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Rapid assessment of *Schistosoma mansoni*: the validity, applicability and cost-effectiveness of the Lot Quality Assurance Sampling method in Uganda

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Summary

Rapid and accurate identification of communities at highest risk of morbidity from schistosomiasis is key for sustainable control. Although school questionnaires can effectively and inexpensively identify communities with a high prevalence of *Schistosoma haematobium*, parasitological screening remains the preferred option for *S. mansoni*. To help reduce screening costs, we investigated the validity of Lot Quality Assurance Sampling (LQAS) in classifying schools according categories of *S. mansoni* prevalence in Uganda, and explored its applicability and cost-effectiveness. First, we evaluated several sampling plans using computer simulation and then field tested one sampling plan in 34 schools in Uganda. Finally, cost-effectiveness of different screening and control strategies (including mass treatment without prior screening) was determined, and sensitivity analysis undertaken to assess the effect of infection levels and treatment costs. In identifying schools with prevalence ≥50%, computer simulations showed that LQAS had high levels of sensitivity and specificity (>90%) at sample sizes <20. The method also provides an ability to classify communities into three prevalence categories. Field testing showed that LQAS where 15 children were sampled had excellent diagnostic performance (sensitivity: 100%, specificity: 96.4%, positive predictive value: 85.7% and negative predictive value: 92.3%). Screening using LQAS was more cost-effective than mass treating all schools (US$ 218 vs. US$ 482 / high prevalence school treated). Threshold analysis indicated that parasitological screening and mass treatment would become equivalent for settings where prevalence exceeds 50% in 75% of schools and for treatment costs of US$ 0.19 per schoolchild. We conclude that, in Uganda,

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LQAS provides a rapid, valid, and cost-effective method for guiding decision makers in allocating finite resources for the control of schistosomiasis.

Keywords

schistosomiasis; *Schistosoma mansoni*; Lot Quality Assurance Sampling; parasitological screening; cost-effectiveness; national control; Uganda

Introduction

Renewed commitment to morbidity control of schistosomiasis provides an important opportunity to re-evaluate and improve control strategies to ensure both cost-effectiveness and long-term sustainability (Utzinger et al., 2003). One key issue for the planning of control is the rapid and accurate identification of high risk communities requiring mass treatment with praziquantel. The use of morbidity questionnaires is well established as an effective and inexpensive means of identifying communities with a high prevalence of *Schistosoma haematobium* (Lengeler et al., 2002). By contrast, the use of questionnaires for *S. mansoni* has proved less promising, and parasitological diagnosis remains the preferred option. However, parasitological screening of individuals incurs significant expenses associated with staff allowances, capital equipment, transport and materials to collect and process faecal samples and as such, there is a need to collect reliable data as rapidly and cheaply as possible.

Parasitological surveys of schools and communities usually rely upon classical statistical approaches (Bennett et al., 1991). Here, sample sizes are fixed in advance of data-collection according to the expected levels of prevalence and the degree of precision required, modified by logistics and resource constraints. Classical analysis such as estimation or hypothesis testing is then performed on the collected data. For example, current WHO recommendations are based on the concept of sample surveys of 50 children per school within defined ecological zones (Montresor et al., 1998). This sample size was selected because it was considered to be the maximum number of children that a survey team could sample and examine in a single day. Such an approach typically involves a survey team of several staff moving with a single vehicle, and necessitates entry and analysis of survey data. It is therefore often considered to be prohibitively expensive for a national programme to sustain parasitological surveys on a large scale where this approach is used.

An alternative sampling approach is Lot Quality Assurance Sampling (LQAS) in which the sample size is not fixed in advance (Lemeshow & Taber, 1991). Instead, observations are collected individually or in small batches and, after each observation, the data are examined to see whether or not a decision, such as whether to intervene, may be made from the accumulated data. LQAS combines data-collection and data-analysis into a single process or sampling plan. This approach can considerably reduce the sample size requirements as well as the data-processing overheads of a survey. LQAS methods are best used in situations where classification (e.g. into prevalence classes) of a population or community is useful and where the emphasis is on decision making (e.g. whether or not to intervene in a particular community) rather than estimation of prevalence and intensity of infection. The use of LQAS has increased in the health field over the last 15 years and has been used to monitor vaccination coverage (Lanata et al., 1990; Sandford. 1993; Singh et al., 1996; Tawfik et al., 2001), HIV prevalence (Houinato et al., 2002) and leprosy elimination (Gupte et al., 2004), and to guide control of lymphatic filariasis (Lakshmi, 2000), malaria (Rabarijaona et al., 2001) and trachoma (Myatt et al., 2003).

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LQAS has recently been used to identify communities in Madagascar with high prevalence of *S. mansoni* (Rabarijaona et al., 2003). Given the potential importance this approach has for national control programmes, there is a requirement for evaluating its usefulness in other settings. Importantly, there is also a need to assess the cost-effectiveness of the approach in comparison to both traditional sampling approaches and to mass treatment without prior screening. To date, studies have only investigated the cost-effectiveness of alternative screening strategies in delivering treatment for *S. haematobium* at the community level (Talaat & Evans, 1996; Ansell & Guyatt, 2002), and for *S. haematobium* (Guyatt et al., 1994) and *S. mansoni* (Carabin et al., 2000) at the individual level. The cost-effectiveness of screening and treatment strategies at the community level has yet to be evaluated for *S. mansoni*. The aim of the present study was to assess the validity of LQAS in classifying schools according categories of prevalence of *S. mansoni* in Uganda, and to explore its applicability and cost-effectiveness in guiding national control efforts.

Methods

Study area and control programme

The study was conducted in the context of a national schistosomiasis and soil-transmitted control programme in Uganda (Kabatereine et al., 2005). This programme was established in 2002 with support from the Schistosomiasis Control Initiative, funded by the Bill and Melinda Gates Foundation. Following WHO guidelines, the programme is classifying communities according to three strategies: (1) in communities with a high prevalence (≥50%) schoolchildren are treated every year and high risk groups, such as fishermen, are treated; (2) in communities with a moderate prevalence (≥20% and <50%) schoolchildren are treated once every two years; and (3) in communities with a low prevalence (<20%) chemotherapy should be available in health facilities for treatment of suspected cases. Because of the widespread distribution of soil-transmitted helminthes (STH) in Uganda, albendazole is co-administered with praziquantel.

The geography and epidemiology of *S. mansoni* in Uganda has recently been reported by Kabatereine et al. (2004). This work shows that no transmission typically occurs in areas where total annual rainfall was <850 mm and altitude was >1400 m. These areas were, therefore, set aside without the need for further surveys. It was also shown that prevalence consistently exceeded 50% in areas within 5km of Lakes Victoria and Albert, and thus in these areas all communities could be justified, with relative certainty, to warrant mass treatment without the need for further surveys. Outside these two ecological areas, where smaller rivers and water bodies are numerous, it is suggested that individual communities are surveyed using parasitological methods (Brooker et al., 2004a). It is in these areas that the LQAS method will be implemented if it is shown to be a reliable, quick and cost-effective method to classify communities according to treatment categories.

Binomial LQAS method

An overview of the method is provided by Maytt *et al.* (2003). In brief, LQAS is used to test the null hypothesis (H_0) that the proportion of individuals (P) infected with *S. mansoni* is lower than some critical level (P_T) according to the requirements for treatment classifications: if $P<P_T$ then H_0 is accepted and no action is required; if $P\geq P_T$ then H_0 is rejected and mass treatment of the population is required. The first objective here is to classify schools according to different prevalence thresholds: 20% and 50% since, as mentioned above, these represent prevalence thresholds which warrant different treatment schedules.

LQAS data are collected and analysed using a sampling plan that specifies a maximum sample size (n) and the number of cases (d) allowed in the sample (so-called lots) before a classification of a community having a high prevalence is made. Here, schools are considered as lots and d represents the number of children found to be infected with *S. mansoni*. A series of sampling plans were developed to select a maximum sample size (n) and the number of cases (d) that are allowed in the sample of n subjects before deciding that a community is a high prevalence community. The combination of maximum sample size (n) and number of defects (d) forms the stopping rules of the sampling plan. Sampling stops when either the maximum sample size (n) is met or the allowable number of cases (d) is exceeded: if d is exceeded then the community is classified as high prevalence and an intervention required; if n is met without d being exceeded then the community is classified as low prevalence and an intervention not required. The values of n and d used in a sampling plan depend upon the threshold values used in the classification system and the acceptable levels of risk (Lemeshow & Taber, 1991).

Using LQAS to provide a granular classification scheme

Ordinarily, LQAS provides a *binary* classification system. A finer classification system may be provided by applying alternative, secondary sampling plans to data already collected and classified, by previously applied sampling plans, as coming from low (<50%) prevalence communities (see Myatt et al. (2003) for a recent application to trachoma). This approach starts by collecting data using a *primary* sampling plan to classify populations into two groups: (1) schools with prevalences likely to be less than 50%, and (2) schools with prevalences likely to be greater than or equal to 50%, based on n and an initial d, termed d_1. The *secondary* sampling is applied to the samples already taken from the populations not classified as high prevalence by the primary sampling plan on the basis of a second d, termed d_2. The secondary sampling plan is designed to classify populations into two groups: (1) schools with low prevalences likely to be less than 20%, and (2) schools with moderate prevalences likely to be greater than or equal to 20% but <50%. Thus, a three class classification scheme may be implemented using two sampling plans.

Computer simulations of the LQAS method

The LQAS method was initially tested using computer-based simulations, implemented in the R language for data analysis and graphics (Ihaka & Gentleman, 1996), using country-wide data from previous, conventional school surveys of schistosomiasis in Uganda (Kabatereine et al., 2004). In all, 13,800 children in 202 schools were sampled. The simulations used one-thousand *with-replacement* simple random samples from each of the sampled schools (i.e., each school in a dataset was surveyed 1000 times). Thus, a total of 202,000 LQAS surveys were simulated for each of the primary sampling plans tested. The use of simple random sampling in the simulations means that the simulations are indicative of how well the simulated LQAS sampling plans are likely to perform when an equal probability selection method (EPSeM) sampling method is used to collect data. EPSeM sampling of children in schools is not difficult since a random or systematic sample of children from school registers may be used. Values for the primary (n, d_1) and secondary (n, d_2) sampling plans were chosen by performing an exhaustive search of cumulative binomial probabilities for combinations of n and d that provide acceptable levels of risk (Lemeshow & Taber, 1991).

The results of the primary sampling plan are presented graphically using (1) an operating characteristic (OC) curve, and (2) an average sample size (ASN) curve (Lemeshow & Taber, 1991). An OC curve summarises the probability of making a decision *not to intervene* at different levels of prevalence. The probability of making a *decision to intervene* is the complement of the OC function. The complement of the OC function (i.e. 1 - OC) is more

intuitive than the OC function since it summarises the probability of making a *decision to intervene* at different levels of prevalence. An ASN curve shows the sample size required to make a classification using the primary sampling plan by the true prevalence in the school being sampled. The average sample size needed to make a decision varies with prevalence, allowing decisions to be made in high prevalence communities with relatively small sample sizes. Each combination of n and d_1 generates a single OC curve and a single ASN curve.

The validity of the primary sampling plans was evaluated by comparing the true prevalence in each school, as assessed by the conventional (reference) survey method and its prevalence classification as returned by the LQAS method. Diagnostic performance was assessed in terms of sensitivity (the percentage of high prevalence correctly classified as such as by the LQAS method) and specificity (the percentage of low prevalence schools correctly classified as such by the LQAS method). Negative predictive value (NPV) is the proportion of communities classified as low prevalence communities that are true low prevalence communities. Positive predictive value (PPV) is the proportion of communities classified as high prevalence communities that are true high prevalence communities. In this context, PPV is a measure of appropriate resource utilisation. The results of the simulations of applying the secondary sampling plan are summarised graphically using a classification plot which plots the range of true prevalences for each classification. The agreement between true prevalence classes and the classifications made using the two sampling plans were calculated and assessed using the Kappa statistic: values of Kappa less than 0.4 indicate poor agreement, values between 0.4-0.75 suggest good agreement, and values above 0.75, excellent agreement. Gross misclassification errors are defined as true low prevalence schools classified as high prevalence by LQAS and true high prevalence schools classified as low prevalence by LQAS.

Field testing

In 2004, field trials were conducted to assess the validity of the selected sampling plans for classifying schools by the prevalence of *S. mansoni* in 12 schools of Kigandalo Subcounty, Mayuge District along the shores of Lake Victoria and 22 schools in Pakwach and Panyimur subcounties, Nebbi District along the Albert Nile. In Nebbi District, a single round of school-based treatment has been undertaken in 2003 whereas no treatment had previously been undertaken in Mayuge District. Survey teams consisted of a driver, a parasitologist and a technician. Ethical clearance was obtained from the Ministry of Health, Uganda and Imperial College, London. It was decided to evaluate a sampling plan of n=15, d_1=7, d_2=2 using the conventional method of sampling. Here, 15 children (as defined by the sampling plan) from class 4 were selected using a random number table and asked to provide stool samples. Subsequently, a survey of 50 children from class 4 (whether or not they had been initially selected) were asked to provide a stool sample, which was processed using the Kato-Katz method and examined using a compound microscope at × 100 magnification. These data were used to evaluate the validity of the LQAS method. The trials also provided information on the operational aspects and time taken to complete each LQAS sampling plan in order to estimate the cost-effectiveness of alternative screening approaches. Microscopic examination of 50 randomly selected schoolchildren using the compound microscope was considered the gold standard for determining treatment strategy, and estimates of sensitivity, specificity, PPV and NPV were calculated. Estimates of PPV and NPV were used in the cost-effectiveness analysis.

Costs and cost-effectiveness

The cost of each sampling strategy was calculated using an itemized-menu approach, whereby costs are calculated according to unit price and quantities used (Guyatt, 1998). Following this approach, items are divided into personnel, capital and consumables. Only

the financial cost to the programme was assessed. Capital costs were assumed to last five years and were annualized using a discount rate of 3% and expressed in dollars (Drummond *et al.*, 1997). All other costs were paid in local currency and their current values were converted into equivalent US$ using the 2003 mid-year exchange rates of Ugandan Shillings 1,943 to US$1. Estimates of quantities were based on fieldwork of the applicability of the LQAS method. The mean treatment dose per child was estimated from treatment registers from the 2003 treatment round.

Cost-effectiveness was assessed in terms of cost per high (≥50%) prevalence school treated based on the different screening and treatment criteria. Costs of screening individual schools and treating according to prevalence categories was compared to the costs of mass treatment of all schools in an entire hypothetical subcounty of 34 schools and 23,188 schoolchildren (based on the average number of schools in a subcounty and the average school enrolment). Using the strategy of mass treating every school, there is 100% sensitivity in identifying high prevalence schools – however the risk that low prevalence schools will inappropriately receive mass treatment (i.e. false positive) is significant. Following parasitological screening (using either LQAS or conventional sampling method), schools are assumed to receive treatment according to the classification provided by the sampling method. These classifications may be successful or not according to the PPV and NPV of LQAS relative to the conventional approach. The values of PPV and NPV are taken from the field validation studies. The financial costs of drug treatment using praziquantel and albendazole were calculated using the ingredient approach and were based on preliminary cost analysis of the control programme in 14 schools in Nebbi District in 2003; no treatment had been implemented in Mayuge District. Screening and treatment costs were estimated for one year. The cost implications are considered from a perspective of the control programme.

One way sensitivity analysis was undertaken to investigate the effect of the proportions of schools with prevalence ≥50% and of cost per child treated on the cost-effectiveness of the alternative sampling methods compared to a mass treatment strategy, assuming the delivery costs remain constant. Threshold analysis was undertaken to determine the critical values central to cost-effectiveness.

Results

Computer simulations

Eleven sampling plans were evaluated (Table 1). With all sampling plans, LQAS provides the ability to identify communities with a high prevalence of *S. mansoni* with high levels of sensitivity and specificity, even at very small maximum sample sizes. For example, the sampling plans with a maximum sample size of eight had a sensitivity of 95.2% and a specificity of 95.0%. In contrast, sampling plans with such small maximum sample sizes had low positive predictive values in the test populations. Sampling plans with larger maximum sample sizes had slightly higher sensitivities and specificities and considerably better positive predictive values.

LQAS also provides an ability to classify communities into more than two prevalence categories. Performance of sampling plans with very small maximum sample sizes had low proportions of correct classification but made few gross classification errors (i.e. high prevalence communities being classified as low prevalence communities and vice-versa). Sampling plans with larger maximum sample sizes provided higher proportions of correct classification and made no gross classification errors. For the purposes of identifying communities with high prevalences of *S. mansoni*, sampling plans with small maximum sample sizes may be used when moderate levels of positive predictive values are acceptable. For finer classifications, sampling plans with moderate maximum sample sizes (i.e. $n \geq 15$)

provide acceptable proportions of correct classification coupled with extremely low probabilities of making gross classification errors.

Following a consideration of logistics and cost, it was decided by the control programme to evaluate a sampling plans of n=15, d_1=7, d_2=2 in the field. The OC curve from the simulations and the ASN curve for the primary (n=15, d_1=7) sampling plan and the sample size needed to make a classification in each simulation by prevalence is shown in Figure 1. This shows that the probability of deciding to intervene is zero at low prevalences (<20%) and one at very high prevalences (>80%) and increases both smoothly and rapidly around a critical prevalence. The average sample size needed to make a decision decreases with increasing prevalence. This allows classifications to be made in high prevalence communities with relatively small sample sizes and reduce the time required to conduct the survey. The results of the simulations of applying the secondary sampling plan are summarised graphically in Figure 2 which presents a classification plot which plots the range of true prevalences for each classification. This confirms Table 1 and shows that a most schools were correctly classified by LQAS according to their true prevalence category: 97.6% of low prevalence schools; 63.0% of moderate; and 88.5% of high. From 202,000 simulations, only five low prevalence schools were grossly incorrectly classified as high prevalence and 14 high prevalence schools classified as low prevalence (Figure 2).

Field testing of the n=15, d_1=7, d_2=2 sampling plan

A total of 1,687 schoolchildren aged 8-14 years from 34 schools were included in the exhaustive parasitological survey. The overall prevalence of infection was 28.0%; 31.2% in schools in Mayuge District and 26.2% in schools in Nebbi District (Table 2). In both districts combined, 18 schools were classified as low prevalence, 10 as moderate prevalence, and 6 as high prevalence.

Overall, the ability of the sampling plan to discriminate between <50% and ≥50% had a sensitivity of 100%, a specificity of 96.4%, a PPV of 85.7% and a NPV of 92.3%. The observed agreement between true prevalence and the classifications (low, moderate and high) made with the sampling plan are shown in Table 2. The overall observed agreement between true prevalence and the classification made by the two sampling plans (d_1=7, d_2=2) was 76.5% (Kappa=0.615). The level of agreement for schools classified as low, moderate and high prevalence was 77.8%, 60% and 100%, respectively. Importantly, no high prevalence schools were grossly misclassified as low prevalence or vice-versa. Table 2 indicates that LQAS had better diagnostic performance in Mayuge schools than in Nebbi schools.

Operational aspects

The field studies found that in a single day six LQAS surveys and two conventional surveys could be completed. All of the technicians took great interest in the LQAS method and encountered no problems in its use. They had no doubt that they would be able to use the approach for targeting treatment, especially since they saw the obvious benefits of LQAS over conventional sampling approaches.

Costs and cost-effectiveness

The itemized financial costs of the LQAS and conventional sampling plans are summarized in Table 3, which shows that the total financial costs were US$ 20.04 per school for LQAS and US$ 56.20 per school for conventional sampling. The financial saving of LQAS was due principally to lower per diem and reduced drug costs from wastage. During 2003, the control programme had treated 38,052 individuals (12,185 schoolchildren and 25,867 community members) in Nebbi District. The estimated financial cost per schoolchild treated

in 14 schools was US$ 0.29 for both praziquantel and albendazole, where 70.1% of total costs were delivery costs (Table 4).

The costs and cost-effectiveness of alternative screening and treatment strategies for a single subcounty on a yearly basis are presented in Table 5. The most expensive option is mass treatment of all schools without prior parasitological screening. In this approach, 23,188 schoolchildren would have been treated at a total cost of US$6,725. The most cost-effective option was parasitological screening using LQAS, where only 8,184 children are treated (US $218/high prevalence school treated, assuming 41% of schools have prevalence >50% and a PPV of 86%). Assuming a PPV of 67-100%, as found respectively in Nebbi and Mayuge districts, the equivalent cost ratio is US$ 246-176.

The effect of varying proportions of schools with a high prevalence (here defined as ≥50%) on the cost-effectiveness of parasitological screening relative to mass treatment of all schools is shown in Figure 3. As expected, the cost-effectiveness of mass treatment is inversely and non-linearly related to the proportion of schools with a high prevalence. Only when over 75% of schools have prevalence ≥50% does screening using LQAS become less cost-effective compared to mass treatment. In practice, 41% of schools in Kigandalo subcounty Mayuge (where no treatment had previously been undertaken) had prevalence ≥50% and nationally 21.4% of schools surveyed by Kabatereine et al. (2004) had a prevalence ≥50%.

Assuming 41% of schools have prevalence ≥50%, the effect of varying cost per schoolchild treated is shown in Figure 4. Mass treatment is only cost-effective relative to screening using LQAS for a treatment cost per schoolchild of less than US$ 0.19; the current cost per schoolchild treated by the Uganda programme is estimated to be US$ 0.29.

Discussion

This study has investigated the validity, applicability and cost-effectiveness of LQAS as a rapid assessment method for targeting mass treatment with praziquantel for the control of schistosomiasis as implemented by the Uganda National Schistosomiasis Control Programme. Mass treatment is currently provided to all schools in known or suspected high-risk subcounties. One of the consequences of delivering mass treatment to all schools within subcounties identified as at risk is that low prevalence schools will inappropriately receive mass treatment and this may waste drug and other resources. Consequently, mass treatment is not necessarily more cost-effective than screening of individual schools. Especially where high prevalence communities are highly localised within an area, there is a possibility that the cost of treating schools which do not require treatment outweighs the cost of parasitological screening of individual schools. The results presented here show that LQAS is a simple, rapid, reliable and cost-effective approach to guide decision makers in allocating finite resources for the control of schistosomiasis.

We demonstrate that LQAS has particular value in classifying schools in Uganda by treatment strategies according to the categories of infection prevalence: <20%, 20-49% and ≥50%. The LQAS approach requires a much smaller sample size than conventional sampling approach as currently proposed (Montresor et al., 1998). In the present study, a sampling plan of n=15, d_1=7 reliably classified schools into high (≥50%) and low prevalence (<50%). An earlier study showed that a LQAS sampling plan of n=16, d_1=6 provided the optimal sampling plan for identifying high *S. mansoni* prevalence (>50%) schools in endemic areas of Madagascar (Rabarijaona et al., 2003). Here, we have extended such a binary classification method to provide a finer classification system as is required by the national control programme in Uganda. In particular, schools identified as high

prevalence by the first sampling plan are classified as high prevalence, schools identified as high prevalence by the second sampling plan are classified as moderate prevalence, the remaining schools are classified as low prevalence. The use of LQAS to provide a three-class classification system has reliably been used to classify communities according to the prevalence of active trachoma in Malawi (Myatt et al., 2003).

The reason that two settings were selected for field testing was to evaluate LQAS in different transmission settings in Uganda, and also in areas where control had not previously been implemented (Mayuge District) and where a single round of mass treatment had been provided in 2003 (Nebbi District). Sensitivity was 100% in both settings. However, specificity and the performance of the secondary sampling plan were poorer in Nebbi District. This is suggested to be due to the lower intensities of infection in Nebbi District as a consequence of previous treatment (Table 2). Notwithstanding these differences, it is argued that LQAS is a reliable method in both pre- and post-treatment settings. Its performance after multiple rounds of treatment is an issue for further investigation.

In implementing LQAS, we propose that parasitological screening takes place only in areas of potential schistosomiasis risk. To help identify areas of potential *S. mansoni* risk, the national programme has been using geographical information systems (GIS) and remote sensing (RS) as geographic decision making tools for determining large-scale patterns of infection for guiding control and help exclude areas where *S. mansoni* risk is unlikely to be prevalent on the basis of rainfall and altitude (Kabatereine et al., 2004). We have earlier demonstrated that a GIS/RS approach could be of particular value in excluding areas where *S. haematobium* is unlikely to be prevalent in Tanzania, and so help focus on priority areas where school questionnaire surveys should be undertaken to more precisely target control (Brooker et al. 2001a, 2002).

The selection of a screening approach relies not only on its diagnostic reliability but also on its costs and cost-effectiveness. For *S. haematobium*, using self-reported schistosomiasis and self-reported blood in urine to identify high-prevalence schools for mass treatment has been shown to be more cost-effective than parasitological diagnosis using urine filtration (Ansell & Guyatt, 2002). This study conducted in Tanzania found that the cost/infected child treated was US$ 1.33 for the questionnaire approach and US$ 2.30 for the urine filtration approach, and only 8% of the infected children would not have been treated. Using symptoms to identify schools with a high *S. mansoni* prevalence has been shown to be less reliable (Brooker et al., 2001b; Lengeler et al., 2000; Utzinger et al., 2000). In terms of cost-effectiveness, Carabin et al. (2000) found that screening all individuals using a Kato-Katz smear and treating only the ones found to be infected was more cost-effective than treating all symptomatic patients presenting at Primary Health Care Centres (PHCCs) in Burundi. The present study is the first to assess the cost-effectiveness of parasitological screening to identify high-prevalence schools for mass treatment.

It should be noted that the estimates of cost-effectiveness are used for illustrative purposes and not meant to comprehensively estimate the overall cost-effectiveness for a specific national control programme. Nonetheless, our sensitivity analysis showed that parasitological screening using the LQAS method would remain cost-effective relative to mass treatment for settings where the percentage of schools with prevalences of 75% or above and for cost per treatment below US$ 0.18. Similar results for treatment costs were obtained in the study from Burundi where providing treatment on the basis of symptoms of individuals presenting at PHCCs would only be more cost-effective than parasitological screening for a drug price per treatment of less than US$ 0.21 (Carabin et al., 2000). However, although treatment costs may fall below these thresholds, it is extremely unlikely that a given area would have more than 75% of schools having a high prevalence. For

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example, based on national survey data, it is estimated that 5% of schools in Cameroon (Ratard et al., 1990), and that 8.8% of schools in Mali (Gryseels, 1989) have prevalence >50%. These data accord with the known geographical focality of schistosomiasis, and emphasize that the cost-effectiveness of screening is principally determined by the epidemiology and geography of infection rather than treatment costs.

Our economic analysis is based on a single screening of schools at the start of the control programme. In practice however screening may be undertaken every two years to assess the impact of the control programme in reducing the proportion of schools requiring mass treatment (see Brooker et al. (2004b) for a discussion of the assessment of programme impact). Such an approach would result in even more cost savings since high prevalence schools would become low prevalence schools and no longer necessitate mass treatment. However, it is worth stressing that economic factors alone should not guide treatment strategies. There may be value for mass treating all schools in a given subcounty to help mobilize the community, but thereafter parasitological screening may be used to guide treatment strategies

We can conclude that, in Uganda, LQAS may provide national programme managers with a valid, straightforward and cost-effective method with which to assess the distribution of *S. mansoni* and hence ensure that treatment is targeted cost-effectively. Full programmatic implementation of the LQAS method will require evaluation of the method in other endemic *S. mansoni* areas. National programmes currently being implemented in Burkina Faso, Mali, Niger, Tanzania and Zambia, with support from the Schistosomiasis Control Initiative, provide an ideal opportunity to assess the usefulness of LQAS as a rapid assessment tool for *S. mansoni*. As indicated above, the cost-effectiveness of the approach will depend on the epidemiology and geography of infection and as such, the relative cost-effectiveness may differ in other countries. Rapid mapping methods are already implemented for assessing the distribution of onchocerciasis (Noma et al., 2002), and for assessing the distribution of *Loa loa* and hence which communities are at high risk of severe adverse reaction following drug treatment for onchocerciasis (Addiss et al., 2003). As well as improving our understanding of the distribution of *S. mansoni*, data collected through the LQAS method may also prove useful in assessing treatment coverage, akin to the widespread use of LQAS to monitor vaccination coverage.

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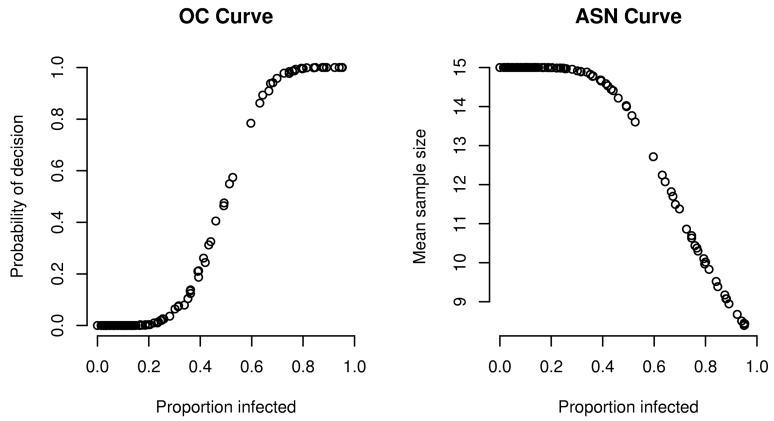

Figure 1.

(a) Probability of classifying school as having prevalence 50% or greater by prevalence, and (b) sample size required to make classifications in each simulation by prevalence for the sampling plan of n=15, d_1=7 based on 202,000 simulated surveys.

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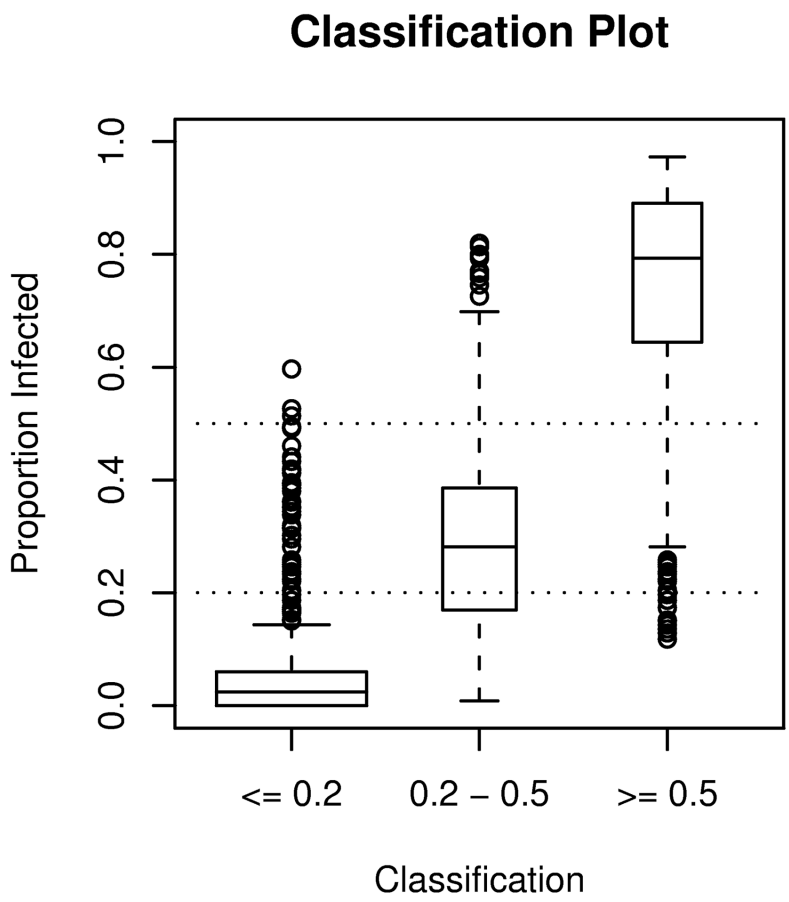

Figure 2.
Box plot of true proportion infected by classification scheme (low, moderate and high) for a sampling plan of n=15, d_1=7, d_2=2 based on 202,000 simulated surveys. The horizontal line within each box represents the median; the lower and upper bounds of the box correspond to the 25- and 75 percentiles; the whiskers correspond to the range of non-outlying data. Width of boxes is proportional to the number in each category. Upper dashed line represents the 50% prevalence threshold and lower dashed line the 20% prevalence threshold.

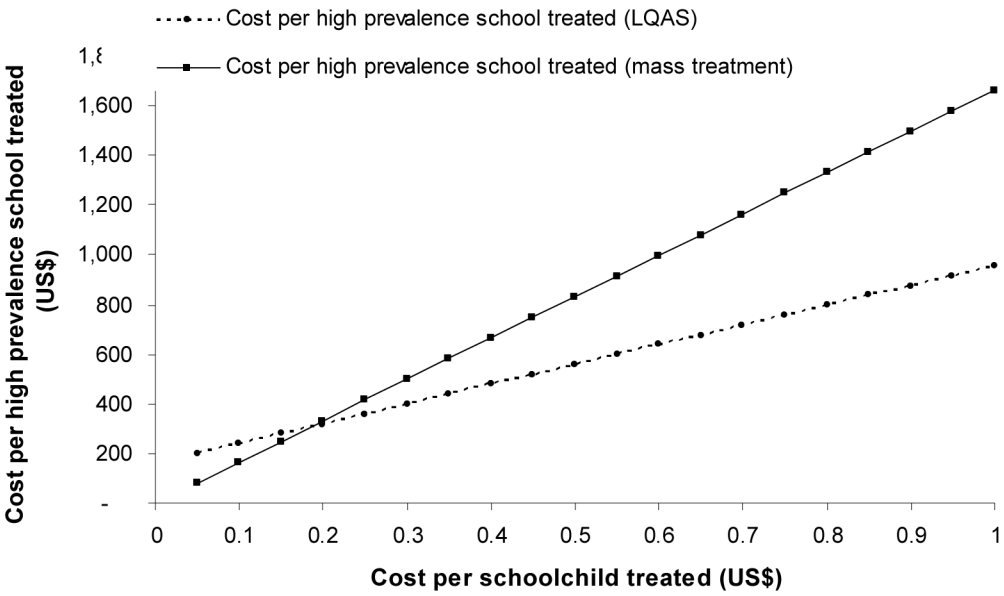

Figure 3.
Cost-effectiveness of screening using LQAS relative to mass treatment of all schools without prior screening in a hypothetical population of 23,188 schoolchildren in 34 schools on a yearly basis as a function of the proportion of schools having a prevalence of 50% or greater.

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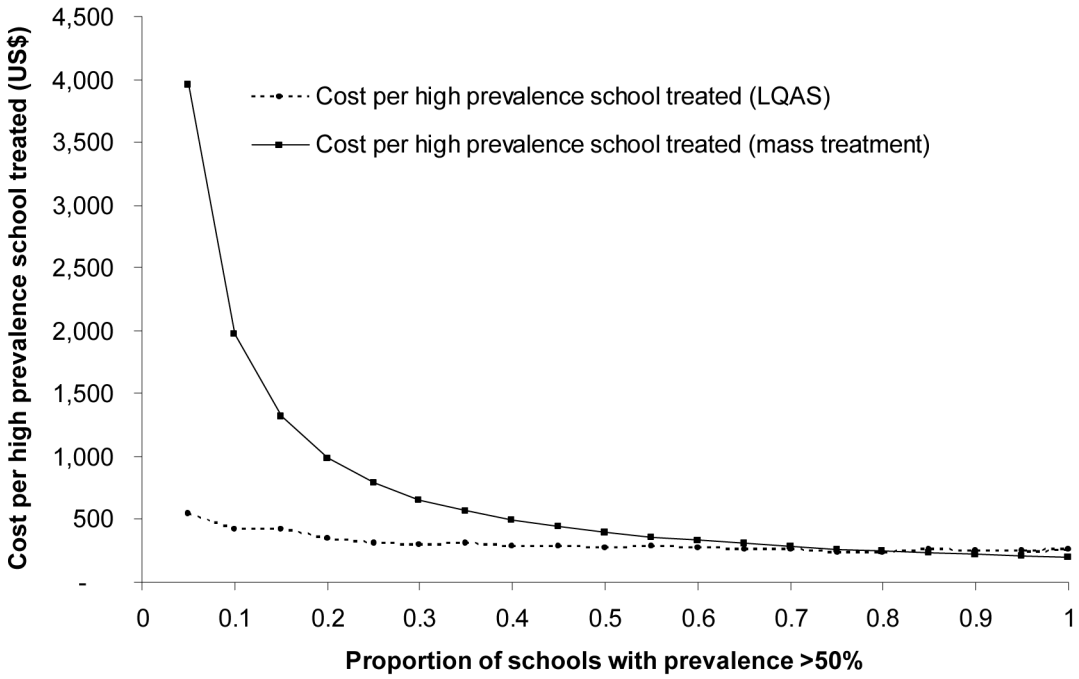

Figure 4.
The effect of different costs per child treated on the cost-effectiveness of the LQAS method to screen schools and provide treatment according to low and high prevalence categories relative to a mass treatment approach in a hypothetical population of 23,188 schoolchildren in 34 schools on a yearly basis, where 21.4% of schools are assumed to have prevalence ≥50%.

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Table 1

Summary performance measures for eleven sampling plans simulated using survey data on 13,800 children in 202 Ugandan schools (1,000 replacements each). Sampling plan selected for field-testing highlighted in bold.

Plans			Primary Sampling Plan[1]					Secondary Sampling Plan[2]			
			Screening Indices[3]					Proportion Correctly Classified[4]			
n	***d*$_1$**	***d*$_2$**	**Sens**	**Spec**	**PPV**	**NPV**	**ASN**	**Low**	**Moderate**	**High**	**All**
8	3	0	0.952	0.949	0.787	0.990	7.4	0.988	0.364	0.787	0.799
10	4	1	0.954	0.956	0.812	0.990	9.3	0.973	0.536	0.812	0.876
12	5	1	0.958	0.962	0.831	0.991	11.2	0.983	0.511	0.832	0.869
15	**7**	**2**	**0.948**	**0.975**	**0.885**	**0.989**	**14.2**	**0.976**	**0.630**	**0.885**	**0.906**
20	9	3	0.967	0.973	0.875	0.993	18.8	0.978	0.679	0.875	0.917
25	12	4	0.961	0.982	0.913	0.992	23.6	0.981	0.719	0.913	0.931
30	14	5	0.971	0.979	0.904	0.994	28.2	0.982	0.749	0.904	0.936
35	17	6	0.966	0.985	0.926	0.993	33.0	0.983	0.768	0.927	0.943
40	19	7	0.974	0.982	0.918	0.994	37.6	0.984	0.788	0.918	0.946
45	22	8	0.970	0.987	0.938	0.994	42.5	0.985	0.800	0.938	0.951
50	24	9	0.975	0.985	0.929	0.995	47.1	0.985	0.812	0.929	0.952

[1] Used to classify schools into <50% and ≥50%.

[2] Used to classify schools into three prevalence classes: low (<20%), moderate (≥20% and <50%) and high (≥50%).

[3] Sens = sensitivity, Spec = Specificity, PPV = Positive Predictive Value, NPV = Negative Predictive Value

[4] The proportion of schools correctly classified in each prevalence class by LQAS according to true prevalence estimated from conventional sampling.

Table 2

Prevalence, mean sample sizes and diagnostic performance of primary and secondary sampling plans in schools in Mayuge District and Nebbi District, Uganda to assess the validity of the LQAS method to estimate treatment strategies, 2004.

	Mayuge	Nebbi	Both
No. children sampled	616	1071	1687
Mean sample size per school (in reference survey)	51.3	48.9	49.6
Prevalence of *S. mansoni* (range by school)	31.2 (2-84)	26.2 (8-67)	28.0 (2-84)
Mean intensity of infection (epg, 95% confidence interval)	244.3 (197.7-290.2)	37.9 (27.0-48.2)	103.1 (86.6-120.1)
Primary plan[1]			
Sensitivity (%)	100	100	100
Specificity (%)	100	95.0	96.4
PPV (%)[2]	100	66.7	85.7
NPV (%)	100	100	100
Secondary plan[3,4]			
Low	85.7	72.7	77.8
Moderate	100	55.6	60.0
High	100	100	100
All	91.7	68.2	76.5

[1] Used to classify schools into <50% and ≥50%.

[2] PPV = Positive Predictive Value, NPV = Negative Predictive Value

[3] Used to classify schools into three prevalence classes: low (<20%), moderate (≥20% and <50%) and high (≥50%).

[4] The percentage of schools correctly classified in each prevalence class by LQAS according to true prevalence estimated from conventional sampling.

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Table 3

Unit financial cost menu for parasitological screening using LQAS and conventional sampling of 34 schools in Uganda, 2004.

Category	Item	Units	Unit cost (US$)	LQAS		Conventional sampling	
				No. units	Total cost (US$)	No. units	Total cost (US$)
Personnel[1]	Technician	per day	22.96	0.167	3.83	0.5	11.48
	Laboratory assistant	per day	17.22	0.167	2.87	0.5	8.61
	Driver	per day	17.22	0.167	2.87	0.5	8.61
	District official	per day	17.22	0.167	2.87	0.5	8.61
Capital items	Compound microscope	per team	873[2]	0.167	0.14	0.5	0.41
	Templates, buckets etc	per team	180[2]	0.167	0.03	0.5	0.10
Consumables	Slides	per test	0.08	15	1.25	50	4.16
	Malachite Green	per test	0.003	15	0.56	50	1.86
	Disinfectant	per test	0.002	15	0.05	50	0.16
	Glycerin & cellophane	per test	0.04	15	0.03	50	0.09
	Diesel[3]	per km	0.31	7	13.02	7	4.34
	Data forms	per school	0.57	1	0.57	1	0.57
	Drugs	per person	0.08	15	2.81	50	9.38
Total cost per school					20.04		56.20

[1] Assumes six schools are visited per day for LQAS and two schools are visited per day for the conventional sampling method. Cost represents per-diem and not opportunity cost of salary.

[2] Annualised at 3% over 5 years and expressed as cost per day assuming 235 working days per year.

[3] Assumes average of 7 km travelled per school, based on actual distances travelled during field testing.

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Table 4

Cost of school-based delivery of praziquantel and albendazole in 14 schools in Nebbi District, Uganda in 2003. (Breakdown by item is available from the corresponding author.)

Cost area	Cost (US$)	% of total
Sensitization and awareness	89.35	2.5
Teacher training	433.10	12.2
Registration	309.57	8.7
Drug distribution	189.63	5.4
Drug treatment	2,478.53	70.1
Health education material	37.96	1.1
Total	3,538.14	100
Cost per schoolchild treated	0.29	
Delivery cost per schoolchild treated	0.09	

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Table 5

Comparison of annual total costs and the numbers treated according to different screening and control strategies in a hypothetical subcounty of 23,188 children in 34 schools, Uganda. It is assumed that 41% of schools have prevalence <50% and therefore would warrant mass treatment, and that the PPV of LQAS is 86%.

	LQAS survey	Conventional survey	Mass treatment
Total costs (US$)	3,055	4,680	6,725
Costs associated with			
Screening (%of total)	681 (22.3)	1,911 (40.8)	0 (0)
Drug (%of total)	1,637 (53.6)	1,910 (40.8)	4,638 (69.0)
Other (%of total)	737 (24.1)	859 (18.4)	2,087 (31.0)
Estimated no. children treated	8,184	9,548	23,188
Estimated no. schools mass treated	12	14	34
Cost per high prev. school treated (US$)	218	334	482