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School-Based versus Community-Based Sampling for Trachoma Surveillance

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Abstract. Trachoma surveillance is typically performed via random sampling of endemic districts. This strategy minimizes bias and allows examination of preschool children, but is also expensive. Surveillance for some other neglected tropical diseases is carried out in schools, which is logistically easier. In the present study, the prevalence of trachomatous inflammation–follicular (TF) from a population-based sample of children from each of 70 communities in Ethiopia was compared with the corresponding school-based estimate, which was calculated for each community by performing examinations in all primary schools in the district. The overall prevalence of TF was 39.1% (95% confidence interval [CI]: 35.0–43.1%) among children aged 1–9 years in the community-based sample and 18.8% (95% CI: 15.9–21.7%) among children in grades 1–3 of the school-based sample. School-based estimates of TF explained 35% of the variation in the community-based prevalences ($P < 0.001$). When TF prevalence was used as a diagnostic test for detecting a community with > 5% prevalence of ocular chlamydia, the area under the receiver operating characteristic curve was 0.73 (95% CI: 0.60–0.85) for the school-based sample and 0.71 (0.58–0.83) for the community-based sample ($P = 0.76$). Thus, although school-based monitoring was necessarily biased relative to population-based monitoring of 1- to 9-year olds, the two methods provided a similar amount of information about the community burden of ocular chlamydia in this trachoma-hyperendemic setting. The generalizability of these findings to areas with less prevalent trachoma is unclear.

INTRODUCTION

Trachoma elimination efforts require surveillance of endemic areas to make treatment decisions. The World Health Organization (WHO) currently recommends cluster random sampling at the district level for baseline mapping and impact surveys.[1] Although random sampling is rigorous and provides an unbiased assessment of the burden of trachoma in a district, it is also expensive. Surveillance for other neglected tropical diseases (NTDs), such as soil-transmitted helminths (STHs), schistosomiasis, and lymphatic filariasis (LF), incorporates school-based sampling, which is logistically easier and less expensive.[2,3] However, because the burden of trachoma is typically highest among preschool children, it is unclear whether school-based trachoma assessments would reflect the community prevalence of disease.[4,5] In the present study, we assess the relationship between community-based and school-based trachoma assessment to determine the level of bias introduced by purposefully sampling only school-aged children.

METHODS

General study design. This is an ancillary study of a cluster-randomized trial for trachoma (clinicaltrials.gov #NCT01202331). In the trial, we performed annual population-based assessment of trachoma in each of 72 communities in the Goncha Siso Enese *woreda*, Amhara region, Ethiopia. For the present study, we performed trachoma monitoring at primary schools in the study area at the same time as one of the trial monitoring visits and assessed the correlation between the school-based and the community-based sampling strategies. The study was approved by the Committee for Human Research at the University of California, San Francisco; the Emory University Institutional Review Board; and the Ethiopian Ministry of Science and Technology. The study was conducted in cooperation with the Goncha Siso Enese Department of Education; for the school-based sampling, we obtained verbal consent from the head of the Department of Education and each school principal, and verbal assent from each child. For the community-based sampling, we obtained verbal consent from each child's guardian and verbal assent for children 7 years and older.

Population-based trachoma assessment. In the trial, we randomized 72 communities in a single district to one of six different mass azithromycin treatment schedules and monitored annually for ocular chlamydia and clinically active trachoma. We performed an annual population census in all study communities before the monitoring and treatment visits. From this census, we randomly selected for examination 50 children aged 0–9 years, providing a 95% confidence interval (CI) width of ±14% assuming a prevalence of 40%. During the monitoring visit, an experienced trachoma grader everted the right upper tarsal conjunctiva of each participant to assess for trachomatous inflammation–follicular (TF) and intense trachomatous inflammation–intense (TI) according to the WHO simplified grading system. The grader then swabbed the everted tarsal conjunctiva with a Dacron swab.[6] Trachoma graders attended a training session before the monitoring visit and were only allowed to grade in the field if they achieved sufficient agreement with an expert trachoma panel (Cohen's $\kappa \geq 0.6$ on a series of 100 conjunctival photographs). The swabs were stored, transported, pooled, and processed as described elsewhere; we used the Abbott m2000 polymerase chain reaction platform (Abbott Laboratories, Abbott Park, IL) to assess pools of five swabs for ocular chlamydia and then calculated the prevalence of ocular chlamydia in each community using maximum likelihood methods.[7]

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School-based trachoma assessment. We performed school-based assessments in October 2013, at the same time as the annual monitoring visit of the trial. With the assistance of the Goncha Siso Enese woreda Education Office, we identified all primary schools in the study area. Each school served multiple communities. We recorded the age, gender, and community of residence for each child in grades 1 through 4, as reported by principals, teachers, and children. A member of the trachoma grading team from the population-based survey everted the upper right conjunctiva and graded for TF and TI using the WHO simplified grading system as described earlier; these field grades were used for the primary analyses. In addition, the grader took at least two high-quality conjunctival photographs of the everted upper right conjunctiva using a digital SLR camera (D-series camera, Nikon, Inc., Tokyo, Japan) with a 105/2.8*f* macro lens (aperture priority, *f*/32, international standards organization 400, native flash engaged, automatic white balance). Two ophthalmologists graded the photographs for TF and TI according to the WHO simplified grading system; discrepancies in assigned grades were resolved by a third ophthalmologist.[6] Of 2,617 children photographed, 31 (1.2%) had images deemed ungradable by at least two of the ophthalmologists. Agreement between the two primary graders was relatively high; Cohen's κ was 0.65 (95% CI: 0.61–0.69) for the grade of TF (219 of 2,586 photographs required the third ophthalmologist) and 0.66 (95% CI: 0.62–0.70) for the grade of TF and/or TI (245 of 2,586 photographs required the third ophthalmologist). The consensus photographic grade agreed with the field grade to a similar degree (κ for the grade of TF was 0.62, 95% CI: 0.58–0.65, and κ for the grade of TF and/or TI was 0.63, 95% CI: 0.60–0.67). Graders were masked to the identity of the school and community, to the prevalence of trachoma from community-based sampling, and to the grades assigned by the other graders.

Statistical methods. We calculated the prevalence of TF and the prevalence of TF and/or TI (TF/TI) in each community, separately for the school-based sample and the population-based sample. For the population-based sample, we calculated the prevalence among the 1- to 9-year-old population because the WHO recommends making treatment decisions based on this metric. For the school-based sample, we calculated the prevalence of TF and TF/TI for each community using educator- or child-reported community of residence. We reported average prevalence estimates using analytic weights to account for the number of children assessed at each school or community. We computed the difference in the school-based and community-based estimates of trachoma for each community and assessed the correlation of the two estimates with linear regression using analytic weights to account for the total number of children per community in the school-based sample. We assessed the accuracy of the school-based and community-based TF prevalence estimates for identifying communities with ocular chlamydia by constructing receiver operating characteristic (ROC) curves that used varying community prevalences of ocular chlamydia as the reference standard (e.g., > 0%, > 5%, and > 10%). We determined the optimal cut-point of school-based and community-based trachoma assessments by maximizing the sum of the sensitivity and specificity (i.e., the Youden index).[8]

RESULTS

We performed population-based trachoma monitoring in all 72 communities of the trial, with a mean of 43 children (95% CI: 41–45) aged 1–9 years per community. The mean prevalence of TF among 1- to 9-year olds was 37.6% (95% CI: 33.4–41.8%) and the mean prevalence of ocular chlamydia among 0- to 9-year olds was 9.6% (95% CI: 6.7–12.5%). We performed school-based trachoma monitoring at 40 schools representing 70 communities of the trial. Table 1 shows the characteristics of the school-based population stratified by grade. We examined an average of 37 children (95% CI: 32–42) per community. The mean prevalence of TF was lower than that in the community-based sample, ranging from 25.7% (21.0–30.3%) in grade 1 to 13.2% (10.0–16.4%) in grade 4 (Table 1). Although we collected data on all four primary school grades, we restricted subsequent analyses only to grades 1–3 (mean of 30 children per community, 95% CI: 26–34) because the prevalence in this subpopulation correlated best with that of the population-based sample. The prevalence of TF in the subpopulation of grades 1–3 was 22.0% (95% CI: 18.9–25.0%).

We calculated the difference between the school-based and population-based samples for each community to investigate systematic differences between the two sampling strategies. On average, the school-based sample from grades 1–3 underestimated the prevalence of TF relative to the 1- to 9-year-old community-based sample by 14.5% (95% CI: 1.1–17.8%; Figure 1). This was expected, given the mismatch in ages between the two sampling populations. In a second analysis, we compared only the subset of 7- to 12-year olds from each sampling strategy and found that the school-based sample (mean 34 children examined per community, 95% CI: 29–38) underestimated the prevalence of TF in these older children by 1.1% (95% CI: 4.0% underestimate to 2.0% overestimate) relative to the population-based sample (mean 23 children examined per community, 95% CI: 31–24). Of note, the most recent study census documented a mean of 52 (95% CI: 46–57) children aged 7–12 years per community, meaning that the number examined during the school-based sampling was on average 25.8% lower (95% CI: 13.3–38.3%) than the total number of children per community.

In a linear regression analysis weighted for the number of school-based examinations performed per community, the prevalence of TF in grades 1–3 explained just over one-third of the variation in the community prevalence of TF among 1- to 9-year olds ($R^2 = 0.35$; $P < 0.001$; Figure 2). Similar results were observed when TI was added to the outcome ($R^2 = 0.40$) or when photographic grades were used to determine the school-based prevalence of TF ($R^2 = 0.34$).

We constructed ROC curves to determine how school-based trachoma surveillance compared with community-based surveillance for detecting ocular chlamydia. We treated the prevalence of TF in grades 1–3 as the diagnostic test and categorized the prevalence of ocular chlamydia among 1- 9-year olds into three separate reference standards (> 0%, > 5%, and > 10%). Figure 3 shows the ROC curves and the trachoma prevalence cut-points that optimized the sensitivity and specificity for detecting ocular chlamydia. Although school-based cut-points were consistently lower than community-based cut-points, we detected no significant differences in the areas under the curve of the school-based and community-based monitoring ($P = 0.59$ for the 0% threshold, $P = 0.23$ for the 5% threshold, and $P = 0.96$ for the 10% threshold). Results were similar when using TF/TI as the diagnostic test or when using photographic grades to determine

TABLE 1
Characteristics of the school-based trachoma surveillance sample, stratified by grade level

	Grade 1, *N* = 697	Grade 2, *N* = 708	Grade 3, *N* = 683	Grade 4, *N* = 529
Class size (mean)	21.8 (15.8–27.7)	22.8 (16.5–29.2)	21.3 (15.5–27.2)	21.3 (15.5–27.2)
Age, years (mean)	7.9 (7.7–8.2)	9.2 (9.0–9.4)	10.5 (10.3–10.8)	11.5 (11.2–12.0)
Female (%)	45.3% (41.1–50.7%)	52.5% (49.2–55.7%)	55.3% (51.5–58.6%)	50.7% (45.9–55.1%)
TF (%)	25.7% (21.0–30.3%)	21.8% (17.5–26.0%)	18.4% (14.9–22.0%)	13.2% (10.0–16.4%)
TI (%)	3.0% (1.3–4.7%)	2.8% (1.6–4.1%)	1.8% (0.6–2.9%)	2.1% (0.7–3.5%)
TF and/or TI (%)	26.1% (21.4–30.8%)	22.0% (17.7–26.4%)	18.9% (15.3–22.5%)	14.4% (10.9–17.8%)

TF = trachomatous inflammation–follicular; TI = trachomatous inflammation–intense, as assessed by field graders.

the prevalence of clinically active trachoma (Supplemental Figure 1).

DISCUSSION

In this study of Ethiopian communities with hyperendemic trachoma, the prevalence of clinically active trachoma assessed in primary schools was significantly correlated with the prevalence obtained from a random sample of children from the community. The relationship was not perfect, with the school-based prevalences explaining just over one-third of the variance in the community-based samples. The source of the remaining variance is unclear but may include the different ages of the populations, measurement error, and chance. Despite the imperfect correlation, the school-based and community-based methods performed similarly in terms of determining the burden of ocular chlamydia in a community.

On average, the prevalence of clinically active trachoma assessed from schools underestimated the prevalence estimate from the community-based sample. This was expected because the community-based sample contains preschool children, who generally have a higher burden of trachoma than school-aged children.[4,5] When we restricted the community-based sample to only school-aged children (7–12 years), the prevalence estimates were much more similar, with the school-based sample only underestimating the community-based sample by approximately 1%. This was not expected because previous work in Ethiopia has demonstrated that children who self-report attending school are less likely to have the clinical signs of trachoma, presumably because school attendance is associated with higher socioeconomic status and, therefore, a lower risk of trachoma.[9,10] It is unclear why our findings were different. The present study was conducted in a different area of Ethiopia with more prevalent trachoma, so it is possible that school-going children have a more similar risk of trachoma in areas where the force of infection is high. School absenteeism may also have been lower in our study area compared with the previous report (25% versus 36%), which may have made our school-based population more representative of the underlying community.[9]

We observed a relatively high prevalence of clinically active trachoma in school children in this region of Ethiopia. One-fourth of all first graders sampled had TF and/or TI. This

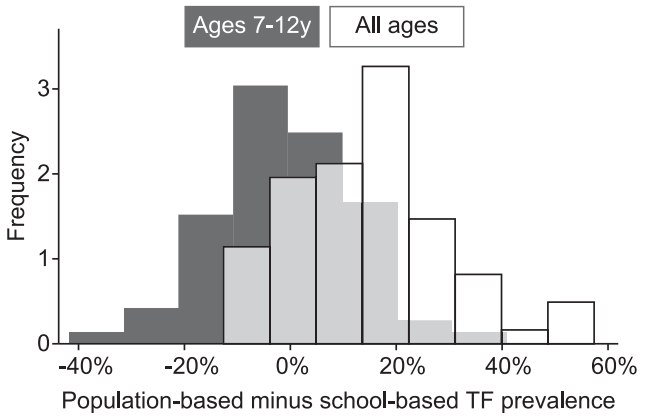

FIGURE 1. Distribution of the difference between the community-based TF prevalence estimate and school-based TF prevalence estimate in 70 Ethiopian communities. The white histogram represents the difference of the community-based sample among 1- to 9-year olds and the school-based sample among grades 1–3. The dark gray histogram represents the difference of the community-based sample among 7- to 12-year olds and school-based sample among 7- to 12-year olds. Positive numbers indicate a higher community-based prevalence of trachomatous inflammation–follicular (TF).

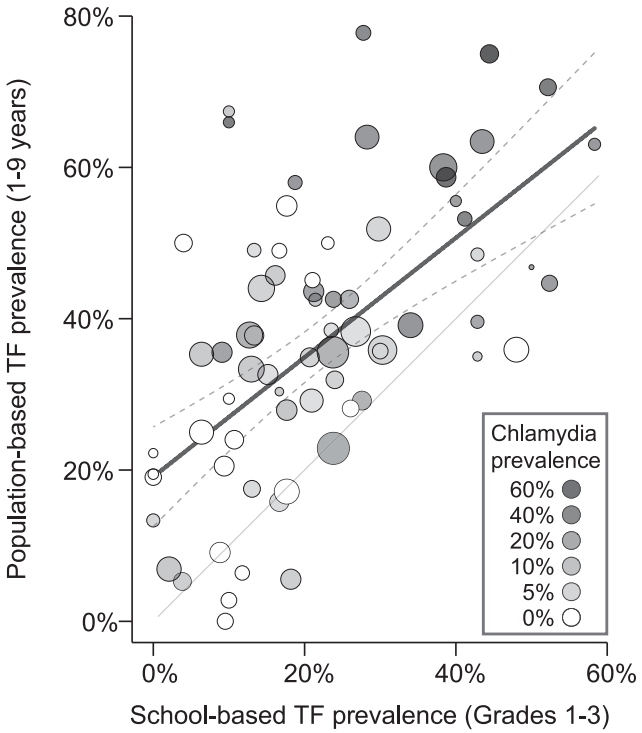

FIGURE 2. School-based vs. community-based prevalence of trachomatous inflammation–follicular (TF) in 70 Ethiopian communities. Each marker represents a single community. The size of the marker is a monotonic indicator of the number of school-based examinations performed from each community and the shading of the marker signifies the prevalence of ocular chlamydia from the community-based monitoring. The solid black line represents the mean predicted population-based prevalence over the range of school-based prevalences and the dotted lines the 95% confidence interval for the predicted means.

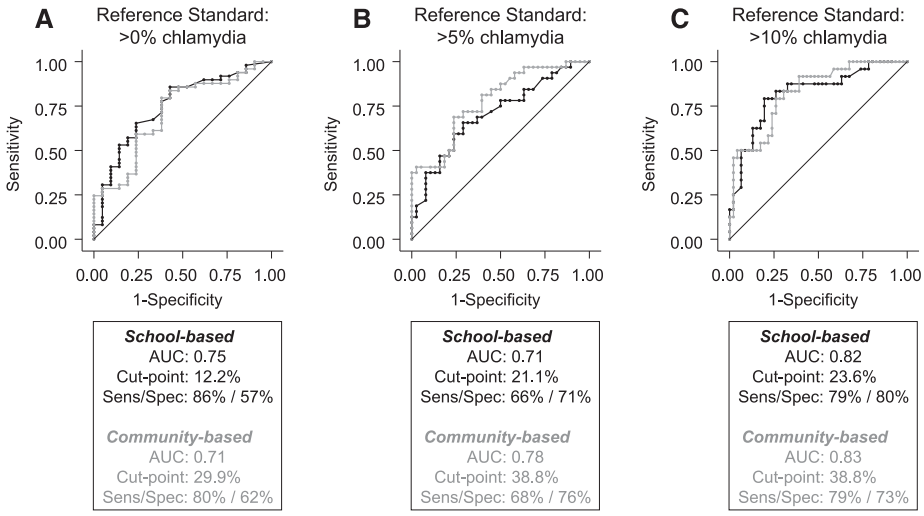

FIGURE 3. Receiver operating characteristic (ROC) curves assessing the diagnostic accuracy of school-based and community-based estimates of TF prevalence. Each column assumes a different dichotomous reference standard to gauge accuracy, with the reference standard based on the estimated prevalence of ocular chlamydia infection as assessed in the population-based sample. Each plot shows an ROC curve for school-based (in black; calculated from grades 1–3) and community-based (in gray) trachoma surveillance in which the community prevalence of trachomatous inflammation–follicular (TF) is treated as the diagnostic test. Below each curve are listed the areas under the curve, the optimal cut-point to maximize diagnostic information, and the sensitivity and specificity at the cut-point.

suggests that schools may be a site of trachoma transmission in this area of Ethiopia and argues for inclusion of the entire school district when designing programmatic activities and clinical research in settings with hyperendemic trachoma. It is possible that school-based transmission of ocular chlamydia could account for some of the persistent infection seen in previous cluster-randomized trials in Ethiopia that enrolled clusters smaller than a school district.[11]

School-based surveillance has been promoted for several NTDs, including schistosomiasis, STHs, and LF.[2,12] These helminthic infections are most commonly found among school-aged children, and interventions are often targeted to schools. Thus, although school-based sampling omits children not attending school, the approach is efficient. By contrast, the highest burden of trachoma is typically among preschool-aged children and interventions are distributed to the entire community. Most experts discourage the use of school-based surveys for trachoma.[13] However, our study suggests that school-based surveys could provide some information about the community burden of ocular chlamydia infection, at least in places with hyperendemic trachoma. The utility of school-based surveys would likely diminish in settings with less prevalent trachoma or when trying to assess elimination. Nonetheless, if school-based surveys are being performed for other diseases, a program could consider additionally screening for trachoma given the low expense of adding conjunctival examination to the screening protocol.

This study has several limitations. We attempted to conduct school-based sampling the way it would be conducted by a trachoma program. Primary schools in this part of Ethiopia have a morning session and afternoon session, with a different set of children attending each half-day. We collected data at each half-day session for each of the sampled schools, but did not return on a subsequent day to examine children who were absent during any given half-day session. We did not record the number of students enrolled at the schools, and hence cannot explore the representativeness of the school-based samples, nor the diagnostic accuracy relative to examination coverage. It is possible, for example, that schools in which a higher proportion of students were examined would have estimates closer to the population-based sample. The study was conducted in a region with hyperendemic trachoma, and its generalizability outside of this specific setting is unclear. Areas with less prevalent trachoma may have little or no trachoma in school children, which could greatly alter the relationship between the school-based and community-based samples.[14,15] Repeating this study in an area with meso- or hypoendemic trachoma would be worthwhile.

In conclusion, we found that school-based samples were correlated with community-based samples in a region with hyperendemic trachoma and that they provided a similar amount of information about the prevalence of ocular chlamydia in the community. Although by definition the school-based sample will be biased relative to the community-based sample, school-based sampling is logistically simpler and less expensive. School-based sampling may be useful in areas of hyperendemic trachoma where screening for other NTDs is being performed anyway because conjunctival examinations add little cost and may provide valuable information about community ocular chlamydia infection. Further study of the association between school-based and community-based surveillance samples in areas with less prevalent trachoma would be helpful to assess the generalizability of these findings.

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