SPATIAL AND TEMPORAL VARIATIONS IN LOCAL TRANSMISSION OF SCHISTOSOMA HAEMATOBIIUM IN MSAMBWENI, KENYA

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Abstract. As part of an extensive study of the eco-epidemiology of urinary schistosomiasis along the southern coast of Kenya, spatial and temporal transmission patterns were associated with various ponds infested with Bulinus snails. The household-level spatial pattern of infection for children of various age groups in 2000 was contrasted with historical data from 1984. Significant local clustering of high and low infection levels among school age children was detected, and the spatial extent of clusters and their direction from specific water sources were measured. High infection levels were clustered around ponds known to contain Bulinus nasutus snails that shed Schistosoma haematobium cercariae, and low infection levels were concentrated near a river where intermediate host snails were rarely found. The spatial patterns of infection varied between 2000 and 1984 and between age groups. High levels of infection were clustered around different transmission foci in the two study periods, and, for younger children in 2000, were clustered nearer to the transmission foci than for the older children. Simultaneous consideration of the effects of different foci on transmission will allow for targeted application of control measures aimed at interrupting S. haematobium transmission at a local level.

INTRODUCTION

Chronic infection with Schistosoma haematobium is a significant cause of morbidity and premature mortality affecting more than 100 million people1,2 and causing hydrenephrosis and hematuria; pain, diarrhea, undernutrition, and anemia are also associated with infection. Morbidity increases with infection intensity, but can be mitigated with chemotherapy (praziquantel). The intermediate hosts for S. haematobium are various species of bulinid snails of the Africanus complex (Bulinus africanus, B. globosus, B. nasutus).3

Substantial spatial and temporal variation in transmission of schistosomiasis occurs within human populations.4,5 Human infection patterns vary as a function of water contact patterns, immunity, the presence of competent intermediate snail hosts,6 and the availability of suitable aquatic habitats for water use. Along the southern coast of Kenya, human exposure to S. haematobium occurs at snail habitats (ponds and streams) infested with the intermediate host snail Bulinus nasutus. Complicating the effective targeting of control measures in coastal Kenya is the use by residents of a variety of different ponds for bathing, swimming, and washing laundry.7 As Chandiwana and Woolhouse8 and others9–11 have shown, the frequency and intensity with which people use a diversity of contaminated and uncontaminated water sources affects transmission patterns. Because water use of different ponds is not independent, the association of the human population with various ponds in the area needs to be considered when analyzing spatial patterns of infection.

Clennon and others12 described the spatial clustering of S. haematobium infection around one infested pond in a single rural village in Msambweni. To better understand the influence of multiple transmission sources on infection patterns, retrospective and current spatial patterns were examined at the household level by integrating human infection and snail habitat locational data, and applying spatial analyses in 10 villages throughout Msambweni Division, Kwale District, Kenya.

METHODS

Study area. The study area consists of 10 villages (Nganja, Milalani, Vidungeni, Marigiza, Mabatani, Sawa Sawa, Bomani, Mwaembe, Kisimachande, and Vingujini) located in Msambweni Division, Kwale District, Coast Province, Kenya (Figure 1) approximately 50 km south of Mombasa on the coastal plain along the Indian Ocean. According to a demographic survey conducted in 2000, the 10 villages have 2,813 households and 16,790 people. Most residents are Moslem and are affiliated with the Wadigo tribe. Subsistence agriculture predominates with maize, cassava, sweet potatoes, and rice as the main crops. Rice cultivation occurs throughout the area in valleys that connect rain-filled ponds. An irrigation canal, constructed in 1954, enhances water drainage to a large area in the western portion of the study area where family-based rice farming has replaced commercial sugar cultivation (Figure 1).

Water sources used by Msambweni residents. Within Msambweni Division, residents depend on a variety of water sources. These include ponds, spring fed rivers, and a stream, as well as human-made open wells and boreholes. Natural water sources in the area include a perennial river, the Mukumuzi, and a seasonal stream, the Lukungwi, that flow through Msambweni. Until recently, access to piped-water has been quite limited, but in 2003 the Kenyan government began a substantial water project to expand access of piped-water in the area. Residents in the area have a preference for pond and stream/river water over the hard water from boreholes and open wells for laundry and for other uses, including swimming and playing. Additionally, boreholes and open wells in the area have been plagued with water quality problems related to bacterial contamination. Water-borne infections such as cholera, typhoid, and Escherichia coli among others are prevalent along the southern coast of Kenya.13,14 The quality of water in boreholes and open wells in Msambweni is affected by the poor drainage of waste water.15

Nine water bodies were monitored for human water contact, snail distribution, and environmental conditions. Moni-

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tored water sources included six ponds (Kiziamkala Pond, Maridzani Pond, Bovo Pond, Nimbozde Pond, Mwachiangwa Pond, and Mwamagongo Pond), a rice field, the Mukurumudzi River, and the Lukungwi Stream (Figure 1). When the ponds contain water, a variety of snail species can be collected, including B. nasutus, the intermediate host of S. haematobium in the study area. During the 1980s, B. nasutus snails were found at every water source at least once, with the river being the least favorable habitat. Most snails found shedding S. haematobium cercariae were from Kiziamkala and Maridzani Dams, followed by Bovo, Nimbozde and Mwagiza ponds. The percentages of B. nasutus found shedding cercariae were generally less than 2%, even at Kiziamkala and Maridzani Dams. In 2001, Nimbozde Pond had the greatest numbers of B. nasutus (approximately 3%) shedding S. haematobium cercariae, followed by Maridzani, Kiziamkala and Mwamagongo ponds. Bovo and Mwamagongo ponds were also found to have B. nasutus shedding, but in lower numbers. Along the stream, B. nasutus snails were found, but none shed.

Ethical oversight. Prior to collecting urine samples for determining S. haematobium infection status, informed consent was obtained from area residents (or for children their parents). These studies were performed under human investigations protocols approved by the Ethical Review Board of Kenya Medical Research Institute (Nairobi, Kenya) and by the Human Investigations Review Board of University Hospitals (Cleveland, OH).

Infection prevalence. Residents submitted two 10-mL urine specimens at noon a week apart for examination for S. haematobium infection during 2000–2002. Infections were detected using Nuclepore filtration, and measured up to 1,000 eggs per urine specimen. Aggregated household infection levels are reported as geometric mean density (number of parasites per person in a household regardless of infection status), which is a function of both prevalence (the proportion of people infected in a household) and geometric mean intensity (the geometric mean number of parasites for only infected people infected in a household). Schistosoma haematobium infection patterns in the population of Milalani Village were originally described by Clennon and others. These data were compared with those collected in the 1980s by King and others.

Statistical analysis. Our study population comprised children 6–17 years of age, the age group that exhibits the highest infection levels, and who unlike older residents were not previously enrolled in a school-based schistosome chemotherapy program. Differences in prevalence between age groups were tested using the homogeneity chi-square test. Correlation was used to assess the correspondence of eggs counts between urine tests. Logistic regression (forward conditional) was used to appraise the relationship between whether children were infected with sex, age (continuous from 6 to 17 years), age-by-sex interaction, the nearest household distance to an alternative water source (open well, borehole, piped-water), known school attendance, total household population, and number of children per household. A follow-up univariate logistic regression using age as a factor (6–9, 10–13 and 14–17 years) was used to calculate odds ratios for each age group. Stepwise linear regression was then used to evaluate the relationship of individual infection levels with those variables. These non-spatial statistical analyses were performed using SPSS version 11.5.0 software (SPSS Inc., Chicago, IL).

Geospatial processing. Households and water sources were mapped as described by Clennon and others using a high-resolution satellite image comprised of 1-m² panchromatic and 4-m² multi-spectral images of Msambweni. During the 2001 house-to-house demographic survey, each household was given a village affiliated household identification (HID) number that was marked on the exterior of the home, and each person was assigned a individual identification (ID) number incorporating the HID. Demographic information collected on each individual included name (common and tribal), sex, year of birth, mother’s name and ID, mother’s mother name, father’s name and ID, and father’s father name. When urine samples were submitted, the participant’s name, ID (or at least HID), sex, and year of birth were again recorded so that the infection data could be correctly linked with demographic data. When household locations were mapped, homes were identified based on roof type (thatch, tin, rusty-tin), household relationship to other homes and landmarks (e.g., roads, walking paths, trees by type water sources) in the pan-sharpened Ikonos image. The HID were then marked directly upon the Ikonos image in the field, and digitized in the GIS later the same day. When there was any uncertainty, a GPS reading was taken and a small sketch map of the location was drawn.

To identify 1984 household locations, village workers familiar with the residents in the area went to the participant’s (identifiable by name, date of birth, sex, and prior school attendance and past participation) current homes and inquired if the home where they currently resided was their home in 1984 or if they have since moved. In cases when the participant had moved, they were asked about the previous home’s location (if they knew who was currently residing there or if they could show them the location). We were able to locate 1,014 homes from the 1980s.

Household and water source locations were joined with demographic, parasitologic, malacologic, and environmental data. Locational data were georectified to the Universal Time System.
Transverse Mercator (UTM) zone 37S projection, 1984 datum, in the GIS software package ArcGIS 9.0 (Environmental Systems Research Institute, Redlands, CA).

**Spatial statistics.** For spatial analyses, children were grouped by age (6–9, 10–13, and 14–17 years). Global, focal, and directional spatial analyses were used to examine the spatial structure of *S. haematobium* infection patterns and identify significant clustering of elevated infection levels in the study area. Global Ripley’s K-function, global weighted K-function, local G*(d), and focal G*(d) were applied to human infection patterns using Point Pattern Analysis (Chen and Getis) and ClusterSeer (TerraSeer, Ann Arbor, MI) software.

Global second-order (K-function and weighted K-function) spatial analyses that compare the observed pattern of points with a homogenous Poisson process were used to classify spatial patterns over the entire study area as being random, clustered, or uniformly dispersed (tending towards regular), with significance determined using Monte Carlo simulations. The observed point pattern in a K-function analysis is composed of a 0/1 distance matrix that includes points according to distance, over a range of distances. The weighted K-function considers values in each location (e.g., household density of infection), and permutations that randomize these values among household locations are used to determine significance, thus rendering it independent of site locations. We used global K-function to assess the general distribution of household locations, and weighted K-function to evaluate the overall submission distribution and spatial pattern of infection.

The local statistic G*(d) was applied to describe local variation in the spatial structure of infection within the study area. Local G*(d) and G*(d) spatial statistics detect significant autocorrelation or clustering around each point by comparing point values (e.g., household infection density) to the overall mean. Mathematically, the values at each point are weighed according to distance (1 = within the considered distance; 0 = outside the considered distance) using a circular extent (Figure 2A). The G*(d) and G*(d) statistics yield normal standard variables. To account for multiple comparisons, significance levels for local G*(d) analyses were determined according to Ord and Getis. Clennon and others have demonstrated that the local G*(d) spatial statistic can be applied as a focal statistic by only evaluating the spatial association of point values (infection density, infestation levels) at different distances surrounding unique locations of interest.

Centroids for suitable (Nimbodze Pond, Maridzani Pond, Kiziamkala Pond, Bovo Pond, Mwamagongo Pond, Mwachiangwa Pond) and unsuitable *B. nasutus* water sources (Mukurumudzi River) were used as source points for such focal cluster analyses. A cluster was deemed significant when G*(d) exceeded and maintained a value of 1.96, the standard normal cutoff for significance at 0.05. A critical distance for a cluster diameter was defined by a peak and subsequent decay of G*(d). Clustering was considered up to a realistic walking distance of 2,500 meters surrounding specific transmission foci, where snails shedding *S. haematobium* cercariae have been found, and low infection levels near aquatic habitats where *B. nasutus* is rarely found. Focal spatial statistics that use circular extents in weighting distances in their calculations can give somewhat misleading results when there are directional differences in a spatial pattern (anisotropy). Directionality can be incorporated into the weight matrix by including an additional condition for a point to also be at a particular direction (or angle) from the focal point being assessed (Figure 2B). Centroids for Nimbodze and Kiziamkala ponds were used as source points for directional analyses to limit the number of tests performed. The critical level for significance was set at 2.13 for n = 3 (4 directions -1). In this study, we used local G*(d) as a focal, directional statistic to identify directional clustering occurring near two known foci of *S. haematobium* transmission (Nimbodze Pond and Maridzani Dam).
The 2000 data were compared with data from a 1984 school survey from 1,647 households that could be located\(^\text{19}\) and for which spatial statistics could be applied to school age children of three age groups (6–9, 10–13, and 14–17 years).

RESULTS

In 2000, we were able to determine the locations of 2,292 households with 13,609 residents (Figure 1). From those households, 9,260 (68.0\%) residents submitted urine samples that were tested for *S. haematobium* eggs and 3,000 (32.4\%) of these samples were positive. The mean ± SD number of school age children tested per household was 2 ± 1.5. Egg counts between urine specimens from school age children corresponded significantly (\(r = 0.66, P < 0.001\)).

The logistic regression of infection of school age (6–17 years) children adequately fit the data (Hosmer and Lemeshow \(\chi^2 = 9.7, P > 2.29\)), but explained only 12\% of the variance (Nagelkerke pseudo-\(R^2\)). Age (as a covariate) was the only significant variable (Wald = 90.6, \(P < 0.0001\)), and had positive association with infection (\(\beta = 0.21\)). When age groups (as a factor) were further examined using univariate logistic regression, both adolescents (14–17 years of age) (odds ratio [OR] = 2.55, 95\% confidence interval [CI] = 2.15–3.02) and 10–13 years-old persons (OR = 1.69, 95\% CI = 1.69–2.32) had higher odds of being infected than 6–9 year-old children. Although linear regression explained less than 10\% of the variance (\(P < 0.0001\)) in infection levels, it detected a significant positive relationship between age and infection level (\(\beta = 0.36, t = 9.13, P < 0.0001\)). Other factors such as sex (\(t = -0.74, P > 0.46\)), distance to nearest alternative water source (\(t = 0.23, P > 0.82\)), and school attendance (\(t = 0.85, P > 0.40\)) did not have significant relationships with degree of infection.

Spatial infection patterns. Household locations were highly aggregated (K-function, \(P < 0.01\)) at distances up to 2,500 meters, and submission of urine samples by children was evenly distributed. Household density of infection in each age group was not aggregated (weighted K-function) during both study periods.

During 2000, significant local spatial autocorrelation of high infection levels at 500 meters occurred near Nimbozde Pond for all age groups (Figure 3A). Additional clustering at 500 meters also occurred near Maridzani Dam among older children (10–17 years of age) and Mwachiangwa Dam only for adolescents (14–17 years of age). At distances greater than 500 meters, a significant positive autocorrelation was detected throughout the area between Nimbozde, Kiziamkala, and Mwachiangwa ponds, with additional clustering among young children (6–9 years of age) occurring south of Lukungwi Stream near Nimbozde Pond.

In 1984, local patterns of infection density exhibited high levels of clustering for each age group around Maridzani Dam and the neighboring Bovo Pond to a greater degree than in 2000 (Figure 3B). There was no significant clustering of high infection levels around Nimbozde Pond for any age group up to a distance of 1,000 meters in 1984. Significant positive clustering at 1,500 meters was detected between Nimbozde, Maridzani, and Mwachiangwa ponds for older children (10–17 years of age) in 1984. In the youngest children, a significant positive autocorrelation occurred halfway between Maridzani Dam and Nimbozde Pond. Additionally, significant negative autocorrelation was detected in 10–13 year-old persons between the river and Kiziamkala Dam at a variety of distances, and the center of this clustering moved southeast as the distance considered increased.

Focal clustering of infection. Focal clustering of infection density around the different water sources varied by age and between the two study periods. In 2000, high levels of infection in children 6–9 years of age were clustered starting and peaking in close proximity to Nimbozde Pond with clustering persisting past 1,500 meters (Figure 4A). High infection levels were also clustered among older children (10–13 and 14–17 years of age) around Nimbozde Pond, but the degrees of clustering were much lower initially and peaked farther from Nimbozde Pond (Figure 4A). During 2000, the greatest degree of clustering around Maridzani Dam was detected among 10–13 year-old persons, with clustering highest close to the dam and significant levels up to a distance of 650 meters (Figure 4B), as was the clustering of infections in ado-
lescents (14–17 years of age). In contrast, clustering among 6–9 year-old children was significant only between 350 and 450 meters (Figure 4B). Near the river in 2000, significant clustering of low levels of infection was detected for 10–13 and 14–17 year-old persons (Figure 4C).

In 1984, high levels of infection were clustered around both Nimbodze Pond (Figure 4D) and Maridzani Dam (Figure 4E) for all age groups. Among 6–9 year-old children, significant clustering of high infections around Nimbodze was detected up to 550 meters from the pond and for older children it persisted beyond 1,000 meters. Around Maridzani Dam in 1984 (Figure 4E), high infection levels for all age groups were significantly clustered from 500 to 800 meters, but the degree and extent of clustering was higher for the younger children (6–13 years of age) than for older children (14–17 years of age). Around the river water site in 1984, low levels of infection were clustered for all age group (Figure 4F), with clustering persisting in older children (10–13 and 14–17 years of age) up to 1,500 meters and beyond.

When patterns of recent infection density are compared with data from 1984, differences in the patterns of clustering are apparent. In 1984, clustering of high infection density among all age groups was focused to a greater degree and more extensively around Maridzani Dam, rather than around Nimbodze Pond (Figures 4D and 4E). In 2000, significant clustering of high infection levels occurred more extensively around Nimbodze Pond (up to a distance of 1,000 meters) than around Maridzani Dam (Figures 4A and 4B).
**Directional clustering near transmission foci.** When directionality was considered in the focal cluster analyses, most of the clustering of high household infection density occurred from east of Nimbozde Pond to west of Maridzani Dam. During 2000, all age groups showed significant clustering extending east from Nimbozde Pond, peaking at 750 meters (Figure 5A), decreasing until 1,250–1,500 meters (the halfway mark between Nimbozde Pond and Maridzani Dam), and then increasing until 2,250–2,500 m (the distance to Maridzani Dam). Although the general trend of $G_i(d)$ values in 1984 was similar (significant clustering early with a subsequent decrease in levels that bottom out at approximately 1,250 meters before they increase again) (Figure 5B). Only at distances of 500–750 meters east of Nimbozde Pond was infection significantly clustered for children 6–9 and 10–17 years of age.

Westwards from Maridzani Dam, clustering peaked at distances of 750–1,000 meters for each age group in 2000 (Figure 5C). The overall level of clustering between 1,000 and 2,000 meters was higher in older children and adolescents compared with 6–9 year-old children. In 1984, significant clustering of high household infection densities was also identified as extending west from Maridzani Dam (Figure 5D) with peak $G_i(d)$ values occurring between 500 and 750 meters. Although $G_i(d)$ values in 10–13 and 14–17 years-old persons remain steady past 1,250 meters, a decrease in the degree of clustering occurs among 6–9 years-old children.

Some clustering of infection density was detected in other directions around Maridzani Dam. Clustering of high infection levels extended north 500 meters among 10 to 13 year-old persons in both 2000 and 1984. Additional clustering to the east of Maridzani Dam was detected in 1984 through to 2,500 meters in older children (10–13 and 14–17 years of age) but not in children 6–9 years of age.

**DISCUSSION**

Within Msambweni, *S. haematobium* infection levels varied among children by age, between the two study periods and as a function of the spatial associations of their homes with contaminated and uncontaminated water sites. Global spatial statistics enabled us to determine that although households were clustered overall, there was no general trend of clustering for *S. haematobium* infection densities throughout the area. Local and focal spatial statistics were used to detect significant autocorrelation and clusters of high or low levels of infection density of *S. haematobium* among children at the household-level. The application of focal spatial statistics allowed us to assess transmission levels around various water sources, both contaminated and uncontaminated. By accounting for directionality in assessing clustering around known *S. haematobium* transmission foci, major differences in clustering by direction became apparent.
Our findings suggest that infection levels of human urinary schistosomiasis are clustered as a function of the spatial distribution of water sources that are contaminated, as well as those that are not contaminated (e.g., the river) with S. haematobium-infected snails. The effects of main transmission sources on household infection density were significant through 1,500 meters, which is well within the known distance range that people will travel to ponds in the area. Significant directional patterns of clustering can be attributed to most clusters being located between two transmission foci (Nimbodze Pond and Maridzani Dam). The sharp gradient in levels of focal clustering (Figure 4B) was greatly reduced in the directional focal analysis (Figure 5C), which demonstrates the strong anisotropy of the data. The clusters of low infection levels are likely associated with the use of uncontaminated water sources that allow people to avoid infection (e.g., rivers and streams).

By considering two study periods 16 years apart and children’s ages, a temporal shift in the primary source of S. haematobium transmission was identified. The spatial patterns of infection in 1984 can be attributed to more intense transmission that was occurring around Maridzani and Bovo Ponds. In 2000, clustering was found primarily around Nimbodze Pond. The change in clustering pattern between 1984 and 2000 suggests a shift in the primary source of transmission in the area, which may be associated with changes in environmental conditions affecting intermediate host snails in the ponds, or with shifts in patterns in human use of ponds. Some spatial heterogeneity in infection patterns during 1984 may not have been recognized because households (linked with infection data) could not be mapped as extensively as the current data.

Although Kiziamkala Dam was found to have many B. nasutus shedding S. haematobium cercariae during the 1980s, people living east of the dam would frequent the river where no B. nasutus have been found shedding cercariae. The clustering of intense infections between Bovo Pond and Maridzani Dam, and not by Kiziamkala Dam, suggests that the use of a non-cercarial infested water source (the river) mitigated infections levels. Only limited 2000 era water contact data was collected in 2001 because of drought conditions and subsequent drying of the primary water bodies used by residents.

Differences in clustering among children of different age groups reflect the effects of exposure to waters contaminated with S. haematobium cercariae, as well as of acquired immunity. The most dramatic shift in local and focal clustering patterns was seen among children 6–9 years of age, those with limited exposure to Maridzani and Bovo ponds before the contribution of these two ponds to transmission was apparently reduced. Variations in exposure to S. haematobium-contaminated water sources among the different age groups are likely due to differences in water-use activities and in walking distances to water sources.

Maridzani Dam (with interaction with Bovo Pond) appears to have been the primary S. haematobium transmission epicenter in the 1980s, and Nimbodze Pond acted as a main focus in 2000. Our results also suggest that older children in 2000 are carrying infections acquired when Maridzani was still the prominent transmission focus. It is possible that with an increasing number of households built in closer proximity to Nimbodze Pond, the epicenter for S. haematobium transmission shifted from Maridzani Dam to Nimbodze Pond. However, changes in snail distribution patterns suggest that the shift in parasite transmission and the resulting infection clustering pattern are more likely associated with climatic and environmental changes.\(^4,16\)

During 2000, more snails and more snails shedding cercariae were found at the Nimbodze Pond water contact sites compared with Maridzani Dam, and the reverse was observed in 1984. This may be related to an El Niño event during 1997–1998. The flooding that occurred in 1997–1998 was devastating in many parts of Kenya including Kwale District, where the Msambweni study area is located, and was associated with significant environmental degradation (e.g., soil erosion), as well as more small temporary ponds. It is possible that the snail habitats at Maridzani Dam were more negatively affected by soil erosion. During El Niño years, much of the area surrounding Nimbodze Pond, which is more level than the area around Maridzani Dam, was flooded; this likely increased the amount of snail habitat in that part of the study area. It is also possible that the intensity of S. haematobium transmission was decreased at Maridzani Dam because people living in the vicinity of the pond began using small temporary ponds created by the 1997–1998 El Niño flooding. In addition, the conversion of sugar cane fields to rice fields (which requires an aquatic environment) west of Nimbodze during the 1990s increased the connectivity of the B. nasutus source and sink habitats of Nimbodze Pond, leading to a more stable intermediate host population, which subsequently led to increased S. haematobium transmission.

Applying spatial statistics, Clennon and others\(^12\) determined that S. haematobium infection was clustered around a single pond (Nimbodze) known to be contaminated with S. haematobium cercariae. Age-related water contact behaviors and acquired immunity were the most probable determinants underlying the observed pattern of clustering of high density of infection. By moving upscale and expanding our study area to include neighboring villages and additional ponds in the study presented here, we were able to account for the area-wide nature of household use of water sources. By applying the same spatial analysis and a directional focus statistic to data from an earlier study period, we could consider changes in transmission patterns over time. Because of sharp discontinuity in transmission habitats (and infection patterns) and that the process driving infection in Msambweni is not intrinsically stable, a risk map was not constructed.

Based on the complex interactions between study period, age, and spatial associations with water sources, we conclude that a range of spatial and temporal scales needs to be considered for an understanding of S. haematobium transmission patterns in an area. As environmental and social conditions change, spatial analyses allow control programs to better focus interventions targeting schistosomiasis transmission in space and time.

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