**Schistosomiasis sampling**

**Abstract**

**Introduction**

Schistosomiasis is chronic parasitic disease affecting over 200 million individuals globally and causing over XXX Disability Adjusted Life Years (GBD Ref). The majority of the burden occurs in Sub-Saharan Africa, with over 150 million individuals estimated to be infected with either *Schistosomiasis haematobium* or *S. mansoni* [1]. Determined by distribution and contact with freshwater snail habitats and access to clean water and sanitation, schistosomiasis transmission is highly focal, with disease risks varying markedly within small spatial areas [2, 3].

To reduce morbidity, preventative chemotherapy with praziquantel remains the cornerstone of control programmes [4, 5]. Mass drug administration targets high risk groups living in endemic areas, including school aged children (SAC, ages 5-15 years), pregnant women and individuals with occupational risks [6]. Prior to treatment, epidemiological data on infection prevalence are required to identify high risk communities; prevalence is assessed and treatment assigned at a spatial unit referred to as the implementation unit (IU). Although there is no standard definition for IUs, these are typically defined as districts or ecological zones consisting of multiple subdistricts [7]. Current World Health Organization guidelines recommend estimating prevalence using two stage cluster-based school surveys, recommending sampling 50 children per school for five schools per IU [6, 7]. This survey design is easily implemented and analysed, using simple random sampling from lists of schools per IU without requiring additional spatial information on schistosomiasis distribution. Alternatively, with increasing availability of spatially referenced prevalence data, model-based geostatistical approaches (MBG) can be used to design more efficient sampling approaches by exploiting spatial correlation in prevalence [8]. Based on these surveys, preventive chemotherapy is administered every year for mapping units with over 50% prevalence, every two years if the prevalence is between 10 – 50% and not administered if prevalence is below 10% [6] (WHO 2011 – add description if revised?).

Modelling studies have been used to illustrate how alternative sampling strategies can improve estimates of prevalence, maximising cost efficiency by more accurately targeting preventive chemotherapy [9-12]. Using geostatistical simulations of baseline prevalence estimated from existing survey data, effects of different sampling strategies can be evaluated against known parameters generated from spatially realistic simulated datasets, allowing assessment of a wide range of survey designs. For schistosomiasis, this approach has been used to explore the accuracy and cost effectiveness of varying the number of schools and number of children sampled under current two-stage cluster design surveys [13]. Additionally, a previous study explored the performance of two sampling strategies for classifying school-level schistosomiasis prevalence: lot quality assurance sampling (LQAS), sampling small numbers of children from all schools within a given area, and MGB, using spatial modelling approaches to predict prevalence based on a small number of sampled schools [9].

Building on this work, we use geostatistical simulations to evaluate how survey and treatment strategies can be targeted to capture spatial heterogeneity at finer spatial scales. As countries move towards elimination targets [5], there is increasing recognition of the focality of schistosomiasis transmission and the need to implement preventive chemotherapy at subdistrict levels [14]. Previous studies have demonstrated a substantial proportion of schools are misclassified and incorrectly treated based current WHO guidelines due to variation within districts [15]. To explore how control programmes can address this heterogeneity, we assessed the use of district and subdistricts as IUs across a range of spatial distributions for *S. haematobium* and *S. mansoni* in a simulated country. Applying these findings to conditional simulations of data collected in three African countries, we then compare the accuracy and cost-effectiveness of two-stage cluster surveys using subdistricts as implementation units and MGB approaches.

**Methods:**

*Simulation of representative country data*

To explore the implications of different sampling strategies on estimates of prevalence, we obtained polygon boundaries of all schistosomiasis IUs in Sub-Saharan Africa (SSA) from the World Health Organization Expanded Special Project for Elimination of Neglected Tropical Diseases (ESPEN) portal [16]. We first generated a hypothetical representative country in SSA using the mean country area (km2). Using the median ratio of numbers of IUs to country area and estimating three subdistricts per IU, we randomly assigned districts and subdistricts. We simulated the distribution of schools based on the density of schools per area in Uganda, assuming 500 SAC per school and at least 5 schools per district.

Binomial geostatistical models were fitted to *S. haematobium* and *S. mansoni* prevalence data retrieved from the ESPEN portal for 24 countries in SSA, with the intent to capture the heterogeneity of the spatial variability and spatial extent of the disease under different settings (ADD TO SI). Using conditional simulations and combining the different ranges of spatial parameters obtained from geostatistical models, we created a gold-standard dataset of prevalence under different scenarios with a range of spatial variances and scales.

* Add equations?

*Comparison of subdistrict and district level implementation units*

* Current version has categorised – need to rerun with 10% cutoff?

*Conditional simulations using country data*

* Data sources
* Methods

*Cost analysis*

* Data sources from SCI – include assumptions
* Table of itemised costs

The mapping survey design cost was estimated using the ingredients method using capital resources data obtained from school-based mapping surveys [13]. We considered only financial costs and excluded expenditures related to general programme operating costs or costs borne by the beneficiaries. Expenditures related to the reassessment mapping were extracted for two surveys conducted in 2016-2017 and 2017-2018 in Malawi and Uganda and one survey conducted in 2017-2018 in Tanzania (REF SCI?). Consumable item costs were calculated based on the quantity used for each diagnostic method and number of children surveyed, assuming 10% wastage. We defined capital items as items with a typical life expectancy of over one year; the costs of these items were annuitized based on the useful life expectancy in years estimated by survey personnel (SCI).

We assumed an average of one school per day would be visited by the survey team, including a half day to register children and collect samples and a half day of sample processing. Based on reported survey activities, teams included one driver, one team leader, one district officer and one central officer with two technicians would be required to sample 30 – 40 children and three technicians would be required to sample 50 children. Per diems for sample teams were estimated based on reported country specific expenditures. We calculated mean costs per school based on reported district level fuel costs and numbers of schools covered, assuming vehicle maintenance was conducted once during the survey period. No capital costs for vehicle purchase were included.

Need to add 40 children – other diagnostics?

|  |  |  |
| --- | --- | --- |
| Diagnostics | Number sampled per school | Cost per school, GBP  mean (range) |
| All (KK, UF, CCA) | 30 | 466.23 (415.55 – 504.70) |
| Routine (KK, UF) | 30 | 431.05 (382.00 – 471.17) |
| All (KK, UF, CCA) | 50 | 670.12 (604.51 – 708.07) |
| Routine (KK, UF) | 50 | 611.47 (548.59 – 652.11) |

Costs per treatment were estimated based on district-level treatment data obtained from Burundi, Malawi, Uganda and Tanzania for treatments administered from 2016- 2017 and 2017- 2018 (need more information about data). We estimated the mean treatment cost per child from the number of children treated per district and total district level costs.

* Add sensitivity analysis for subdistrict costs?

All expenditures were obtained in the local currency and converted into British pounds (Need to convert to USD) using the Consumer Price Index and current exchange rates.

|  |  |
| --- | --- |
| Country | Cost per child treated, GBP  mean (range) |
| All | 0.33 (0.01 – 3.37) |
| Burundi | 0.05 (0.01 – 0.12) |
| Malawi | 0.22 (0.05 – 1.86) |
| Tanzania | 0.37 (0.06 – 1.09) |
| Uganda | 0.62 (0.05 – 3.37) |

*Evaluation of sampling strategies*

* MBG methodology + random sampling
* Variation in numbers of children sampled, etc

**Results:**

District vs subdistrict

* Polygon of schools generated with districts and subdistricts
* Summary descriptions of model results – spatial range, variance
* Estimates of prevalence using wider spatial parameters – include in SI
* Proportions of schools correctly classified vs implementation units
* Spatial parameters?

Sampling accuracy – proportions correctly classified

* AUC figures
* Numbers correctly classified/ treatment/ cost (final results)

Cost efficiency

* Estimated costs – total summaries
* Cost per survey designs – using IQR?

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