Predictive Value of School-Aged Children's Schistosomiasis Prevalence and Egg Intensity for Other Age Groups in Western Kenya

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Abstract. World Health Organization recommendations for the timing and target population for mass drug administration (MDA) for schistosomiasis are based on the prevalence of infection in school children within a given community. In a large study comparing MDA approaches for *Schistosoma mansoni* control, we evaluated whether prevalence of infection and egg burdens in 9- to 12-year-old students reflected infection levels in young children and adults in the same community. Cross-sectional surveys of preadolescents (9–12 years old) were compared with those of first year students (5–8 years old) in 225 villages and adults (20–55 years old) in 150 villages along the Kenyan shores of Lake Victoria. Village schistosomiasis prevalence and intensity levels in preadolescents strongly correlated ($P < 0.0001$) with prevalence and infection intensity for other age groups in the community. Our findings suggest that *S. mansoni* prevalence and intensity among 9- to 12-year-olds are valid for community sampling purposes in mapping for MDAs.

INTRODUCTION

In 1998, the World Health Organization (WHO) formulated an operational model to guide national, regional, and local health authorities with regard to the planning and execution of schistosomiasis surveillance and control programs at the community level.¹ This model was further refined² and incorporated into the recommendations of the Expert Committee of the WHO,³ which focused on endemic countries that were having difficulty attaining their goals. A revised second edition was published in 2011.⁴ The strategy recommends testing school-aged children (SAC) for both baseline and follow-up surveys to assess the prevalence of schistosomiasis and determine the intervention needs for the community as a whole. The recommendations provide for targeted distribution of praziquantel (PZQ) based on the prevalence of infection in SAC.^{3,5–7} Areas where $\geq 50\%$ of SAC have schistosome eggs detected in their stool are considered at high risk, and mass PZQ treatment should be provided to SAC yearly. Furthermore, adults in these areas, from special at-risk groups to the whole community, should also be treated. For moderate risk areas with 10–49% SAC prevalence, mass treatment of SAC is recommended once every 2 years, along with adults considered at risk. For areas with 1–10% prevalence, SAC should be treated at least twice during the primary school years. The strategy also recommends that in the high-risk areas, mass drug administration (MDA) should be combined with sanitation improvement, environmental management, and health education.^{5,8}

Before implementation of any control activities for soil-transmitted helminths (STHs) and schistosomiasis, a baseline survey is needed.⁹ This allows for a situational analysis and determination of intervention strategies based on prevalence of infection. Thereafter, follow-up surveys are used to monitor the impact of mass treatments. The Kato-Katz test¹⁰ on stool collected from representative samples of schoolchildren is the methodology currently recommended by WHO for monitor-

ing prevalence of intestinal schistosomiasis and STH. School children are considered ideal subjects for baseline surveys because schools are easily accessible and SAC bear the highest burden of these infections. Moreover, prevalence and intensity levels in this group are believed to be representative of the community, and therefore, the SAC prevalence can be used to make intervention decisions for other age groups.

Although WHO and other partners have provided basic information for each country online,^{11–13} that information may not be current or sufficiently detailed at the implementation unit level. Individual countries should conduct baseline prevalence surveys to adapt the recommended strategy for local situations and to allow for comparisons in subsequent monitoring and evaluation. The WHO recommendations may not be always applicable to the reality in some settings if the 6- to 15-year-old age group does not truly reflect the prevalence of the disease and the need for intervention in the community as a whole.¹⁴

In Kenya, the current control strategy for STHs and schistosomiasis is school-based mass chemotherapy with albendazole (since 2009) and PZQ (since 2012), administered in prioritized areas by a national control team with cascaded support at the county and subcounty levels. Prioritization of targeted areas is based on historical data generated from these areas, and implementation is accompanied by baseline surveys. Because different segments of a community may be infected depending on prevailing economic activities, it is important to determine the extent of disease among age groups that are not targeted by current strategies. Moreover, while there are already vast amounts of data on infection in SAC, there are much less community-based data available to inform intervention decisions at the community level. Therefore, we sought to determine whether SAC constitute an effective reference group to assess the *Schistosoma mansoni* prevalence in the overall community in endemic areas of western Kenya.

METHODS

Ethics statement and eligibility criteria. This study was reviewed and given scientific and ethical clearance by the departmental and institutional Scientific Steering Committees of Kenya Medical Research Institute (KEMRI) and the

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KEMRI National Ethics Review Committee. The Institutional Review Boards of both the Centers for Disease Control and Prevention (CDC) and the University of Georgia also reviewed the study protocol and deferred to the KEMRI National Ethics Review Committee. Written informed consent was obtained from parents or guardians of children eligible for inclusion, along with written assent from the 5- to 14-year-old participants. Adults living in the same communities as the primary schools were included into the study once they provided written informed consent.

Study area and inclusion of study villages into the study.

Cross-sectional data were collected from students attending schools within approximately 10 km of Lake Victoria in the Nyanza Province of Kenya based on historical data that showed a high prevalence of *S. mansoni*, but very few *Schistosoma haematobium*, infections in the area.^{15–18} No school-based MDA for schistosomiasis had been performed in the study area prior to collection of the data; however, one round of MDA for STHs had been carried out in the area by the national deworming program 1 year prior to the study. As part of two larger Schistosomiasis Consortium for Operational Research and Evaluation (SCORE) projects designed to evaluate the impact of different MDA strategies, 13- to 14-year-old children were screened in 300 schools to determine eligibility of villages for the study. A single stool was examined (two slides per stool) by the Kato-Katz fecal thick smear technique from 50 children in each school. If between 5 and 12 children were positive for *S. mansoni* eggs, the community was eligible for entrance into the Sm1 study evaluating MDA approaches in villages with moderate prevalence (10–24%); if 13 or more children were positive, the community was eligible for the Sm2 study that was designed to evaluate MDA in high prevalence (> 25%) villages. Based on the *S. mansoni* infection prevalence in 13- to 14-year-olds and the larger study designs, there were 75 villages included in the Sm1 study and 150 villages included in the Sm2 study. MDA with praziquantel (40 mg/kg) was provided to the villages included in the studies.

Stool examination. For all villages included in either study, we sought to enroll 100 first-year students (generally 5–8 years old) and 100 students 9- to 12-years old. For the Sm2 study, 50 adults were also enrolled in each village. First year students and adults were given stool containers and asked to provide a single fresh stool sample. The 9- to 12-year-old students were asked to provide stool on 3 consecutive days; however, to provide comparable sensitivity among the different age groups, only the data from the first day's stool was used for the analyses in this study. Samples were transported to the CDC/KEMRI laboratory where they were processed and examined by the Kato-Katz technique for detection of parasite eggs, 41 mg per slide and two slides per stool. The presence of *S. mansoni*, *Ascaris lumbricoides*, and *Trichuris trichiura* eggs was recorded. Egg counts were quantified for *S. mansoni* only. The arithmetic mean of egg counts was calculated from the two slides and multiplied by 24 to express data as eggs per gram (EPG). Each stool evaluation was performed by trained microscopists blinded to prior stool results.

Data handling and analysis. EpiCollect Application (Imperial College, London, United Kingdom) was installed on smartphones and was used to collect demographic data that were then uploaded to a dedicated database maintained on a central server. Laboratory data were collected on paper

forms and entered via the smartphones into the same database. Data were analyzed using R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria). For each participant, the results of testing on a single stool were used for determination of schistosome infection, presence, and intensity. For each village, the proportion of positive test results, an arithmetic mean of the EPG for positive individuals, and a geometric mean of the EPG for all individuals were calculated. For geometric means, 1 was added to all participants to allow for inclusion of those with an EPG of 0. In addition to the overall village data, prevalence and intensity were determined for the age groups of interest. For village age groups with small sample sizes, which occurred most often with the first-year students, we used weighted least squares regression. Village age groups with a sample size of 20 or greater received a weight of one and village age groups with fewer than 20 people sampled were given a weight of the sample size divided by 20. This allowed us to reduce the contribution of villages with age groups that may have unstable estimates and bias model results. Analyses exploring the relationships between village-level data were performed using thin-plate regression splines and cubic regression splines.¹⁹ Exploratory analyses revealed that most relationships could be adequately explained with weighted least squares regression models using polynomials of first, second, or third degree. Selection of the optimal degree was performed using the Bayesian information criterion.²⁰ All tests and confidence intervals used the 5% level of significance. At the end of data analysis for each survey, a report containing the results from the survey was provided to the Ministry of Public Health and Sanitation, and the Ministry of Education at the national and district levels. Each school received a report showing prevalence and intensity levels for that school.

RESULTS

The 225 villages selected for the Sm1 and Sm2 studies were distributed through 9 subcounties (formerly districts) along the shores of Lake Victoria. Within these villages, 29,619 individuals were examined for *S. mansoni* infections. Of these, 6,334 were first-year students, representing 21.4% of the total sample, 16,157 (54.5% of total sample) were children aged 9–12 years in classes 3–6 (preadolescent), and 7,128 (24.1%) were adults ≥ 25 years of age. The prevalence of schistosomiasis varied from 26.51% (95% confidence interval [CI]: 21.44, 31.57) in first-year children to 35.10% (CI: 31.52, 38.68) among preadolescents, and 43.95% (CI: 40.93, 46.98) in adults. *Schistosoma mansoni* infection intensity (as measured by EPG) varied from a mean (±SD [standard deviation]) of 53.29 (±8.27) in first-year children to 71.98 (±6.87) among preadolescents and 67.76 (±4.99) in adults. Although the prevalence of *S. mansoni* infections among adults appears higher than that of the 9- to 12-year-olds, it should be noted that the adult data were only collected from the 150 Sm2 schools, that is, those schools with a prevalence > 25% in 13- to 14-year-olds, while the data from the 9- to 12-year-olds includes a total of 225 schools with selection criteria prevalence as low as 10% in 13- to 14-year olds.

The STH prevalence levels were much lower than for *S. mansoni*. For *A. lumbricoides* infection, mean (95% CI) prevalence was 4.83% (CI: 3.89, 5.76) for first-year students, 3.25% (CI: 2.72, 3.79) for 9- to 12-year-olds, and 1.85%

TABLE 1
Means and SDs of village-level prevalence and intensity of infection for schistosomiasis among different age groups in western Kenya

	First year students mean $\pm$ SD (N)	9- to 12-year-old children mean $\pm$ SD (N)	Adults mean $\pm$ SD (N)	Overall mean $\pm$ SD (N)
<i>Schistosoma mansoni</i> mean prevalence	21.17 $\pm$ 21.44 (225)	32.92 $\pm$ 25.25 (225)	43.94 $\pm$ 18.88 (150)	30.66 $\pm$ 22.11 (225)
<i>S. mansoni</i> intensity (arithmetic mean EPG)	39.69 $\pm$ 69.82 (225)	65.99 $\pm$ 88.88 (225)	67.83 $\pm$ 61.25 (150)	56.07 $\pm$ 66.25 (225)
<i>S. mansoni</i> intensity (geometric mean EPG)	8.36 $\pm$ 25.45 (225)	13.15 $\pm$ 29.20 (225)	10.64 $\pm$ 13.33 (150)	8.39 $\pm$ 16.43 (225)
<i>S. mansoni</i> intensity (positives only, arithmetic mean EPG)	178.27 $\pm$ 77.69 (182)	172.47 $\pm$ 91.79 (222)	145.00 $\pm$ 75.06 (150)	160.41 $\pm$ 73.99 (222)
<i>S. mansoni</i> intensity (positives only, geometric mean EPG)	101.10 $\pm$ 54.47 (182)	87.57 $\pm$ 53.45 (222)	73.34 $\pm$ 35.56 (150)	76.76 $\pm$ 40.26 (222)

EPG = eggs per gram; SDs = standard deviations.

Estimates are at the village level and are weighted by the sample size, where villages with a sample size ≥ 20 receive a weight of one and village with a sample size < 20 receive a weight of the sample size divided by 20. Fewer (150) villages were used for calculating village mean prevalence and intensity for adults as only the Sm2 study collected adult data. For 43 villages, there were no *S. mansoni* egg-positive first-year students; 31 of these villages were in Sm1 and 12 were in Sm2.

(CI: 1.39, 2.32) for adults, resulting in an overall prevalence of 3.14% (CI: 2.70, 3.58). The prevalence of *T. trichiura* infection was 7.45% (CI: 6.19, 8.71) for first-year students, 6.05% (CI: 5.24, 6.86) for 9- to 12-year-olds, and 1.87% (CI: 1.41, 2.33) for adults; the overall prevalence was 5.06% (CI: 4.44, 5.68).

Arithmetic means of *S. mansoni* infection prevalence and intensity of village-level data (Table 1) were similar to the individual-level data. Mean village-level prevalence was 21.17% (± 21.44) in first-year children, 32.92% (± 25.25) among preadolescents, and 43.94% (± 18.88) in adults. The *S. mansoni* infection intensity was 39.69 (± 69.82) in first-year children, 65.99 (± 88.88) in preadolescents, and 67.83 (± 61.25) in adults. We observed a strong, statistically significant correlation ($r^2 \geq 0.96$; $P < 0.001$) between prevalence and geometric mean EPG for all age categories (Figure 1). The village mean prevalence levels of the 9- to 12-year-old age group were also significantly correlated to those of the first-year students ($r^2 = 0.74$; $P < 0.001$), adults ($r^2 = 0.26$; $P < 0.001$), and combined groups ($r^2 = 0.52$; $P < 0.001$) (Figure 2). When we

compared the correlation between the geometric mean egg intensity of each age group with that of the 9- to 12-year-old age group, there was again a positive correlation with the adults and first-year populations ($r^2 = 0.67$; $P < 0.001$) as well as with the first-year students ($r^2 = 0.82$; $P < 0.001$) and adults ($r^2 = 0.26$; $P < 0.001$) (Figure 3). Adults (Table 2) and first-year students (Table 3) living in villages with 9- to 12-year-olds with *S. mansoni* prevalence $> 50\%$ had significantly higher infection levels than those living in villages with $< 50\%$ prevalence among 9- to 12-year-olds.

DISCUSSION

We took advantage of the large ongoing SCORE projects in western Kenya to revisit the question of whether SAC are a suitable reference group for predicting infection levels in the overall community. Such a reference group needs to be representative of the MDA target population and the community. The strong correlations between the prevalence and EPG of all the age groups as well as correlation in both prevalence

FIGURE 1. Relationship between prevalence of infection and intensity of infection as expressed by geometric mean eggs per gram feces + 1. Village-level estimates are weighted by the sample size, where villages with a sample size ≥ 20 receive a weight of one and village with a sample size < 20 receive a weight of the sample size divided by 20. Each dot represents one village with the size of the dot proportional to the number of participants in that village. The legend provides examples of symbol size for a given number of village participants.

FIGURE 2. Relationships between prevalence of infection in 9- to 12-year-olds and other age groups. Village-level estimates are weighted by the sample size, where villages with a sample size ≥ 20 receive a weight of one and village with a sample size < 20 receive a weight of the sample size divided by 20. Each dot represents one village with the size of the dot proportional to the number of participants in that village. The legend provides examples of symbol size for a given number of village participants.

and intensity of the other age groups to the 9- to 12-year-old age group confirmed the validity of the WHO recommendation to use the 9- to 12-year-old age group as a reference.^{1,3,21} The sharp increase in first-year student infection prevalence and intensity (Table 3, Figure 2) in villages where *S. mansoni* infection prevalence was greater than 50% in 9- to 12-year-olds is particularly noteworthy and supports calls to provide treatment to preschool-aged children, in those villages.^{22,23}

Because logistic and economic issues are a large consideration in parasitologic surveys, obtaining community prevalence

and infection intensities has to be considered against accessibility of the sampling group, ease of specimen collection, and cost-benefit ratios. Specimens from children were collected at schools with the help of a health teacher. Only one project staff person was required to be present at each school to collect up to 100 specimens per age category, per school per day. Schoolchildren and their parents/guardians, as well as the school administration, were generally accessible and receptive to testing. In addition, the participation rate was high, with only minimal refusals from either parents/guardians (declined

FIGURE 3. Relationship between intensity of infection in 9- to 12-year-olds as expressed by geometric mean eggs per gram feces + 1 and the other age groups. Village-level estimates are weighted by the sample size, where villages with a sample size ≥ 20 receive a weight of one and village with a sample size < 20 receive a weight of the sample size divided by 20. Each dot represents one village with the size of the dot proportional to the number of participants in that village. The legend provides examples of symbol size for a given number of village participants.

TABLE 2
Prevalence and intensity of infection in adult group compared with 9- to 12-year-olds

% Positive 9- to 12-year-olds in village	Villages	Adults tested	% Positive	0 EPG	1–99 EPG	100–399 EPG	400 + EPG
< 10%	3	142	30.28 (8.50, 52.06)	69.72 (47.94, 91.50)	26.76 (7.87, 45.65)	2.82 (0.50, 5.13)	0.70 (0.00, 1.84)
10–49%	88	4,173	38.27 (34.85, 41.69)	61.73 (58.31, 65.15)	24.63 (22.59, 26.67)	9.73 (8.04, 11.42)	3.91 (2.70, 5.11)
≥ 50%	59	2,800	53.25 (48.43, 58.07)	46.75 (41.93, 51.57)	31.61 (28.94, 34.27)	15.68 (13.07, 18.28)	5.96 (4.19, 7.73)
χ^2 (P)	—	—	24.64 (< 0.0001)		56.81 (< 0.0001)		

EPG = eggs per gram.

Both tests are Rao-Scott χ^2 values to account for village-level clustering. Analyses are at the individual level, and no weights are included.

consent) or children (declined assent). By contrast, adult samples were collected from home compounds and involved door-to-door walking to seek out adults. It took up to 3 days for project staff members accompanied by a village elder or community health worker to collect 50 samples from adults. Many adults contacted at their homes declined to participate in the study. Collecting specimen from adults therefore required more personnel, took longer hours, and it was more difficult to obtain follow-up specimens. Even though the prevalence and infection intensity among the adult group was very similar to that of the overall population, the logistical challenges and cost implications make this group less appropriate for baseline surveys.

Previous studies have reported reduced costs in school-based studies where activities are concentrated in a specific physical space.²⁴ With school enrollment in Kenya currently very high because of a policy regarding provision of free primary education, the SAC group is most appropriate as the target group for baseline surveys. Furthermore, this age group was very representative for both prevalence and intensity levels in comparison to the overall population. Other studies, including Rodrigues and others reporting data collected in Minas Gerais, Brazil, validate the use of prevalence among SAC in the 7- to 14-year-old age group to predict *S. mansoni* infection prevalence in the community and confirm that it can be used to guide treatment strategies in the endemic areas.²⁵ Traore and others surveyed 323 villages in Mali and showed a strong relationship between the community prevalence of infection with *S. haematobium* and the prevalence rate in the 7–14 years age group.²⁶ Guyatt and others observed a consistent relationship between community prevalence and SAC prevalence for different parasites from varied sites.²⁷ They further showed that degrees of overestimation of community prevalence were dependent on the parasite species and the intensity level of infection, and even though this can be reduced by more age-specific surveys,²⁸ the SAC still provide a reliable reference and cost-effective group for estimating level of risk of infection in the community and for making intervention decisions.²⁷

By contrast, the study of Evans and others of *S. haematobium* infections in Nigeria demonstrated similar adult levels of infection and hematuria in villages with SAC prevalence between 20% and 49% as in villages with SAC prevalence > 50%.¹⁴ However, in both settings the median adult prevalence was lower than for SAC (~20% for both groups) whereas in our study the adult prevalence was more similar to the SAC prevalence. This may represent differences in the longevity of *S. haematobium* and *S. mansoni* worms, increased resistance to reinfection in adults infected with *S. haematobium*, or simply differences in age-related water contact patterns between the two study settings. Despite the differences in the pattern of the data in the two sites, we are in agreement with the authors' call for greater access to treatment of adults.¹⁴

Using 9- to 12-year-old SAC in baseline surveys may also facilitate measurement of the impact of treatment, especially with nested cohorts to follow for detailed monitoring and evaluation.²⁹ Furthermore, the school setting provides an environment to empower children as agents of health behavior change and an entry point for other community members to access MDA benefits.^{30–32} Because several other health programs also operate from schools, it is possible to incorporate these surveys into the routine activities.^{33,34}

In conclusion, our findings show that prevalence and intensity indicators among the 9- to 12-year-olds are comparable to other population groups in the same settings as well as overall community prevalence and are a valid age group to use for sampling purposes for baseline data to determine MDA. However, because of possible regional differences, it is advisable for program managers in other settings to conduct similar operational research assessments where resources permit to determine how WHO guidelines apply to their particular circumstances.

Received June 25, 2015. Accepted for publication August 20, 2015.

Published online September 28, 2015.

Acknowledgments: We appreciate the support from the Ministry of Education, Ministry of Public Health and Sanitation, and the Provincial administration in Nyanza province. We thank the head

TABLE 3
Prevalence and intensity of infection in first-year student group compared with 9- to 12-year-olds

% Positive 9- to 12-year-olds	Villages	First-year students tested	% Positive	0 EPG	1–99 EPG	100–399 EPG	400 + EPG
< 10%	43	913	5.82 (4.31, 7.34)	94.18 (92.66, 95.69)	3.42 (2.19, 4.66)	1.94 (1.02, 2.86)	0.46 (0.03, 0.88)
10–49%	122	3,185	13.38 (11.25, 15.50)	86.62 (84.50, 88.75)	9.64 (7.99, 11.29)	2.61 (1.94, 3.27)	1.13 (0.67, 1.59)
≥ 50%	60	2,236	53.71 (46.48, 60.95)	46.29 (39.05, 53.52)	25.89 (22.90, 28.89)	17.40 (13.80, 0.99)	10.42 (7.09, 13.75)
χ^2 (P)	—	—	1,337.05 (< 0.0001)		1,406.26 (< 0.0001)		

EPG = eggs per gram.

Both tests use Pearson χ^2 values because the design effect was not positive. Analyses are at the individual level, and no weights are included.

teachers, teachers, and pupils in each of the schools that participated in this study, as well as the community health workers and adults in the community based study. We also thank all the SCORE Kenya staff for their assistance in the field and laboratory work. We would like to acknowledge the help of Division of Vector-Borne and Neglected Tropical Diseases (DVBNTD) personnel, Kisumu, and in particular Blasto Kwanya, Otieno Oloo, and Charles Odah for their assistance with microscopy.

Financial support: This study was made possible by the generous support from the University of Georgia Research Foundation, Inc., which is funded by the Bill and Melinda Gates Foundation for this SCORE project.

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