visit, the median prevalence of ocular chlamydia had decreased to 13.1% (IQR = 7.7–14.8%). At this time, the proportion of households with recent latrine use on inspection ranged from 20% (95% CI = 2.5–55.6%) to 90% (95% CI = 55.5–99.7%) (Figure 1). Over the next 12 months, the prevalence of ocular chlamydia infection increased by a median of 2.0% (IQR = 2.7% reduction to 6.6% increase).

In univariate analyses, we found a correlation between the proportion of households with evidence of recent latrine use at 12 months and the change in prevalence of ocular chlamydia over the subsequent year (2.0% decrease [95% CI = 0.2–3.9% decrease] in the community prevalence of ocular chlamydia for each 10% increase in community latrine use, $P = 0.04$). The inclusion of several potential confounders did not change the magnitude of the association (Table 1). In contrast, we found no association between the proportion of households using a latrine and the change in the prevalence of TF/TI over the subsequent year (Figure 1 and Table 1).

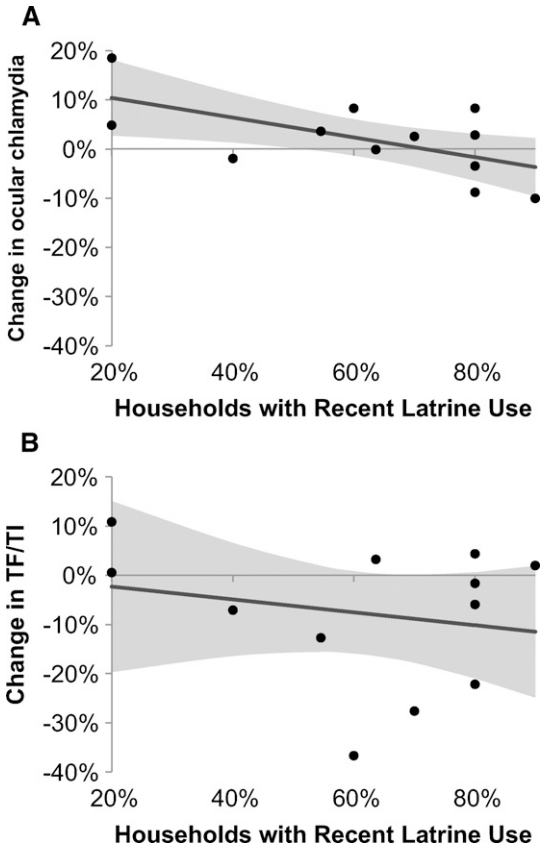

FIGURE 1. Scatter plot of the proportion of households using a latrine versus the change in the prevalence of (**A**) ocular *Chlamydia* and (**B**) clinically active trachoma in 12 months after assessment of latrine use. Clinically active trachoma was defined as TF and/or TI according to the simplified WHO grading system. The dark grey line represents the regression line, and the light grey bars are the 95% CIs.

TABLE 1

Multivariate sensitivity analyses assessing the influence of various confounders on the association between latrine use and trachoma

Covariate included in regression model	Change in prevalence of ocular *chlamydia* per 10% increase in latrine use	Change in prevalence of clinically active trachoma per 10% increase in latrine use
No covariate	–2.0% (–3.9% to –0.2%)	–1.3% (–5.5% to 2.9%)
Elevation, m	–2.2% (–5.1% to 0.6%)	0.4% (–6.0% to 6.7%)
Distance to city, km	–3.3% (–5.5% to –1.1%)	–2.6% (–8.4% to 3.3%)
Distance to road, km	–2.2% (–4.8% to 0.4%)	–0.3% (–6.0% to 5.5%)
Percent ages 0–9 years	–2.4% (–4.4% to –0.3%)	–0.0% (–4.2% to 4.3%)
Percent female	–2.1% (–4.1% to –0.1%)	–2.4% (–5.2% to 0.3%)
Population	–1.8% (–3.9% to 0.3%)	–0.5% (–5.1% to 4.1%)

Values represent the regression coefficient for latrine use; coefficients for each of the individual covariates are not shown.

DISCUSSION

In this secondary analysis of a randomized clinical trial, we found that the higher the proportion of households using a latrine, the greater the reduction in ocular chlamydia in the community over the subsequent year. This association could not be attributed to several measured confounders.

Latrines have long been considered an important intervention for trachoma control. Cross-sectional studies have consistently found that lack of a household latrine is a risk factor for trachoma.[14–20] A randomized trial found that latrines reduced the burden of the eye-seeking fly *Musca sorbens*, a likely vector for ocular chlamydia.[3] However, there have been few longitudinal interventional studies that have assessed ocular chlamydia as an outcome, and it is possible that the relationship between latrine ownership and trachoma is simply a result of confounding: poorer households may be less likely to have a latrine and more likely to have trachoma. In the current study, the proportion of households using a latrine was a significant predictor of the change in ocular chlamydial infection over the subsequent year. The longitudinal nature of this study provides a higher level of evidence for a causal relationship between latrine use and trachoma than previous cross-sectional studies.

It is important to note that the randomized trial comparing these 12 communities to 12 control communities did not find a significant difference in ocular chlamydia in the two treatment arms, despite a much higher level of latrine use in the latrine promotion communities (average of 61.5%) compared with the control communities (average of 15.8%).[8] The randomized nature of the trial greatly reduced the influence of unmeasured confounders and therefore represents the best way to test the hypothesis without bias. However, despite being more prone to bias, this cohort study may also be more capable of detecting a true effect if latrine promotion only becomes effective after a high enough proportion of the community starts using latrines. It is plausible that this scenario could be the case, because the purpose of latrines is to reduce the community burden of flies, and a meaningful reduction in a

community's fly population may occur only after the vast majority of households have adopted latrines.

In contrast to the ocular chlamydia outcome, we found no relationship between latrine use and clinically active trachoma. The most likely reason for this finding is the long duration of clinically active trachoma, especially in areas with hyperendemic trachoma.[21] Thus, in this Ethiopian setting, a follow-up period of 1 year may not be sufficiently long enough to detect a reduction in the clinical signs of trachoma.

This study had several limitations. The sample size was relatively small. The latrine survey was performed in a sample of only 10 households per community, reducing the certainty of the latrine use estimates. Nonetheless, because these households were randomly selected, the estimate provides an unbiased measure of community latrine use. The presence of feces in the pit does not mean that all members of the household were using the latrine, and it does not guarantee that there was no disposal of feces outside of the latrine.[22] The intervention contained no education component, and therefore, it is possible that latrines were not used as intended. Finally, we measured only a small number of potential confounding variables, which limited the multivariate analyses.

This study provides some evidence that the degree to which latrines are adopted by a community may be important for trachoma control, although this finding should be interpreted with caution given the negative clinical trial result using the same data. Additional research will be important to better characterize the role of the combined SAFE package for trachoma control.

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