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Spatial co-distribution of neglected tropical diseases in the East African Great Lakes region: revisiting the justification for integrated control

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Summary

OBJECTIVE To determine spatial patterns of co-endemicity of schistosomiasis mansoni and the soil-transmitted helminths (STHs) *Ascaris lumbricoides*, *Trichuris trichiura* and hookworm in the Great Lakes region of East Africa, to help plan integrated neglected tropical disease programmes in this region.

METHOD Parasitological surveys were conducted in Uganda, Tanzania, Kenya and Burundi in 28 213 children in 404 schools. Bayesian geostatistical models were used to interpolate prevalence of these infections across the study area. Interpolated prevalence maps were overlaid to determine areas of co-endemicity.

RESULTS In the Great Lakes region, prevalence was 18.1% for *Schistosoma mansoni*, 50.0% for hookworm, 6.8% for *A. lumbricoides* and 6.8% for *T. trichiura*. Hookworm infection was ubiquitous, whereas *S. mansoni*, *A. lumbricoides* and *T. trichiura* were highly focal. Most areas were endemic (prevalence ≥10%) or hyperendemic (prevalence ≥50%) for one or more STHs, whereas endemic areas for schistosomiasis mansoni were restricted to foci adjacent large perennial water bodies.

CONCLUSION Because of the ubiquity of hookworm, treatment programmes are required for STH throughout the region but efficient schistosomiasis control should only be targeted at limited high-risk areas. Therefore, integration of schistosomiasis with STH control is only indicated in limited foci in East Africa.

keywords *Schistosoma mansoni*, *Ascaris lumbricoides*, hookworm, *Trichuris trichiura*, neglected tropical diseases, integrated control programmes

Introduction

The neglected tropical diseases (NTDs) (Molyneux *et al.* 2005; Hotez *et al.* 2007) form part of a vicious cycle, whereby they are both the result of, and contributors to, poverty in endemic communities (Hotez 2007). Different NTDs can occur in the same poor populations, encouraging support for an integrated approach to their control (Engels & Savioli 2006). Effective and inexpensive chemotherapeutic agents are available for treating urinary and intestinal schistosomiasis, caused by *Schistosoma haematobium* and *Schistosoma mansoni*, respectively; soil-transmitted helminth (STH) infections, including roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworms (*Necator Americanus* and *Ancylostoma duodenale*); lymphatic filariasis (LF), caused by *Wuchereria bancrofti*; and onchocerciasis, caused by *Onchocerca volvulus* (Molyneux *et al.* 2005; Hotez *et al.* 2006). Effective methods for the control of trachoma, caused by *Chlamydia trachomatis*, have also been developed, based on the SAFE strategy (i.e. Surgical correction of inverted eyelids, treatment with Antibiotics, promoting Facial hygiene and Environmental improvements in hygiene and sanitation).

Renewed interest in the NTDs has led to the development of new, donor-funded, disease-specific (i.e. vertical) control initiatives. These large-scale programmes are increasingly targeting the same populations, indicating a need for cooperation and possibly integrated distribution of chemotherapeutic agents (Fenwick 2006). Integrated

control can present efficiency and cost-effectiveness benefits (Lammie *et al.* 2006; Hotez 2007) and possibly other synergistic effects (e.g. effectiveness of drugs for multiple parasite species and collateral effects of treatment on other diseases). By contrast, isolated vertical programmes can lack sustainability, compatibility with existing health systems and local ownership (Nicoll 2000; Mahendradhata & Moerman 2004; Fenwick 2006; Hotez *et al.* 2007). Integrated disease surveys are starting to be conducted to inform multi-disease control programmes, such as those for trachoma and malaria in Ethiopia (Emerson *et al.* 2008).

One of the bases of integration of vertical control programmes is spatial overlap in the distribution of the targeted diseases (Molyneux *et al.* 2005; Fenwick 2006; Brooker *et al.* 2006b). Development of rapid mapping approaches is one of the challenges identified for implementation of integrated NTD control (Hotez *et al.* 2007). Although many countries are endemic for multiple NTDs, a sub-national evaluation is required to determine overlap of the different diseases and projected benefits of integration (Lammie *et al.* 2006; Brooker & Utzinger 2007; Kolaczinski *et al.* 2007). This objective can be achieved using georeferenced epidemiological data, spatial statistical analysis and geographical information systems.

Recent reports have demonstrated prediction of NTD distributions using Bayesian geostatistical models with climate (Raso *et al.* 2005; Clements *et al.* 2006a,b, 2008a) and socioeconomic variables (Raso *et al.* 2006a). However, few studies have analysed the spatial co-distribution of multiple diseases. Raso *et al.* (2006b) investigated the spatial distribution of co-infection with hookworm and *S. mansoni* in Côte D'Ivoire, and Kazembe and Namangale (2007) and Kazembe *et al.* (2008) investigated the spatial distribution of co-morbidity with fever, diarrhoea and pneumonia in Malawian children. We have also recently predicted the spatial distribution of hookworm and *S. mansoni* co-infection in East Africa (Brooker & Clements 2009). While co-infection and co-morbidity are clinically and epidemiologically important (Drake & Bundy 2001; Ezeamama *et al.* 2005; Pullan & Brooker 2008), the main operational issue for integrated control planning is co-endemicity of diseases in the community. Basic qualitative maps of NTD co-endemicity in Ugandan districts have been presented (2007), and co-endemicity of *Plasmodium falciparum* malaria and hookworm has been estimated at a high spatial resolution across the African continent (2006). However, maps of co-endemicity have yet to be developed to inform an integrated NTD control programme.

Following our reports on the distribution of schistosomiasis and hookworm in East Africa (Clements *et al.* 2006a,b, 2008a; Brooker & Clements 2009), here we present additional NTD data from national surveys in Burundi and predict the prevalence of four helminth infections (*A. lumbricoides* and *T. trichiura*, for which spatial predictions have not been previously reported in this region, plus hookworm and *S. mansoni*) across the Great Lakes region of East Africa. We aim to demonstrate sub-national variation in the distribution of each parasite infection, and areas where the geographical distributions of the different infections overlap (i.e. areas of co-endemicity). The objective is to determine the need for integrated schistosomiasis and STH control in different areas of East Africa and to inform efficient targeting of resources for integrated programmes.

Methods

The Schistosomiasis Control Initiative (http://www.sci-ntds.org/) supports integrated NTD control programmes in Burundi, Burkina Faso, Mali, Niger, Rwanda, Tanzania and Uganda. With the exception of Rwanda and Burundi, these programmes are described in detail elsewhere (Garba *et al.* 2006; Kabatereine *et al.* 2006), and the principles of control are similar in both Rwanda and Burundi.

Here, we specifically consider *S. mansoni* and STHs because high-quality regional pre-intervention datasets are available for these parasitic infections. These data were collated from randomised primary school-based field surveys in Uganda (2002–2005), northwest Tanzania (August–November 2004), southwest Kenya (1998 and February–March 2005) and Burundi (October–November 2007). Survey design and sampling methods for the Ugandan, Tanzanian and Kenyan datasets are described elsewhere (Clements *et al.* 2006a; Kabatereine *et al.* 2006; Brooker & Clements 2009; Kabatereine *et al.* 2004, 2005), but the data from the Burundian national surveys have not been previously described. We used a three-staged randomised cluster survey design, where 22 cercles (the second administrative level) were selected randomly, one school was selected randomly from a register of schools in each cercle, and 60 children (30 boys and 30 girls) were selected randomly from an assembly of all available children in each school. A single stool sample was obtained from each child, and two slides prepared from each sample were examined microscopically using standard Kato–Katz methods. Detection of one or more eggs for each parasite species on either slide indicated positive infection status. The data were entered in standardised paper forms in the field and transferred to an electronic database. The location of each school (latitude, longitude) was obtained using a hand-held global positioning system. The combined regional dataset covered a large

geographical area (approximately 1190 × 650 km), and included data from 404 schools and 28 213 schoolchildren.

Data analysis

Spatial prediction was based on multivariable models. An initial candidate set of covariates was considered for inclusion. Age (categorised into 5–9, 10–14 and 15–19 years) and sex of survey participants were recorded in the surveys. Distances of survey locations from the nearest perennial inland water body (PIWB) were derived from an electronic map obtained from the Food and Agriculture Organization (and originating from the US National Imagery and Mapping Agency). Satellite-derived mean land surface temperature (LST) and normalised difference vegetation index (NDVI; a proxy for rainfall) for 1982–1998 were obtained from the National Oceanographic and Atmospheric Administration's Advanced Very High Radiometer (see Hay *et al.* 2006 for how these datasets were derived). Elevation was obtained from an interpolated digital elevation model from the Global Land Information System of the United States Geological Survey (http://edcwww.cr.usgs.gov/landdaac/gtopo30/). An electronic map of degree of urbanisation (urban, periurban, rural and extreme rural) was provided by the University of Oxford (Tatem *et al.* 2005). Variable selection was performed using fixed-effects logistic regression models in STATA/SE 10.0 (StataCorp, College Station, TX, USA) with backwards elimination.

Spatial models were developed in WINBUGS version 1.4 (MRC Biostatistics Unit, Cambridge, and Imperial College London, UK) (Appendix 1). The models were logistic regression models with the covariates described earlier, and a geostatistical random effect that modelled spatial correlation using an isotropic, stationary exponential decay function (Diggle *et al.* 1998). Covariates were standardised to have mean = 0 and standard deviation = 1, to improve identifiability. Predictions of infection prevalence were made at the nodes of a 0.1 × 0.1 decimal degree (approximately 12 × 12 km) grid covering the study area. This was performed in WINBUGS using the *spatial.unipred* command, which implements an interpolation function (kriging) for the spatial random effects. Predicted prevalence was calculated by adding the interpolated geostatistical random effect to the sum of the products of the covariate coefficients and the values of the covariates at the prediction locations. For the individual-level fixed effects (age and sex), separate calculations were performed, where the coefficient for each age and sex group was added. The overall sum was then back-transformed from the logit scale to the prevalence scale, giving prediction surfaces for prevalence of each infection in each age and sex group.

Model validation was performed by randomly allocating the survey locations to one of four subsets (each containing approximately 25% of the total dataset) and training the geostatistical models on three subsets while simultaneously predicting prevalence of infection at the survey locations of the fourth, excluded subset. This was repeated four times, each time excluding and predicting prevalence at the survey locations of a different subset, giving an observed and a predicted prevalence value for all 404 survey locations, for each parasitic infection. Validatory statistics included area under the curve (AUC) of the receiver operating characteristic (a plot of sensitivity *vs.* one minus specificity), where predicted values were compared to observed values dichotomised at prevalence thresholds of >0%, ≥10%, ≥20% and ≥50% to assess discriminatory performance of predictions, and mean error and mean absolute error to assess bias and accuracy of predictions.

Results

For the combined regional dataset, the prevalence of infection was: *S. mansoni*, 18.1%, hookworm, 50.0%, *A. lumbricoides*, 6.8% and *T. trichiura*, 6.8%. Descriptive maps are presented showing raw prevalence of each helminth species (Figure 1). Covariate effects differed markedly between the helminth species (Table 1). Males and older children had a significantly higher prevalence of hookworm and *S. mansoni* infections than females and younger children, but there was no significant association between age or sex and prevalence of infection with *A. lumbricoides* or *T. trichiura*. Increasing distance from a PIWB was significantly and negatively associated with *S. mansoni* and hookworm infection prevalence, but not *A. lumbricoides* or *T. trichiura*. Elevation and NDVI were only significantly associated with *S. mansoni* infection prevalence. A significant quadratic association was found between LST and both *S. mansoni* and hookworm infection prevalence, but not *A. lumbricoides* or *T. trichiura*. Being in a more extremely rural area was significantly and negatively associated with *A. lumbricoides* and *T. trichiura*, positively associated with hookworm and not associated with *S. mansoni* infection prevalence. The variance of the geostatistical random effect (also called the sill, indicating propensity for clustering) was lower for hookworm, and the rate of decay of spatial correlation was higher for hookworm (indicating smaller clusters), than the other parasite infections.

Prediction maps were created for each age–sex group and for each parasite species; illustrative examples are shown for infections in boys aged 15–19 (Figures 2–5). Clusters of high prevalence of *S. mansoni* infection (Figure 2) were located in the Albert Nile area of Uganda,

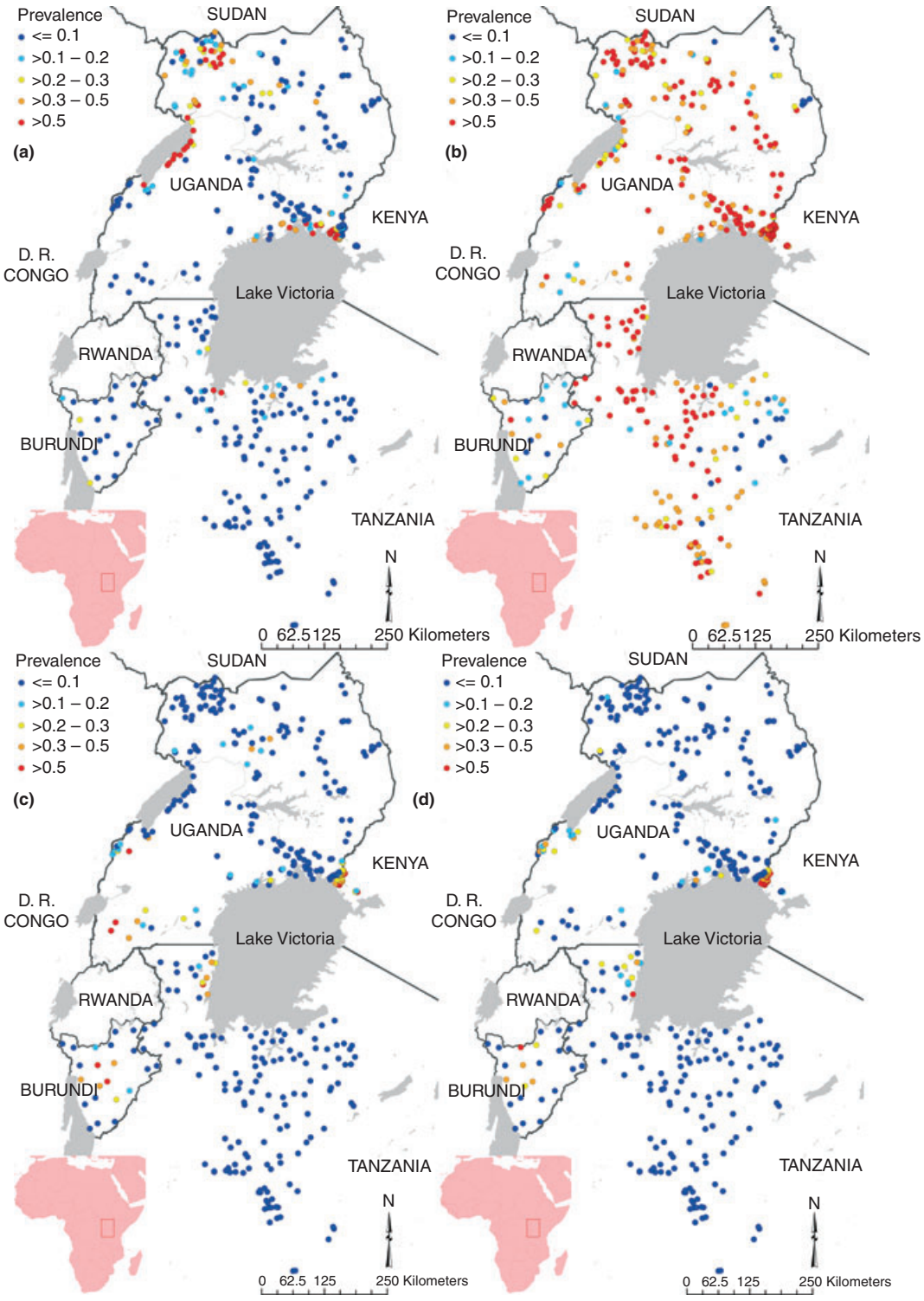

Figure 1 Prevalence of (a) *Schistosoma mansoni*; (b) hookworm; (c) *Ascaris lumbricoides* and (d) *Trichuris trichiura* in school-aged children, Great Lakes region, East Africa 1998–2005.

Table 1 Bayesian geostatistical logistic regression models of *Schistosoma mansoni* and soil-transmitted helminth infections in school-children, Great Lakes region, East Africa 1998–2007

	Posterior mean (95% CI)			
Variable	*S. mansoni*	Hookworm	*Ascaris lumbricoides*	*Trichuris trichiura*
Female (*vs*. male)	0.77 (0.70, 0.84)	0.89 (0.84, 0.94)	0.92 (0.82, 1.03)	0.95 (0.84, 1.07)
Age 10–14 years (*vs*. 5–9 years)	2.01 (1.79, 2.25)	1.42 (1.32, 1.54)	0.88 (0.73, 1.04)	1.41 (1.16, 1.70)
Age 15–19 years (*vs*. 5–9 years)	2.49 (2.02, 3.03)	1.63 (1.45, 1.83)	0.80 (0.63, 1.01)	1.29 (1.00, 1.63)
Distance to PIWB	0.38 (0.23, 0.57)	0.79 (0.65, 0.97)	0.86 (0.46, 1.41)	0.52 (0.25, 1.06)
Elevation*	0.33 (0.22, 0.49)	0.92 (0.75, 1.15)	1.33 (0.90, 1.88)	0.98 (0.65, 1.36)
NDVI	0.57 (0.47, 0.69)	1.00 (0.87, 1.14)	0.97 (0.79, 1.17)	1.24 (0.99, 1.53)
LST*	0.57 (0.37, 0.83)	0.73 (0.59, 0.91)	0.62 (0.39, 1.01)	0.59 (0.27, 1.00)
LST^2*	0.64 (0.50, 0.80)	0.84 (0.74, 0.94)	1.03 (0.82, 1.27)	0.97 (0.69, 1.25)
Rural (*vs*. urban/periurban)	0.67 (0.37, 1.09)	1.10 (0.81, 1.43)	0.93 (0.55, 1.50)	0.50 (0.27, 0.84)
Extreme rural (*vs*. urban/periurban)	0.87 (0.46, 1.47)	1.48 (1.07, 2.01)	0.37 (0.17, 0.72)	0.36 (0.16, 0.68)
Intercept (log odds scale)	−3.61 (−4.11, −2.78)	−0.58 (−0.92, −0.24)	−4.03 (−4.96, −3.16)	−5.09 (−6.34, −4.17)
φ (rate of decay of spatial correlation)	3.29 (1.98, 5.05)	5.70 (3.63, 8.58)	2.49 (1.01, 4.64)	3.35 (1.35, 6.74)
σ^2 (variance of spatial random effect)	5.09 (3.52, 7.57)	1.34 (1.05, 1.73)	4.77 (2.79, 8.85)	5.58 (3.23, 10.01)

CI, Bayesian credible interval; NDVI, normalised difference vegetation index; LST, land surface temperature; PIWB, perennial inland water body.
*Variables were standardised to have mean = 0 and standard deviation = 1.

the shores of Lakes Kyoga and Victoria and, in Burundi, the shores of Lake Tanganyika (particularly the northern shore) and Lakes Cohoha and Rweru (in the far northeast of the country). Hookworm infection (Figure 3) was virtually ubiquitous in the study area, excluding small areas in north-eastern Uganda, central and northern Burundi and the Shinyanga region of north-western Tanzania. *Ascaris lumbricoides* and *T. trichiura* infections (Figures 4 and 5) had similar distributions, with high prevalence clusters in south-western and south-eastern Uganda, south-western Kenya, the western coast of Lake Victoria (in the Kagera region of Tanzania) and central Burundi.

For each parasitic infection, the models consistently had an AUC of >0.8 for all observed prevalence thresholds, and in most instances an AUC of >0.9, indicating excellent discriminatory performance (Table 2). Mean error of model predictions was <0.5% for each infection suggesting little overall bias in predictions. Mean absolute error was generally proportional to the overall prevalence value, being low for *A. lumbricoides* and *T. trichiura*, moderate for *S. mansoni* and higher for Hookworm.

Co-endemicity of schistosomiasis mansoni and STHs

Figure 6 is a map of the Great Lakes region showing overlays of areas of hyperendemic (prevalence >50%) and endemic (prevalence >10%) status for *S. mansoni* and one or more STH infections. The distribution of *S. mansoni* was highly focal with hyperendemic areas restricted to locations near the Nile River and the Great Lakes. While *A. lumbricoides* and *T. trichiura* were highly focal, the ubiquity of hookworm meant that most areas were endemic or hyperendemic for one or more STH.

Discussion

Infections with *A. lumbricoides*, *T. trichiura* and *S. mansoni* were highly focal in the Great Lakes region of East Africa, whereas hookworm infection was widespread. Because of the ubiquitous nature of hookworm infection, mass administration of benzimidazole drugs is indicated throughout the region. Given these drugs are the treatment of choice for *A. lumbricoides* and *T. trichiura* infections, widespread mass benzimidazole administration would also control these parasites. The highly focal nature of *S. mansoni* suggests that efficient control of intestinal schistosomiasis should involve targeted distribution of praziquantel in high-risk areas only. We did not investigate the distribution of *S. haematobium* in this study, but our recent report (Clements *et al.* 2006a) demonstrated a large focus of *S. haematobium* infection in north-western Tanzania, and mass distribution of praziquantel is also required in this area. However, urinary schistosomiasis is not thought to be a major public health problem in Uganda (Bradley *et al.* 1967) or Burundi.

Our models gave several insights into the epidemiology of helminths in East Africa. The associations between each of the helminth infections and environmental variables, such as temperature, distance from water bodies and

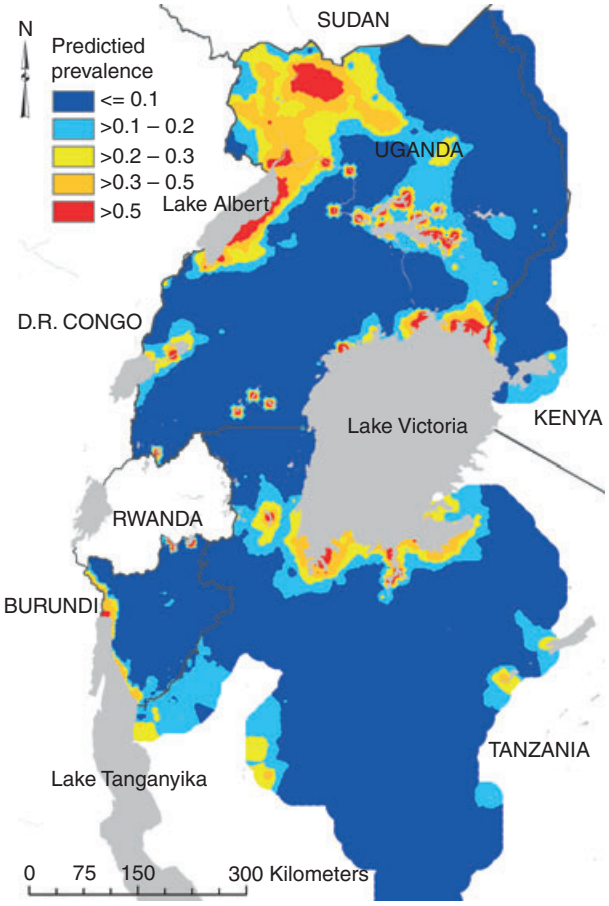

Figure 2 Predicted prevalence of *Schistosoma mansoni* infection in boys, 15–19 years, East Africa (inset Burundi) 1998–2007. Estimates are the mean posterior predicted prevalence values from a Bayesian geostatistical model.

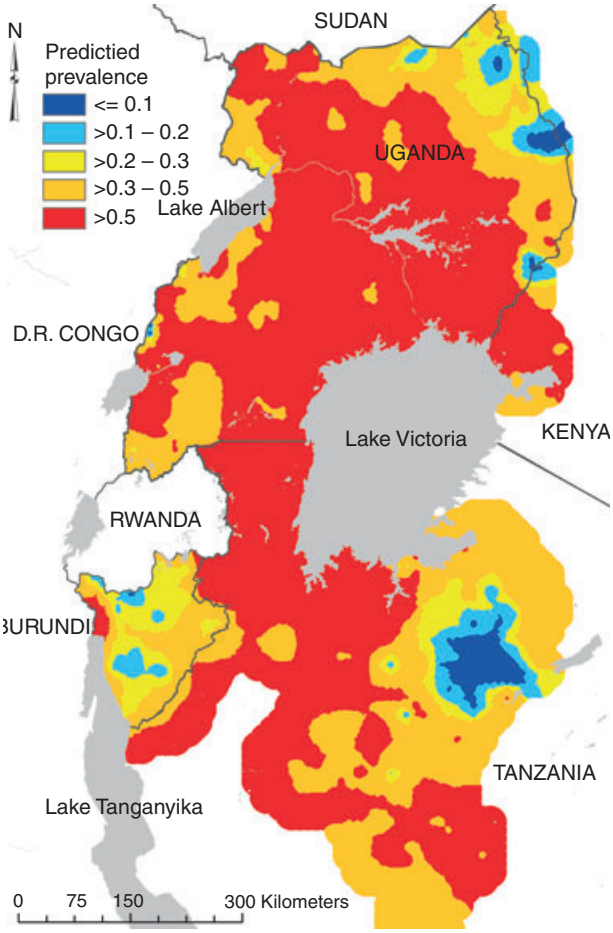

Figure 3 Predicted prevalence of hookworm infection in boys, 15–19 years, East Africa (inset Burundi) 1998–2007. Estimates are the mean posterior predicted prevalence values from a Bayesian geostatistical model.

degree of urbanisation, are well described, as is the focality of schistosome infections (Brooker *et al.* 2006a; Raso *et al.* 2005, 2006a,b; Clements *et al.* 2006a,b, 2008a,b). Residual spatial variation, represented by the spatial random effects, suggests that factors other than the environmental variables included in the models influence the spatial distribution of these parasitic infections. This is particularly true for *S. mansoni*, *A. lumbricoides* and *T. trichiura*, all of which demonstrated strong spatial clustering. Further investigation is required to identify these additional factors, which might be related to poverty, hygiene (particularly of the water supply), ongoing interventions and other environmental variables.

There are many issues that complicate integration of control efforts. These include the potential for emergence of drug resistance, untested drug interactions, differences in target sub-populations (e.g. children *vs.* the whole population, school-based *vs.* community-based control), different treatment frequencies for the chemotherapeutic agents, the need for cooperation between groups that have different needs and objectives, and added complexity in monitoring and evaluation strategies (Molyneux *et al.* 2005; Lammie *et al.* 2006; Kolaczinski *et al.* 2007). The potential impact of large-scale programmes (vertical or integrated) on existing fragile health services, such as drawing away staff and other resources, also needs to be considered. For sustainability, planning, monitoring and evaluation of large-scale NTD control programmes need to have a broader focus than the operational aspects of mass drug administration to include concerted health education activities, incorporating knowledge of local cultural and

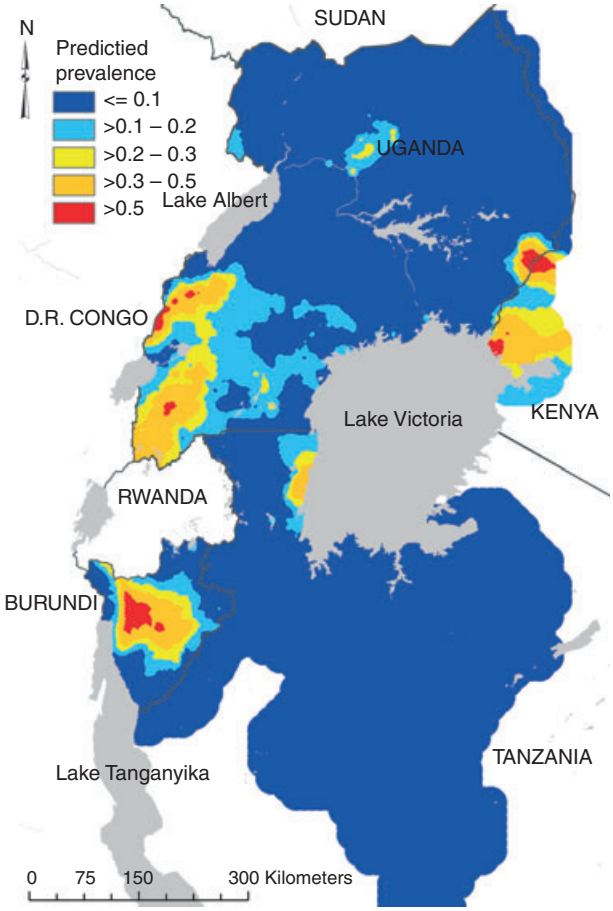

Figure 4 Predicted prevalence of *Ascaris lumbricoides* infection in boys, 15–19 years, East Africa (inset Burundi) 1998–2007. Estimates are the mean posterior predicted prevalence values from a Bayesian geostatistical model.

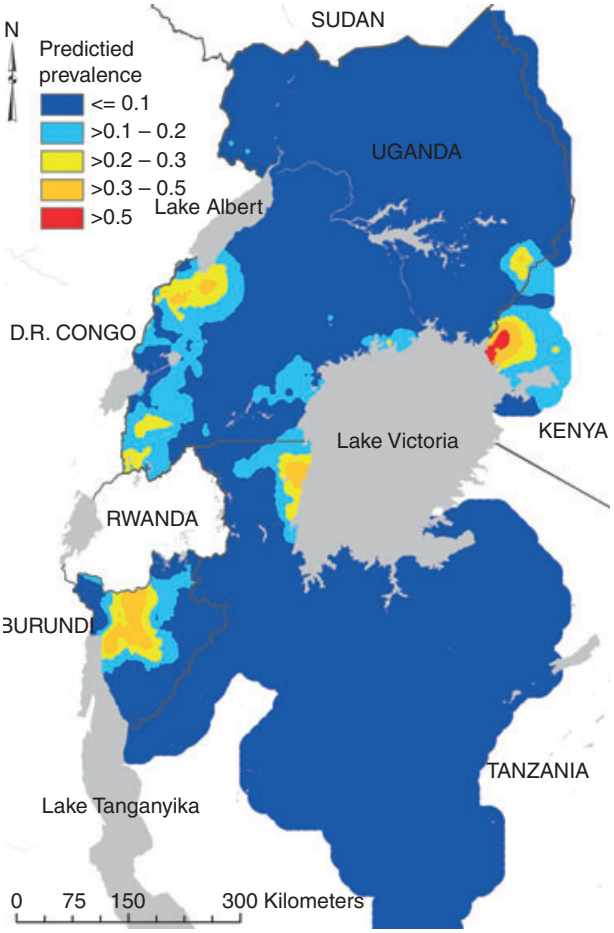

Figure 5 Predicted prevalence of *Trichuris trichiura* infection in boys, 15–19 years, East Africa (inset Burundi) 1998–2007. Estimates are the mean posterior predicted prevalence values from a Bayesian geostatistical model.

societal factors that influence uptake of the intervention (Parker *et al.* 2008).

It should be noted that we only considered the co-distribution of *S. mansoni*, hookworm, *A. lumbricoides* and *T. trichiura* in this study. Recent integrated control programmes are also targeting LF, onchocerciasis and trachoma. Surveys for LF and trachoma were recently conducted in Burundi but these used standard rapid assessment methods that are not randomised and hence not amenable to risk mapping. To plan truly integrated NTD programmes using overlays of risk maps, randomised, geographically stratified surveys need to be conducted for these and other NTDs. A potential limitation is that the current school of enrolment was chosen as the geographical reference for infection exposure; at the large geographical scale of the current study the school location is likely to be sufficiently accurate to represent the probable exposure location of the majority of participants. Migration might have an effect, which is currently impossible to measure.

Integration is indicated where control programmes have a common technical approach, common target populations and collectively high disease burden (Lammie *et al.* 2006; Utzinger & de Savigny 2006; Emerson *et al.* 2008). Integration of control of schistosomiasis with the control of STHs is clearly only warranted in limited areas of the Great Lakes region, near the large inland water bodies, where intestinal schistosomiasis is endemic. Like Kolaczinski *et al.* (2007), who found limited overlap at the sub-national level of three NTDs (intestinal schistosomiasis, LF

Table 2 Validatory measures of discriminatory ability, bias and accuracy of Bayesian geostatistical logistic regression models of *Schistosoma mansoni* and soil-transmitted helminth infections in schoolchildren, Great Lakes region, East Africa 1998–2007

Validation statistic	*S. mansoni*	Hookworm	*Ascaris lumbricoides*	*Trichuris trichiura*
Area under the ROC curve (95% CI)				
0% threshold	0.82 (0.78, 0.86)	0.98 (0.95, 1.00)	0.86 (0.83, 0.90)	0.89 (0.86, 0.92)
10% threshold	0.95 (0.93, 0.97)	0.90 (0.83, 0.97)	0.96 (0.94, 0.98)	0.94 (0.92, 0.97)
20% threshold	0.96 (0.93, 0.98)	0.86 (0.81, 0.91)	0.97 (0.95, 0.99)	0.94 (0.91, 0.97)
50% threshold	0.97 (0.96, 0.99)	0.80 (0.76, 0.84)	0.96 (0.94, 0.99)	0.97 (0.93, 1.00)
Mean error	−0.001	0.003	−0.002	−0.002
Mean absolute error	0.074	0.142	0.042	0.042

ROC, receiver operating characteristic.

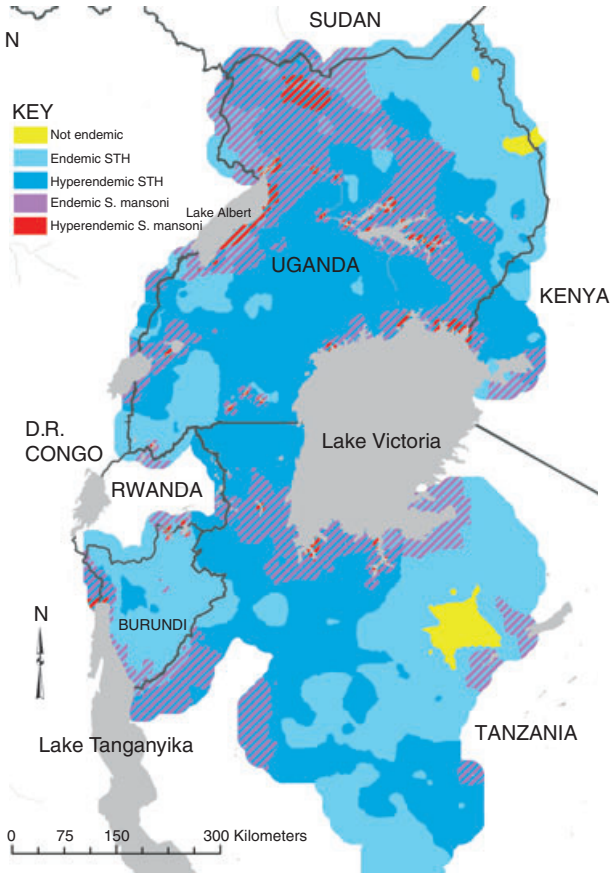

Figure 6 Predicted areas of co-endemicity for *Schistosoma mansoni* and one or more soil-transmitted helminth infections, East Africa. Hyperendemicity is defined as prevalence ≥50%, and endemicity is defined as prevalence ≥10% but <50%. Maps are based on predictions for boys aged 15–19.

and onchocerciasis) in Uganda, our finding suggests that it is important to incorporate local variation of disease risk in integrated control strategies.

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Appendix I

The individual data were aggregated into age and sex groups and by school location. The Bayesian geostatistical models were of the form:

$$Y_{i,j} \sim \text{Binomial}(n_{i,j}, p_{i,j})$$

$$\text{logit}(p_{i,j}) = \alpha + \sum_{k=1}^{p} \beta_k \times x_{i,j,k} + u_i$$

where $Y_{i,j}$ is the number of infection positive children in school i, age–sex group j, $n_{i,j}$ is the number of children examined in school i, age–sex group j, $p_{i,j}$ is prevalence of infection in school i, age–sex group j, α is the intercept, $\sum_{k=1}^{p} \beta_k \times x_{i,j,k}$ is a matrix of covariates, and u_i is a geostatistical random effect defined by an isotropic powered exponential spatial correlation function:

$$f(d_{ab}; \phi) = \exp[-(\phi d_{ab})]$$

where d_{ab} are the distances between pairs of points a and b, and ϕ is the rate of decline of spatial correlation per unit of distance. Non-informative priors were used for α (uniform prior with bounds $-\infty$ and ∞) and the coefficients (normal prior with mean = 0 and precision = 1×10^{-4}). The prior distribution of ϕ was also uniform with upper and lower bounds set at 0.06 and 50. The precision of u_i was given a non-informative gamma distribution.

A burn-in of 4000 iterations was allowed, followed by 1000 iterations where values for the intercept and coefficients were stored. Diagnostic tests for convergence of the stored variables were undertaken, including visual examination of history and density plots of the three chains. Convergence was successfully achieved after 5000 iterations, and the model was run for a further 10 000 iterations, during which predicted prevalence at the prediction locations was stored for each age and sex group. Posterior distributions of model parameters were summarised using descriptive statistics (posterior mean and 95% Bayesian credible interval limits).

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