

Trachoma among children in community surveys from four African countries and implications of using school surveys for evaluating prevalence

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Background: School surveys provide a convenient platform to obtain large child cohorts from multiple communities and are widely used as a proxy to determine community prevalence of neglected tropical diseases. The purpose of this study was to compare trachoma prevalence between preschool- and school-aged children and children who attend and do not attend school.

Methods: We analysed data from community-based trachoma surveys conducted from 2008–2011 in Ethiopia, Mali, Niger and Nigeria. The surveys utilised a cross-sectional, randomised cluster design. Individual-level data on school attendance was collected.

Results: Overall, 75 864 children aged 1–15 years from 2100 communities were included in the analysis. The prevalence of trachomatous inflammation follicular (TF) among these children in surveyed districts was 19.1% (95% CI 17.9–20.2%) in Ethiopia, 6.2% (95% CI 5.4–6.9%) in Niger, 4.6% (95% CI 4.2–4.9%) in Mali and 4.2% (95% CI 3.5–4.9%) in Nigeria. Controlling for age, sex and clustering, the OR of TF for school-attendees compared to non-attendees was 0.64 (95% CI 0.56–0.73) in Ethiopia, 0.67 (95% CI 0.56–0.80) in Mali, 1.03 (95% CI 0.81–1.16) in Niger and 1.06, (95% CI 0.65–1.73) in Nigeria.

Conclusion: Estimating the prevalence of trachoma through examination of only school-going children risks underestimating the true prevalence.

Keywords: Trachoma, Neglected tropical diseases, School attendance, Sub-Saharan Africa, Surveys

Introduction

Surveys are required for mapping, monitoring and the evaluation of neglected tropical diseases (NTDs) that are targeted for control and elimination by preventive chemotherapy and integrated intervention packages.^{1–3} For example, the prevalence of clinical signs of trachoma is typically measured through cluster randomised household surveys to determine the need for, or monitor the impact of, control programmes.⁴ Community-based household surveys generate prevalence estimates of trachomatous

inflammation follicular (TF) based on a representative sample of the community on which programmatic decisions are based according to guidelines issued by the World Health Organization (WHO).⁴ This type of survey is recommended, as it is feasible to implement, requires reasonable financial input, but needs considerable human resources.^{5,6} Recent efforts to integrate mapping of multiple NTDs have utilised or suggest utilising school-based surveys.^{7–10} Indeed, school-based surveys are often used as a proxy to determine community prevalence in NTD control programmes such as schistosomiasis, soil-transmitted helminthiasis

and lymphatic filariasis as they provide the convenience of a readily accessible and assembled cohort of children from multiple communities.^{11–13}

In this study, we utilise large-scale community-based survey data from trachoma control programmes in four African countries to determine whether trachoma prevalence differs among preschool-aged and school-aged children and, among the latter, to determine whether the prevalence differs between those who attend school and those who do not. Additionally, we explore whether school-attendees and non-attendees differ in gender, having a clean face and participation in mass distribution of antibiotics for trachoma control. The implications of our findings are discussed concerning estimating the true prevalence of trachoma for starting, implementing and evaluating control or elimination efforts.

Materials and methods

Sampling methodology

Box 1 defines several terms utilised in this paper to help clarify our methods. We analysed data from cross-sectional, community-based surveys conducted in 2008–2011 in Ethiopia, Mali, Niger and Nigeria. The surveys were designed to measure the prevalence of trachoma clinical signs at the district or other implementation units, as part of ongoing trachoma control programmes. Details of the sampling methodology of each survey have been described elsewhere.^{14–16} In brief, probability sampling was used to randomly select communities (clusters) and households within selected communities aligning with other standardised household survey protocols.^{17,18} At each household, an interview was conducted with the head of household or designated respondent. All household residents were examined for the presence or absence of all five clinical signs (TF; trachomatous inflammation intense [TI]; trachomatous scarring [TS]; trachomatous trichiasis [TT]; and corneal opacity [CO]) of the simplified trachoma grading system in both eyes, using 2.5x binocular loupes and adequate light.¹⁹ Training prior to each survey followed WHO guidelines, which included a rigorous selection process for trachoma graders based on the ability of graders to apply the trachoma grading system.⁴ Graders achieving agreement with a 'gold' standard of $\geq 80\%$ (Nigeria) or a kappa ≥ 0.7 (Ethiopia, Mali and Niger) specifically on the clinical sign TF were selected for clinical grading during the survey.

All residents of selected households present at the time of the interview, including all children were enrolled in the surveys. Prior to examination, each child was asked whether he/she attended school. The definition of school was clarified to exclude religious or informal schools. The faces of children aged 1–9 years were observed for the presence or absence of ocular and nasal discharge. Those children with no ocular and nasal discharge were recorded as having a clean face. In districts where the primary purpose of the survey was to measure impact after control interventions (Ethiopia, some districts in Mali and Niger), children were asked whether they took antibiotics during mass drug administration (MDA) campaigns for trachoma. To improve recall, antibiotics distributed in MDA were shown to the children (tablets or suspension bottle with description of the suspension). For preschool-aged children, the responses of their parents/guardians were accepted.

Box 1. Definitions of common terms referenced

- **Community-based survey:** epidemiological study where people in their households represent the sample population
- **School-based survey:** epidemiological study where children attending school represent the sample population
- **School attendance:** 'yes' response when asked 'do you attend school regularly?' during community-based surveys
- **Preschool-aged:** children aged 1–5 years
- **School-aged:** children aged 6–15 years
- **TF:** trachomatous inflammation follicular
- **TI:** trachomatous inflammation intense
- **Clean face:** absence of ocular and nasal discharge on the face of children aged 1–9 years
- **WHO recommended indicator for trachoma control intervention decisions:** TF among children aged 1–9 years (4)
- **MDA:** mass drug administration

Statistical analysis

To assess age-specific TF prevalence and reported school attendance, stratified by country, we modelled the relationship between age and TF with a polynomial term of age to fit the observed estimates. Robust variance estimation for proportions and means was used to adjust for clustering at the household and community level through the 'survey data' commands in Stata version 12.0 (Stata Corp. College Station, TX, USA). Statistical comparisons between proportions were adjusted also for the cluster design utilising the second-order corrected Pearson statistic.²⁰ We defined statistical significance as p -value < 0.05 . Multilevel logistic regression was employed for analysis of the association between TF and reported school attendance expressed as prevalence odds ratio (OR), controlling for sex, and clustering at both the community and household level separately for each country. We adjusted for age by limiting the analysis to only school-aged children 6–15 years of age and including age as a continuous variable in the models. A fixed effect meta-analysis was then performed using the country-specific ORs and respective confidence intervals to obtain an overall summary OR of TF between school attendees and non-attendees.²¹

We simulated district-level prevalence of TF that might have been identified through school surveys by limiting the analysis to only school attendees and classified districts to either $\geq 10\%$ or $< 10\%$ TF. We then compared these classifications to our gold standard classifications based on actual district-level prevalence of TF among children aged 1–9 years from the surveys as implemented. The following summary statistics and 95% CIs were calculated in Stata: sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). We chose the threshold of 10% as this is the prevalence at which the need for mass antibiotic distribution is determined when mapping and additional sub-district prevalence investigation is warranted after impact assessment surveys.

Ethics statement

The study protocols were reviewed and approved by Emory University Institutional Review Board (IRB protocol #079-2006).

Table 1. Description of data sets by country collected during cross-sectional cluster randomised surveys between 2008–2011

Country	Survey type ^a	Districts	Clusters	Households ^b	Children examined ^c
Ethiopia	Impact	25	711	14 211	29 251
Mali	Mapping or impact	36	647	9656	25 262
Niger	Mapping or impact	23	452	5916	12 825
Nigeria	Mapping	17	290	2610	8526
Total		101	2100	32 393	75 864

^a Sub-district or district-level prevalence surveys conducted pre-intervention (mapping) or post-intervention (impact). Data from Mali and Niger included district-level data from both types of surveys.

^b Households surveyed with children aged 1–15 years.

^c Children aged 1–15 years.

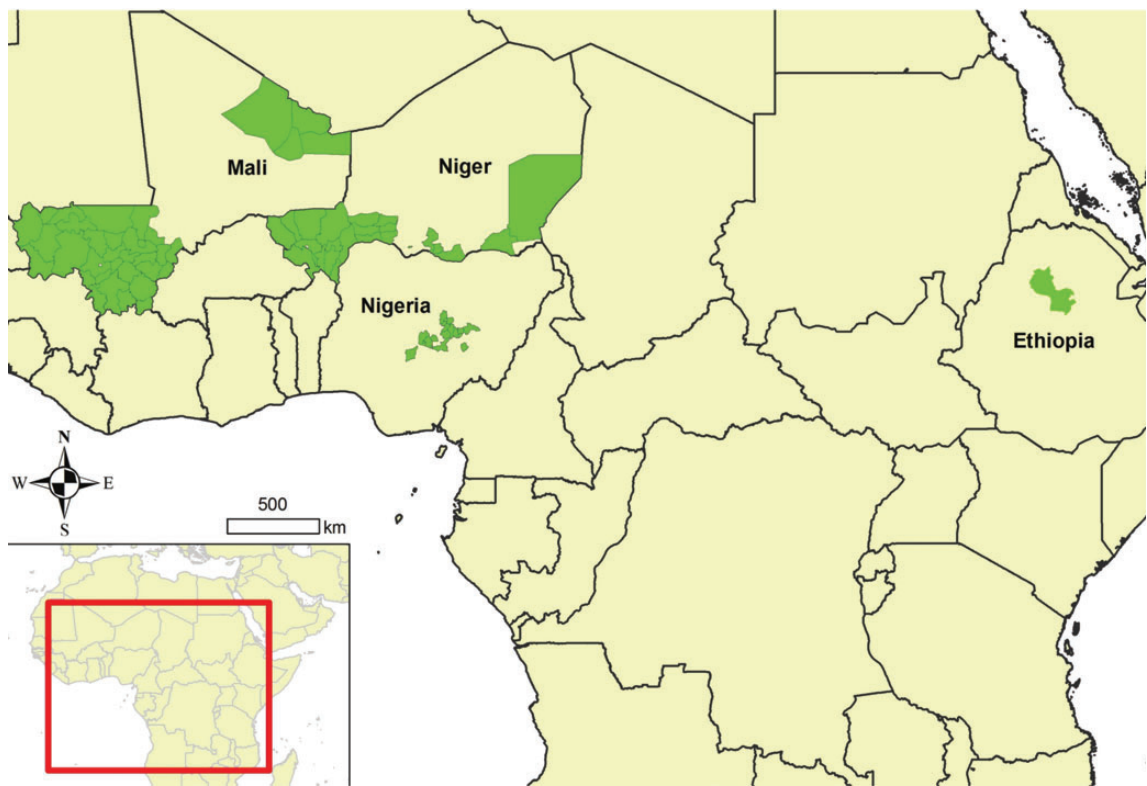


Figure 1. Map of surveyed districts included in analysis

Additionally, the surveys were approved by the local ethical review committee from the health administrations in each country. Verbal informed consent in these surveys was approved in the protocol and recorded prior to data collection rather than written information and a signed statement due to the high level of illiteracy in the surveyed populations. Consent for trachoma examination and interview was obtained from heads of households, individuals and parents/guardians of minors. In addition to parental consent, oral assent for examination and interview was obtained from school-aged children.

Results

Operational results

In total, 75 864 children were examined in 32 393 households from 2100 communities across the four countries (Table 1). Highlighted in Figure 1 are 101 districts from where the data were collected during either baseline mapping or post-intervention trachoma prevalence surveys (impact). Among households with child residents, the mean number of children aged 1–15 years was 3.3 (SD 2.6) in Nigeria; 2.5 (SD 1.6) in Mali; 2.2 (SD 1.4) in Niger; and 2.1 (SD 1.1) in Ethiopia.

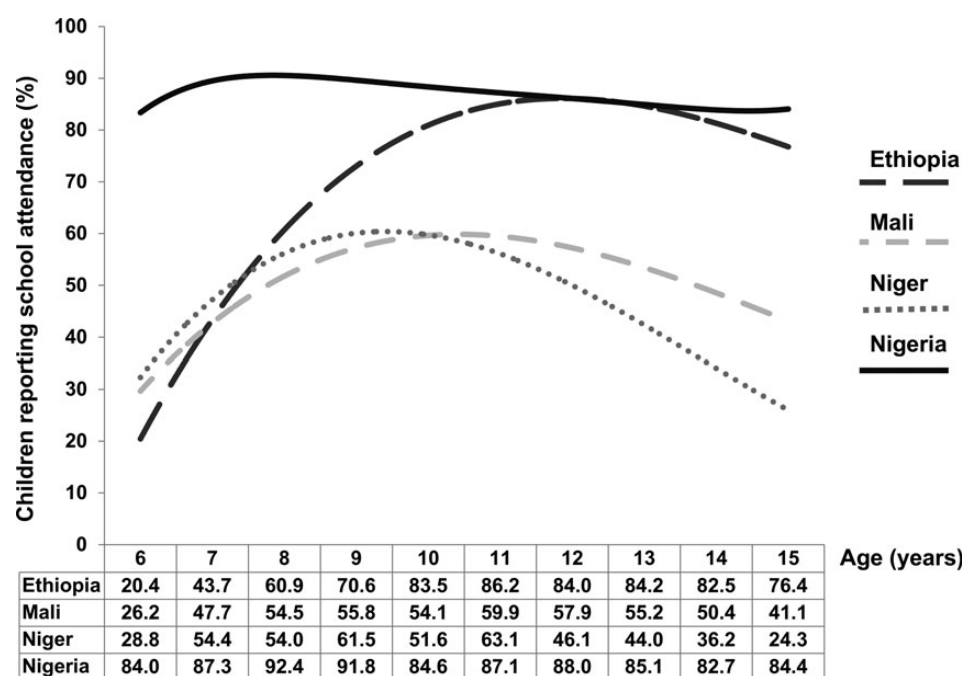


Figure 2. Proportion of school-aged children in surveyed areas reporting to attend school

Table 2. Description of school-aged children (6–15 years) surveyed by reported school attendance by country

	Ethiopia		Mali		Niger		Nigeria	
	Attend	Do not attend	Attend	Do not attend	Attend	Do not attend	Attend	Do not attend
Mean age	10.4	8.4	10.0	9.6	9.4	9.6	9.6	9.8
(SD, IQR)	(2.6, 8–13)	(2.6, 6–9)	(2.6, 8–12)	(2.9, 7–12)	(2.5, 7–11)	(3.0, 7–12)	(2.8, 7–12)	(3.0, 7–12)
Percentage girls	53.9	50.8	45.7	51.4	46.3	60.0	49.3	52.6
(95% CI)	(53.0–54.9)	(49.5–52.2)	(44.6–46.8)	(50.3–52.5)	(44.6–47.9)	(58.4–61.5)	(47.0–51.6)	(48.7–56.6)
Proportion with clean face	89.8	84.8	78.4	79.3	62.7	59.0	57.2	64.5
(95% CI)	(87.6–91.5)	(82.8–86.7)	(76.7–80.1)	(77.7–80.9)	(60.6–64.9)	(56.8–61.1)	(54.1–60.2)	(57.1–71.3)
Proportion taken antibiotics	97.8	87.8	91.7	90.6	95.9	87.6	NA	NA
(95% CI)	(97.3–98.2)	(85.2–90.0)	(89.4–93.6)	(88.1–92.5)	(94.5–96.9)	(84.3–90.3)		
Mean compliance in MDA ^a	85.8	73.8	NA	NA	52.3	50.7	NA	NA
(95% CI)	(84.9–86.8)	(71.3–76.3)			(49.9–54.7)	(48.3–53.0)		
Proportion with TF	10.4	16.6	3.0	5.2	4.6	4.7	3.8	3.6
(95% CI)	(9.5–11.5)	(15.2–18.1)	(2.6–3.4)	(4.7–5.8)	(3.9–5.4)	(4.0–5.5)	(3.1–4.6)	(2.4–5.4)
Proportion with TI	3.2	6.0	0.4	0.7	1.0	1.1	0.2	0.3
(95% CI)	(2.8–3.7)	(5.3–6.8)	(0.3–0.6)	(0.5–0.8)	(0.7–1.5)	(0.9–1.5)	(0.0–0.5)	(0.0–1.1)

MDA: mass drug administration with antibiotics; NA: not applicable, either no MDA had occurred or number of times taken antibiotic in MDA was not recorded.

^a Proportion of possible annual MDA campaigns in which antibiotics were reported taken (up to 3 campaigns).

School attendance

School attendance varied by country. The proportion of school-aged children (6–15 years) attending school was 87.1% (5023/5766; 95% CI 85.2–89.0%), 64.3% (12 928/20 099; 95% CI 62.7–66.0%), 49.7% (9627/19 381; 95% CI 47.7–51.6%), and 47.1% (5066/10 764; 95% CI 44.9–49.2%) in Ethiopia, Mali and Niger, respectively. The age-specific school attendance is shown in Figure 2 for school-aged children by country. Nigeria had the highest attendance rates with >80% of children above age 5 years reporting to attend school. Peak attendance was observed for the ages 10–14 years in Ethiopia, 8–13 years in Mali and 7–11 years in Niger (Figure 2). The proportion of communities surveyed where there were no children reporting school attendance was 9.1% (59/647) in Mali, 7.5% (34/452) in Niger, 1.0% (3/290) in Nigeria and 0.4% (3/711) in Ethiopia.

Description by school attendance

A description of school-aged children is presented in Table 2 for each country by school attendance. School attendees were older than non-attendees in Ethiopia ($t=37.55$, $p<0.001$) and Mali ($t=8.78$, $p<0.001$) and younger than non-attendees in Niger ($t=-3.23$, $p=0.001$). Girls were more likely to report going to school than boys in Ethiopia ($F=15.04$, $p<0.001$). The opposite was found in Mali ($F=48.25$, $p<0.001$) and Niger ($F=144.98$, $p<0.001$) with significantly more boys attending school than girls. There was no statistically significant difference between girls' and boys' school attendance in Nigeria ($F=1.98$, $p=0.160$). Children attending school had cleaner faces than those not attending in Ethiopia ($F=14.77$, $p<0.001$) and Niger ($F=5.44$, $p=0.020$). This difference in facial cleanliness was not observed in Mali ($F=0.58$, $p=0.447$) and Nigeria ($F=3.28$, $p=0.071$). In areas where MDA had been implemented for trachoma control, children attending school in Ethiopia ($F=246.70$, $p<0.001$) and

Niger ($F=61.12$, $p<0.001$) were more likely to have ever taken antibiotics than children not attending school. School-attending children were more compliant in MDA than children not attending school in Ethiopia ($t=10.27$, $p<0.001$), but not in Niger ($t=0.96$, $p=0.336$).

Prevalence of trachoma clinical signs

Among children aged 1–9 years, the prevalence of TF was 23.4% (4870/20 835; 95% CI 22.0–24.7%) in Ethiopia, 8.7% (681/7858; 95% CI 7.7–9.7%) in Niger, 5.7% (889/15 725; 95% CI 5.2–6.1%) in Mali and 5.0% (292/5865; 95% CI 4.1–5.9%) in Nigeria. Age-specific prevalence of TF is plotted in Figure 3 for each country. The prevalence of TF was highest among children aged 2–5 years in Ethiopia and Niger. The same pattern was not as pronounced in Mali and Nigeria. Adjusted for clustering and female gender, TF was more common in preschool-aged children than school-aged children in all countries (OR=4.34, 95% CI 3.99–4.71 in Ethiopia; OR=1.18, 95% CI 1.02–1.37 in Mali; OR=4.48, 95% CI 3.64–5.51 in Niger; OR=1.30, 95% CI 1.01–1.67 in Nigeria). TI was also more common among preschool-aged children than school-aged children in Ethiopia (OR=1.84, 95% CI 1.63–2.08), Mali (OR=1.52, 95% CI 1.06–2.16) and Niger (OR=3.06, 95% CI 1.96–4.79), but not significantly so in Nigeria (OR=2.03, 95% CI 0.83–4.98). Among school-aged children, the prevalence of TF was lower among school attendees (Table 2) in Ethiopia ($F=69.51$, $p<0.001$) and Mali ($F=40.88$, $p<0.001$). No difference in TF prevalence was observed in Niger ($F=0.06$, $p=0.802$) or Nigeria ($F=0.04$, $p=0.835$) between school-aged children attending and not attending school. TI also differed among school-aged children by school attendance in Ethiopia ($F=57.48$, $p<0.001$) and Mali ($F=4.90$, $p=0.027$). Adjusting for age, sex and clustering at the community and household level, the odds of TF among school-aged children attending *versus* not attending

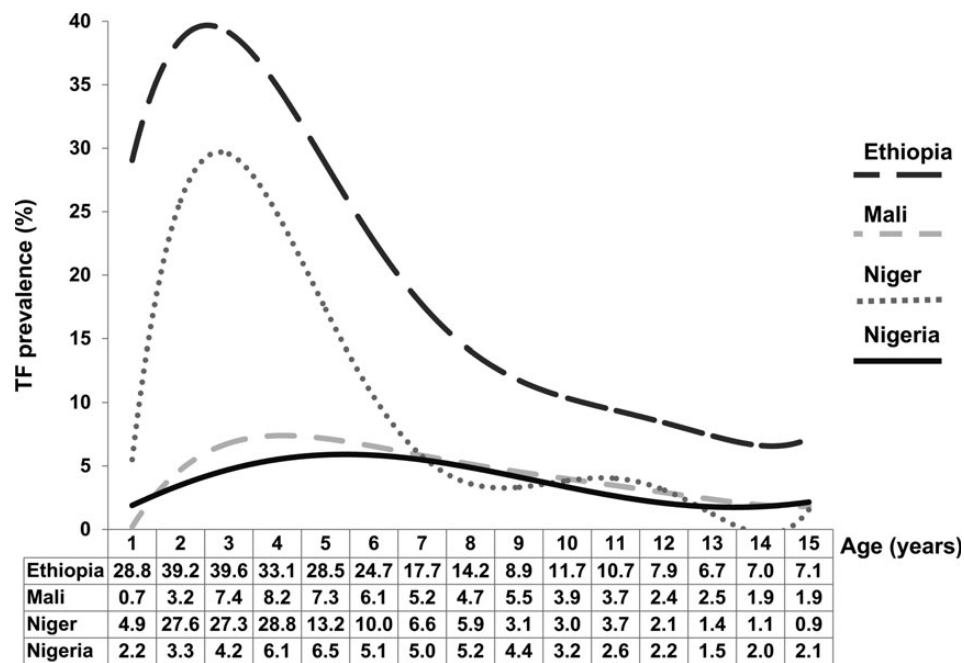


Figure 3. Age-specific prevalence of trachomatous inflammation follicular (TF) by country among children aged 1–15 years

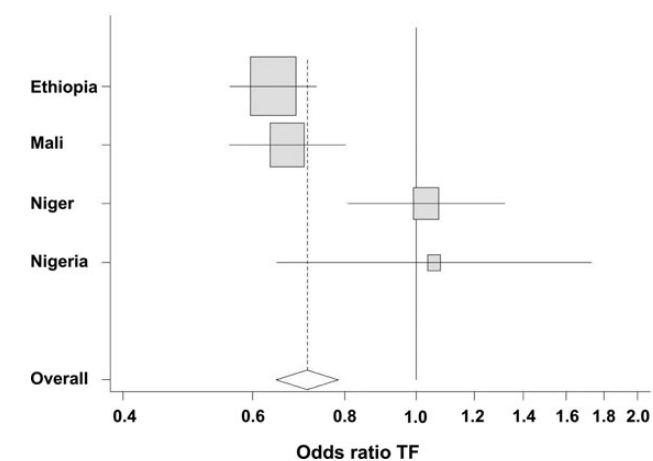


Figure 4. Country-specific and overall adjusted prevalence ORs of trichomatous inflammation follicular (TF) among school-aged children attending *versus* not attending school

Table 3. Diagnostic summary statistics for the classification of surveyed districts (n=101) to $\geq 10\%$ or $<10\%$ trichomatous inflammation follicular (TF) as estimated from analysis of school attendees only compared to classification from the true prevalence of TF among children aged 1–9 years as determined during community-based surveys

Districts classified based on all children aged 1–9 years as surveyed	Districts classified based on school attendees only	
	$\geq 10\%$ TF	$<10\%$ TF
$\geq 10\%$ TF	19	17
$<10\%$ TF	1	64
Summary		
Sensitivity	52.8%	(35.5–69.6%)
Specificity	98.5%	(91.7–99.9%)
Positive predictive value	95.0%	(75.1–99.9%)
Negative predictive value	79.0%	(68.5–87.3%)

school are plotted in Figure 4. School attendees were less likely to have TF than those not attending school in Ethiopia (OR=0.64, 95% CI 0.56–0.73) and Mali (OR=0.67, 95% CI 0.56–0.80). In Nigeria (OR=1.06, 95% CI 0.65–1.73) and Niger (OR=1.03, 95% CI 0.81–1.16) there was no statistically significant difference in having TF between children who attend and do not attend school. The summary OR of TF between school attendees and non-attendees was 0.71 (95% CI 0.65–0.78).

Simulated diagnostic comparison

Table 3 presents the summary findings of the classification of the 101 surveyed districts according to TF prevalence as defined by analysis of only school-attendees *versus* classification based on the actual survey findings. The proportion of districts correctly

classified as $\geq 10\%$ TF from analysis of only school-attendees had a sensitivity of 52.8% (19/36). The proportion of districts classified as $\geq 10\%$ TF by school-attendee analysis that were also identified as $\geq 10\%$ TF in the surveys had a PPV of 95.0% (19/20).

Discussion

Consistent across three of the four study areas, school-attending children differed from their non-school-attending counterparts in sex and age. More school-attending than non-attending children in two of the three countries where trachoma interventions had been implemented had ever taken antibiotics during the community-based MDA. In Ethiopia and Niger, the faces of children attending school were observed to be cleaner than children not attending. The obvious difference observed between countries was the ratio of reported school attendance. We did not observe differences between the school-aged children attending and not attending school in Nigeria, as reported attendance in the surveyed areas was uniquely high, which is consistent with the findings from a previous study determining no difference in TF prevalence estimates between school-based and community-based integrated surveys.⁷

Schools are often targeted for disease assessment and interventions due to the ease of accessibility and availability of children from multiple communities.^{2,11,22} School-based survey methodology is also being promoted in integrated NTD mapping methodology as operationally more feasible than traditional community-based cluster surveys.⁹ However, of immediate importance to trachoma is that school-based surveys exclude adults who are also necessary for determining whether blinding trachoma is a public health problem and upon which to plan sight-saving surgeries.

Our findings raise important questions that warrant consideration by trachoma and perhaps other NTD control and elimination programmes and these are offered for consideration. A first issue is whether school-based surveys provide valid estimates of prevalence in the communities. We simulated a school-based sample by limiting analysis to only school-attendees and estimating TF prevalence. By doing so, we determined a school-based survey strategy would have misclassified nearly half of the districts as not warranting control interventions when actual TF prevalence among children aged 1–9 years indicated control measures were warranted according to WHO guidelines. While school attendance likely influenced this outcome, age also plays a factor. Children attending school are not always the target age group recommended for prevalence assessment. For example, trachoma programme decisions are based on estimates of TF prevalence in children aged 1–9 years.⁴ In this study, the age group with the highest frequency of TF (1–5 year-olds) is considered too young to attend school. A prevalence estimate based on children in school would not provide an estimate of prevalence in the recommended age group and more importantly would then underestimate it and perhaps misclassify communities as areas not needing control interventions as our analysis suggests. Controlling for age-prevalence differences, children attending school in two of the countries included in this study were 33–36% less likely to have TF than children not attending. Our data are not generalisable to other NTDs as the transmission dynamics and infection patterns are often unique for each disease. However, a study in Zanzibar found higher prevalence and twice as many intense

soil-transmitted helminth infections among younger children not in school compared to older children attending school.²³ These findings should be taken into consideration so as not to exclude endemic areas from interventions when initiating or scaling down disease control programmes.

Other crucial questions brought to our attention from the secondary data analysis presented here, are whether children not in school are benefiting as much as school-going children from disease control interventions and whether these control efforts are indeed reaching all children in the community. The higher proportion of clean faces observed in children reporting to attend school may suggest that the desired behaviour of face washing is being practiced more often than among children not in school. In Ethiopia, Mali and Niger, behaviour change communication for trachoma control is being delivered in primary schools as well as through health extension workers and volunteers in the community. MDA for trachoma is community-based from central distribution points, rather than school-based distribution, yet we found higher reported drug coverage among reported school attendees. While it is encouraging to know school-going children may be benefiting from disease control interventions, it is discouraging to observe a disparity between children who do not attend school. Recent monitoring of another MDA programme targeted to control intestinal helminths in Cambodia similarly found that children who were not enrolled or who did not attend school were less likely to receive the drug treatments in a school-based distribution strategy.²⁴ While school-based MDA strategies in Sierra Leone have shown success in reducing intestinal helminth infections among school children, no community-based assessment was conducted in parallel to determine whether similar impact was observed in children not attending school.²⁵ Of note, we observed a small proportion of surveyed communities in each country that had no children reporting school attendance. Hence, school-based disease control programmes must identify additional means to ensure that all children benefit as has been discussed in the literature and warrants renewed attention.^{26–28}

The analysis presented in this study was not the primary purpose of the surveys and we were not able to compare results from actual school-based and community-based surveys as has been done previously.⁷ We used community-based prevalence data from epidemiological rigorous household surveys employing standardised methods basing the analysis on the responses of children and their caretakers of whether the child attended school. The purpose of our study was not to quantify in detail the scholarship of school-aged children and we did not attempt to verify school attendance with enrollment records at schools, but enrollment rates reported by household surveys are often significantly lower than school reports.²⁹ Inquiring about the school-aged child's attendance allowed us to make simple comparisons of prevalence, but also to provide a quick evaluation of school-based behaviour change communication in some of the countries. The response of the child and/or guardian may have introduced bias, but school attendance status collected in household surveys aiming to measure health conditions is not uncommon and used by standardised household surveys such as Demographic and Health Surveys.^{23,30,31} The amount and type of data collected at the household was limited and varied across surveys. Therefore, we are unable to control for other potential confounding or modifying factors that may account for the differences observed. Although we cannot generalise our

findings to other NTDs, we encourage the scientific community and disease control managers to investigate potential disparities among children to ensure disease control/elimination interventions are reaching and benefiting all those in need.

Conclusions

In some areas under community-based trachoma control interventions, school attendees had cleaner faces, less trachoma and reported higher coverage of MDA. The summary odds ratio from our meta-analysis suggests that using a school-based approach to monitor prevalence of trachoma will underestimate true community prevalence, which may result in misclassifying trachoma endemic communities as not warranting control interventions, which is supported by our diagnostic comparison of simulated school-based surveys. The exception was where school attendance is very high and where there is no difference in age-specific prevalence between preschool- and school-aged children. Similar investigations should be conducted to determine whether the finding is consistent across other NTD control programmes.

Authors' contributions: JDK, PO, JU, JN, AEPS, EAC, PME designed the study; JDK, JN, SB, KB, NJ, AWM, EAC coordinated field data collection in the surveys; JDK, AWM conducted the analysis; JDK, PO, JU, JN, AWM, AEPS, EAC, PME interpreted the results; JDK drafted the manuscript, whereas all authors read and approved the final manuscript. JDK is guarantor of the paper.

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Competing interests: None declared.

Ethical approval: The study protocols were approved by Emory University Institutional Review Board (IRB protocol #079-2006). Additionally, the surveys were approved by the local ethical review committee from the health administrations in each country. Verbal informed consent in these surveys was approved in the protocol and recorded prior to data collection. Consent for trachoma examination and interview was obtained from heads of households, individuals and parents/guardians of minors. In addition to parental consent, oral assent for examination and interview was obtained from school-aged children.

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