An outbreak of intestinal schistosomiasis in primary school children living along the shoreline of Lake Malawi, Mangochi District, Malawi

CURRENT STATUS: Under Review

Infectious Diseases of Poverty  ▼ BMC

Sekeleghe Kayuni, Angus M. O’Ferrall, Hamish Baxter, Josie Hesketh, Bright Mainga, David Lally, Mohammad H. Al-Harbi, E. James LaCourse, Lazarus Juziwelo, Janelisa Musaya, Peter Makaula, John Russell Stothard

Sekeleghe Kayuni
Liverpool School of Tropical Medicine

Angus M. O’Ferrall
Liverpool School of Tropical Medicine

Hamish Baxter
Liverpool School of Tropical Medicine

Josie Hesketh
Liverpool School of Tropical Medicine

Bright Mainga
Malawi College of Health Sciences

David Lally
University of Malawi College of Medicine

Mohammad H. Al-Harbi
Liverpool School of Tropical Medicine

E. James LaCourse
Liverpool School of Tropical Medicine

Lazarus Juziwelo
Government of Malawi

Janelisa Musaya
University of Malawi College of Medicine

Peter Makaula
Government of Malawi Department of Fisheries

John Russell Stothard
Department of Parasitology
✉️ russell.stothard@lstmed.ac.uk Corresponding Author
ORCiD: https://orcid.org/0000-0002-9370-3420
Subject Areas

*Infectious Diseases*

Keywords

*Emergence, Schistosoma mansoni, Urine CCA-dipsticks, Faecal occult blood, Co-infection, Urogenital schistosomiasis, Morbidity*
Abstract

**Background:** Intestinal schistosomiasis was not considered endemic in Lake Malawi until November 2017 when populations of *Biomphalaria pfeifferi* were first reported; in May 2018, emergence of intestinal schistosomiasis was confirmed subsequently. This emergence was in spite of ongoing urogenital schistosomiasis control by preventive chemotherapy. In our current investigation, we ascertain if intestinal schistosomiasis is transitioning from emergence to outbreak, to judge whether stepped-up control interventions are needed.

**Methods:** During May 2019, three cross-sectional surveys of primary school children for schistosomiasis were conducted using a combination of rapid diagnostic tests, parasitological examinations and applied morbidity-markers; 1) schistosomiasis dynamics were assessed at Samama (n=80) and Mchoka (n=80) schools, where *Schistosoma mansoni* was first reported, 2) occurrence of *S. mansoni* was investigated at two non-sampled schools, MOET (Mangochi Orphan Education and Training) (n=60) and Koche (n=60) schools, where *B. pfeifferi* was nearby, and 3) rapid mapping of schistosomiasis, and *B. pfeifferi*, conducted across a further 8 shoreline schools (n=240).

**Results:** In total, 520 children from 12 lakeshore primary schools were examined, mean prevalence of *S. mansoni* by urine CCA-dipsticks was 31.5% [95% CI 27.5 – 35.5], with clear associations with faecal occult blood and ova-patent intestinal schistosomiasis. Infection prevalence significantly increased at Samama (RR=1.7 [95% CI 1.4 – 2.2]) and Mchoka (RR= 2.7 [95% CI 1.7 – 4.3]) schools, was confirmed at MOET (18.3%) and Koche (35.0%) schools, and across rapid mapping schools ranged from 10.0% to 56.7%. Several populations of *B. pfeifferi* were confirmed, with two new locations on the eastern shoreline encountered. Mean prevalence of urogenital schistosomiasis was 24.0% [95% CI 20.3 – 27.7].

**Conclusions:** When taken as a whole, we notify that intestinal schistosomiasis, once considered non-endemic in Lake Malawi, is now transitioning from emergence to outbreak. We recommend stepped-up preventive chemotherapy, with increased community-access to treatments, alongside renewed efforts in appropriate environmental control.

**Background**

Lake Malawi is the world’s fourth largest freshwater lake, an important aquatic hotspot of global biodiversity but with urogenital schistosomiasis being endemic along many parts of its shoreline [1]. In Mangochi District, Malawi, the prevalence of *Schistosoma haematobium* infection in school children warrants preventive chemotherapy. This is achieved by annual mass drug administration (MDA) of praziquantel [2] as provided by the Malawi National Schistosomiasis and Soil-Transmitted Helminthiasis Control Programme (https://www.health.gov.mw/index.php/schistosomiasis-sth-control-programme). MDA is typically guided upon country-wide mapping information which is usually developed from inspection of 5 schools per district [3]. By contrast, intestinal schistosomiasis, caused by *Schistosoma mansoni*, is not considered endemic within the lake, as being congruent with the absence of *Biomphalaria pfeifferi*, an obligatory intermediate snail host and keystone snail species for this parasite’s transmission [1, 4, 5].

This appraisal was revised in May 2018 as, since November 2017 *B. pfeifferi* has been repeatedly encountered in the lake, alongside emergence of intestinal schistosomiasis documented in 3 local primary schools [6]. Prevalence of infection by urine CCA-dipsticks was 34.3% [95% CI 27.9–41.3], with ova-patent *S. mansoni* in stool noted at Samama and Mchoka schools [6]. Even with ongoing annual MDA for urogenital schistosomiasis control, the dynamics of intestinal schistosomiasis need further scrutiny here, for this disease could transition from emergence to outbreak.

Transitions from emergence to outbreak are often driven by expansions in the distributions of intermediate snail hosts which, like elsewhere in Africa, can instigate, for example, new transmission foci [7]. Even though an outbreak terminology is rather vaguely defined, common with the epidemiology of other water-borne diseases
[8], it is more so for schistosomiasis as its dynamics also involve unsafe water contact, with per-cutaneous (and oral) entry and infection routes. However, the use of outbreak vernacular can be appropriate, foremost, to spur commensurate public health actions, by example in stepped-up surveillance for the intermediate hosts or with intensified control interventions. This was evidenced in Senegal for intestinal schistosomiasis [9] and more recently in Corsica for urogenital schistosomiasis [10] which were each urged by the use of outbreak terminologies.

To seek an appropriate public health response here on the shoreline of Lake Malawi, our investigation had three linked objectives: 1) to resample Samama and Mchoka schools, ascertaining the dynamics of schistosomiasis infection and morbidity after annual MDA, 2) to confirm intestinal schistosomiasis, also noting faecal occult blood (FOB), at two previously non-sampled schools, MOET (Mangochi Orphan Education and Training) and Koche schools, where in 2018 *B. pfeifferi* was found nearby and 3) to conduct a wider rapid mapping survey for schistosomiasis at 8 further schools (Mtengeza, Makumba, St Martins, Chipeleka, Sungusya, Chikomwe, Ndembo and St Augustine II) to judge if an outbreak of intestinal schistosomiasis was occurring.

### Methods

#### Ethical statement and recruitment

Ethical approvals were granted by the National Health Sciences Research Committee (1805), Mangochi District Health Office Research Committee (26.04.2019) and LSTM Research Ethics Committee (30.04.2019). Following on from previous epidemiological information [6] and sample size calculation with single population proportion formula (http://www.raosoft.com/samplesize.html), estimating a precision of prevalence required (± 10%), to address objective 1, 80 children per school were sufficient, objective 2, 60 children per school were sufficient, while for objective 3, according to WHO recommendations for rapid mapping, 30 children per school were selected [11].

At each school, global position system (GPS) coordinates were taken using an Oregon 650 receiver (Garmin, Olathe, Kansas, USA). The GPS locations for each school in decimal degrees are as follows: Samama (-14.417465 °, 35.217580 °), Mchoka (-14.439481 °, 35.220644 °), MOET (-14.320776 °, 35.131558 °), Koche (-14.330917 °, 35.146186 °), Mtengeza (-14.288932 °, 35.264073 °), Makumba (-14.319806 °, 35.286104 °), St Martins (-14.351401 °, 35.294435 °), Chipeleka (-14.385387 °, 35.292935 °), Sungusya (-14.386472 °, 35.311398 °), Chikomwe (-14.422136 °, 35.265088 °), Ndembo (-14.456385 °, 35.273794 °) and St Augustine II (-14.473926 °, 35.279613 °). A location map of the 12 schools is shown, Fig. 1.

#### Study participants, diagnostics and treatment

The surveys took place during May 2019; after obtaining written informed parental consent for each child, a total of 520 children, aged 6–15, of balanced gender, were enrolled. On the appointed day of survey, each school child provided a mid-morning urine sample and when requested, a stool sample, alongside undertaking a brief interview by questionnaire documenting place of birth, recent travel and praziquantel treatment history. If found infected, each child was provided with praziquantel (IDA Foundation, Amsterdam, The Netherlands) at 40 mg/kg.

For detection of intestinal schistosomiasis, two drops of urine were applied to a CCA-dipstick (Rapid Medical Diagnostics, Pretoria, South Africa). Results were scored visually against a reference colour photograph as negative (-ve), trace (tr) or positive (+ ve) and cross-checked [12]. To augment urine CCA-dipsticks, on-site inspection of collected stool was performed with parasitological methods; at Mchoka, Samama, MOET and Koche schools, all children were asked to provide a stool sample with a total of 265 specimens obtained, Table 1. Following our rapid mapping protocol at 8 remaining schools, stool was only requested from urine CCA-dipstick + ve children, obtaining 70 specimens, Table 1.

### Table 1

| Occurrence of ova-patent *S. mansoni* in stool and prevalence and intensity of *S. haematobium* infections by school. |  |  |
|---|---|---|
|  |  |  |

4
| School          | [sample size] | Stool: Kato-Katz (S. mansoni) | Urine: filtration (S. haematobium) |
|-----------------|---------------|------------------------------|-----------------------------------|
|                 |               | Number of stool samples collected | Infection intensity \(^a\) (epg) | Prevalence (%) [95% CI] | Infection intensity \(^b\) (% per 10 ml) |
| Light           | Medium        | Heavy                        | Light | Heavy |
| TOTAL           | 335           | 20                           | 4     | 3     | 24.0 [20.3–27.7] | 64.0 | 36.0 |

All collected stools, irrespective of CCA status, were examined

| School          | [sample size] | Number of stool samples collected | Infection intensity \(^a\) (epg) | Prevalence (%) [95% CI] | Infection intensity \(^b\) (% per 10 ml) |
|-----------------|---------------|-----------------------------------|-------------------------------|--------------------------|-----------------------------------|
| Mchoka          | 73            | 1                                | 0                             | 18.8 [10.2–27.4]         | 73.3 | 26.7 |
| Samama          | 77            | 4                                | 0                             | 56.3 [45.4–67.2]         | 66.7 | 33.3 |
| MOET            | 56            | 2                                | 0                             | 8.3 [1.3–15.3]           | 60.0 | 40.0 |
| Koche           | 59            | 3                                | 3                             | 1.7 [0.0–5.0]            | 100.0 | 0.0 |

Only selective stools from CCA + ve children were examined

| School          | [sample size] | Number of stool samples collected | Infection intensity \(^a\) (epg) | Prevalence (%) [95% CI] | Infection intensity \(^b\) (% per 10 ml) |
|-----------------|---------------|-----------------------------------|-------------------------------|--------------------------|-----------------------------------|
| St Augustine II | 15            | 3                                | 0                             | 43.3 [25.6–61.0]         | 61.5 | 38.5 |
| Ndembo          | 15            | 6                                | 1                             | 60.0 [42.5–77.5]         | 38.9 | 61.1 |
| Chikomwe        | 10            | 0                                | 0                             | 10.0 [0.0–20.7]          | 33.3 | 66.7 |
| Chipeleka       | 3             | 0                                | 0                             | 26.7 [10.9–42.5]         | 50.0 | 50.0 |
| Sungusya        | 7             | 0                                | 0                             | 16.7 [3.4–30.0]          | 80.0 | 20.0 |
To visualize helminth ova in stool, individual specimens were filtered across a 212 µm metal mesh then applied to produce duplicate thick (41.7 mg) Kato-Katz smears as examined by microscopy (x100). Intensity of *S. mansoni* infection as eggs per gram (epg) was classified as: light (1–99 epg), medium (100–399 epg) and heavy (≥ 400 epg) according to WHO guidelines [11]. To assess putative pathology associated with intestinal schistosomiasis [5], stools were screened for FOB using ALLTEST® cassettes (Access Diagnostic Tests UK Ltd, Aylsham, UK).

For detection of urogenital schistosomiasis, 10 ml of well-mixed urine was filtered by syringe across a circular nylon mesh of 1.5 cm diameter, with 20 µm pore size (Plastok® [Meshes and Filtration] Ltd, Birkenhead, UK). The mesh was stained with Lugol’s iodine, then inspected by microscopy (x100) to count *S. haematobium* ova. Infection intensity was classified as light (< 50 ova per 10 ml) or heavy (≥ 50 ova per 10 ml) according to WHO guidelines [11]. Putative pathology associated with urogenital schistosomiasis was assessed by Siemens Multistix® 10 SG reagent strips (Medisave UK Ltd, Weymouth, UK) for microhematuria [5].

**Malacological surveillance**

During May 2019, all known locations where *B. pfeifferi* was found were re-surveyed, alongside several new locations as visited on the eastern shoreline of the lake, based upon convenience sampling from in-field observations of human water contact. At each site, two collectors searched, for 20 minutes, for *B. pfeifferi* by hand and with metal sieves. Global position system (GPS) coordinates, altitude and location photographs were taken with an Oregon 650 receiver (Garmin, Olathe, Kansas, USA). Water temperature (°C), pH and conductivity (µS) were recorded with a HI-98129 Pocket EC/TDS and pH Tester (Hanna Instruments Ltd, Leighton Buzzard, Bedfordshire, UK). Collected snails were screened for shedding human cercariae by exposure to sunlight under a dissecting microscope (x20).

**Epidemiological analyses**

Demographic, questionnaire and diagnostic data were tabulated with statistical analysis carried out using IBM SPSS® Version 24 (IBM, Portsmouth, UK). Univariate analyses and Chi-square testing were first performed, then binary logistic regression undertaken, calculating adjusted odds ratios with generalised linear models, with stepwise subtraction of variables, to investigate (un)adjusted epidemiological associations.

**Results**

**Prevalence and distribution of intestinal and urogenital schistosomiasis**

The outline map, Figure 1, is a summary of all information obtained from urine CCA-dipsticks with the distribution of intestinal schistosomiasis displayed. When trace was considered infected, mean prevalence was 82.5%, when trace was considered not infected this declined to 31.5%. Common across all school children were very high.
levels of reported weekly water contact (>75%), inclusive of bathing, swimming and drinking. The known distribution of *B. pfeifferi* along the western shoreline, alongside new reports on the eastern shoreline in December 2018 and May 2019, is shown. In locations where *B. pfeifferi* was found, water parameters ranged: pH 7.5 - 8.5, temperature 21.5 - 26.2 °C, conductivity 312 - 458 μS and total dissolved salts 155 – 244 ppm; no collected snail (n=52) was observed to shed human cercariae.

Table 1 shows ova-patent *S. mansoni* and that both medium and heavy intensity infections have been observed. Ova patent urogenital schistosomiasis was detected in all schools, ranging from 1.7% to 60.0%, inclusive of heavy intensity infections, except at Koche, St Martins and Makumba schools. Across our sample, 75 (14.4%) children were considered ‘free’ from schistosomiasis; if urine CCA-dipstick ‘trace’ was considered infected or ‘trace’ was considered not infected, then 109 (36.5%) or 56 (10.7%) children were judged co-infected with intestinal and urogenital schistosomiasis, respectively.

### Risk factors associated with schistosomiasis-associated morbidity

Figure 2 shows significant increases of schistosomiasis at Mchoka and Samama, even though MDA treatment coverage (81.9%), as reported by interview, was good. Relative risk (RR) of infection prevalence of *S. mansoni* significantly increased at Samama (RR=1.7 [95% CI 1.4 – 2.2]) and Mchoka (RR= 2.7 [95% CI 1.7 – 4.3]) schools, indicative of substantive re-infection concurrent with increasing environmental transmission for both types of schistosomiasis.

*a* all total of 200 FOB tests were available being used at Samama, Mchoka and MOET schools

*b* a trace result was considered here as not infected, only +ve urine CCA-dipstick scorings were considered infected; our conservative approach was based upon correlates of urine CCA-dipsticks and duplicate Kato-Katz comparisons, with ova-patent prevalence of *S. mansoni* being ≥ 20%, see Bärenbold et al. [12].

Table 2.

Risk factors analyses for morbidity associated with urogenital and intestinal schistosomiasis upon detection of microhematuria and FOB, respectively.

Table 2 shows an analysis of risk factors associated with schistosomiasis-associated morbidity. Urine CCA-dipstick results and ova-patent *S. mansoni* were significantly associated with FOB, alongside ova-patent *S. haematobium* with microhematuria. Neither age nor gender were associated with these morbidity indicators although a marginal protective effect of MDA, on both FOB and microhematuria, was observed.

### Discussion

Our integrated surveillance approach with three linked cross-sectional surveys, with conjoined malacological inspections, builds a more thorough assessment of the changing epidemiology of intestinal and urogenital schistosomiasis on the Lake Malawi shoreline, Fig. 1 and Table 1. Of note, is that the prevalence of both forms of schistosomiasis is increasing, Fig. 2, indicative perhaps that the force of infection [13] for each parasite is rising, with intestinal schistosomiasis being of newest public health concern here.

The unexpected occurrence of intestinal schistosomiasis elsewhere in Malawi, alongside the more well-known urogenital schistosomiasis, has been encountered before; the surveys conducted by Poole et al. in Chikhwawa during June 2012 noted that 24.9% and 9.1% of mothers and their pre-school-aged children were positive by urine CCA-dipsticks with ova-patent *S. mansoni* infections confirmed [14]. While *Biomphalaria* was not detected in their search for local snails [14], the occurrence of *B. pfeifferi*, as shown here in Fig. 1, adds weight to their postulate of intermittent transmission of *S. mansoni* in Chikhwawa. They suggested that the occasional influx of upstream populations of *B. pfeifferi* in the Shire River, as being swept downstream during seasonal flooding, might then colonize temporary pools in the Lower Shire River flood plain, to spark sporadic transmission in Chikhwawa [14]. By contrast, an enduring presence of *B. pfeifferi* along Lake Malawi and Upper Shire River, gives rise to more sustained opportunities in local transmission of *S. mansoni* in Mangochi District.
| Sample size | n = 520 | n = 191 |
|-------------|---------|---------|
| Prevalence (%) [95% CI] | 31.5 [27.5 - 35.5] | 16.2 [11.0 - 21.4] |

### Microhematuria

| Urine-CCA test\(\text{b}\) | -ve | +ve | -ve | +ve | -ve | +ve |
|----------------------------|-----|-----|-----|-----|-----|-----|
| Unadjusted odds ratio (95% CI) | 1 | 2.0 (1.4 - 3.0) [0.001] | 1 | 1.2 (0.6 - 2.6) [0.607] | 1 | 12.9 (4.3 - 38.7) [0.000] |
| [P-value] | | [0.001] | | [0.607] | | [0.000] |
| Adjusted odds ratio (95% CI) | 1 | 3.0 (1.0 - 8.6) [0.043] | 1 | 11.4 (3.9 - 33.3) [0.000] | 1 | |
| [P-value] | | [0.043] | | [0.000] | | |

### Ova-patent intestinal schistosomiasis (Kato-Katz)

| Ova-patent urogenital schistosomiasis (urine filtration) | -ve | +ve | -ve | +ve | -ve | +ve |
|--------------------------------------------------------|-----|-----|-----|-----|-----|-----|
| Unadjusted odds ratio (95% CI) | 1 | 42.1 (23.2 - 76.5) [0.000] | 1 | 47.9 (22.6 - 101.5) [0.000] | 1 | 1.6 (0.7 - 3.8) [0.248] |
| [P-value] | | [0.000] | | [0.000] | | [0.248] |
| Adjusted odds ratio (95% CI) | 1 | 0.7 (0.5 - 1.1) [0.159] | 1 | 0.7 (0.3 - 1.8) [0.499] | 1 | 0.5 (0.2 - 1.3) [0.185] |
| [P-value] | | [0.159] | | [0.499] | | [0.185] |

### Praziquantel treatment in last 12 months

| Gender | Male | Female |
|--------|------|--------|
| Unadjusted odds ratio (95% CI) | 1 | 1.0 (0.7 - 1.4) [0.850] | 1 | 0.9 (0.5 - 1.8) [0.816] | 1 | 1.1 (0.5 - 2.3) [1.000] |
| [P-value] | | [0.850] | | [0.816] | | [1.000] |
| Adjusted odds ratio (95% CI) | 1 | 0.7 (0.5 - 1.1) [0.159] | 1 | 0.7 (0.3 - 1.8) [0.499] | 1 | 0.5 (0.2 - 1.3) [0.185] |
| [P-value] | | [0.159] | | [0.499] | | [0.185] |

### Age

| Age | Unadjusted odds ratio (95% CI) | 1.0 (0.6 - 1.4) [0.706] | 1.2 (0.6 - 2.3) [0.629] | 1.1 (0.507 - 2.4) [0.811] |
|-----|----------------------|----------------------|----------------------|----------------------|
| 6 - 10 | 1 | 1 | 1 |
| 11 - 15 | 0.9 | 1.2 | 1.1 |

In regard of this lake shoreline setting, we have shown 1) increases in the prevalence of intestinal schistosomiasis at Mchoka and Samama Schools, 2) occurrence of intestinal schistosomiasis at MOET and Koche schools and 3) endemic intestinal schistosomiasis occurring along a 80 km section of Lake Malawi and Shire River shoreline, noting additional populations of *B. pfeifferi* on the lake’s eastern shoreline, Fig. 1. Of particular note is the strong association of *S. mansoni* infection, as detected by urine CCA-dipsticks, with FOB in 16.2% of examined children, see Table 2, indicative of overt intestinal pathology [15]. Combined with the observations of ova-patent infections of moderate- and heavy-intensities at Koche and Ndembo, as well as, ova-patent infections at a further 5 schools, this is pervasive evidence of more sustained local transmission of intestinal schistosomiasis.

Whilst the debate on how to interpret ‘trace’ reactions of urine-CCA dipsticks continues, a ‘positive’ reaction is considered solid evidence of active intestinal schistosomiasis [12]. Therefore, 31.5% [95% CI 27.5–35.5] of our sampled children were suffering from intestinal schistosomiasis but if a ‘trace’ reaction was considered diseased then a total of 82.5% [95% CI = 79.2–85.8] were infected or, at the very least, at-risk. Of particular note in this light is intestinal schistosomiasis at Ndembo and St Augustine II schools, see Fig. 1, where the prevalence of

---

\(\text{FOB}\) is the indicator of the presence of *S. mansoni* in the stool, while Microhematuria is the presence of red blood cells in the urine, as detected by the CCA-dipstick method.
'positive' urine-CCA dipsticks was > 50% and ova-patent S. mansoni infections were encountered, being of light and moderate infection intensities, Table 1; moreover, moderate and heavy ova-patent S. mansoni infections were detected at Koche school where the prevalence of ‘positive’ urine-CCA dipsticks was 35.0%, with B. pfeifferi found nearby.

Our rapid disease mapping surveillance across 8 schools, currently augments district-level information of the NCP, critically revising scientific appraisals concerning the previous absence of intestinal schistosomiasis [1], and better demonstrates the newly defined endemicity of intestinal schistosomiasis along the Mangochi District shoreline. When taken as a whole, we judge that there is now sufficient evidence to notify that an outbreak of intestinal schistosomiasis is occurring. This has immediate bearing on the health of the local populace and tourists who may visit here, as well as, in health advice or diagnostic testing undertaken in local or international medical clinics presently unaware of this new risk of intestinal schistosomiasis.

In terms of environmental surveillance, it is worthy to note that the lake is undergoing ecological change, most easily seen with lake level changes through time, see Fig. 3. Its dynamic shoreline and lake level are manifest, perhaps creating new habitats for B. pfeifferi to colonize and or were facilitating collection of this snail in locations previously too deep to be retrieved by hand. The dispersion of this snail, a keystone species for S. mansoni, like in Senegal [9] or in Ethiopia [7], is a critical epidemiological driver of intestinal schistosomiasis transmission. We therefore recommend increased vigilance for B. pfeifferi, especially along the lake’s eastern shores and in downstream locations on the Shire River, with additional epidemiological inspections of adjacent schools and communities. This will better gauge the full footprint of intestinal schistosomiasis with newly recognized environmental opportunities for associated transmission.

Control of schistosomiasis needs a multisectoral approach and it is often debated how control tactics should be changed [16] or better tailored to aquatic environments [17]. To respond to this outbreak of intestinal schistosomiasis, we propose that current MDA efforts should be intensified, adopting biannual treatment cycles in schools, which has been successfully implemented elsewhere [18], alongside expanded access to praziquantel for all community members with intestinal schistosomiasis, in need of regular treatment throughout the year [19]. From recent surveys of adult fishermen who have urogenital schistosomiasis, making specific reference to male genital schistosomiasis, co-infection with S. mansoni has been noted alongside re-infections within a calendar year [20, 21]. To augment MDA and community-access to praziquantel, it is important to strengthen health education and outreach with suitable WASH interventions [20, 22], better appropriate to this lakeshore setting, noting that even focal application of molluscicides is inappropriate [17], given this lake’s global importance in biodiversity.

**Conclusion**

Despite ongoing annual MDA of praziquantel for urogenital schistosomiasis, an outbreak of intestinal schistosomiasis is occurring in Mangochi District, Malawi. We therefore recommend stepping-up MDA treatment cycles, i.e. from annual to biannual, increasing community access to praziquantel treatment throughout the year, with renewed efforts to mitigate environmental transmission with health education and appropriate WASH interventions, as better tailored towards intestinal schistosomiasis in this lakeshore setting.

**Abbreviations**

CCA: circulating cathodic antigen; FOB: faecal occult blood; MDA: Mass drug administration; EPG: eggs per gram; RR: relative risk.
Declarations

Acknowledgments

We are grateful to the local health and education authorities of Malawi with specific thanks to the headteachers, teachers, children and parents who participated in our study; to our friend and colleague Father Henry Chagoma and his staff of Montfort Mission Lake House for their hospitality and convivial company. We thank Dr Michelle Stanton, LSTM for assistance in interpretation of remote sensing imagery presented in Figure 3. Urine CCA dipsticks were supplied by Rapid Medical Diagnostics, South Africa with manufacturer batch number 180907091, expiry date 09/2020.

Funding

SAK and MHAI-H are funded by PhD scholarships from the Commonwealth Scholarship Commission and Ministry of Health, Kingdom of Saudi Arabia, respectively, and JRS, EJLaC by the Higher Education Funding Council for England (HEFCE).

Availability of data and materials

Data used for the analysis are available from the corresponding author upon reasonable request.

Authors contributions

SAK, EJLaC, LJ, JM, PM and JRS designed the study; SAK, AMO’F, HB undertook the parasitological fieldwork with laboratory support from BM and DL. Malacological studies were undertaken by PM, JH, MHAI-H and JRS. Data entry and analyses were undertaken by SAK, AMO’F, HB and JH as overseen by EJLaC, LJ, JM, PM and JRS. All authors read and approved the manuscript for publication.

Ethics approval and consent to participate

Research approvals were granted in Malawi by the National Health Sciences Research Committee (1805), Mangochi District Health Office Research Committee (26.04.2019) and in the UK by LSTM Research Ethics Committee (30.04.2019). Written informed guardian consent was obtained for each school child before participation in surveys.

Consent for publication

All authors have provided consent for publication of the manuscript.

Competing interests

The authors declare that they have no competing interests.

Author details

1 Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, L3 5QA, UK. 2 Medi Clinic Limited, Medical Aid Society of Malawi (MASM), 22 Lower Sclatter Road, P.O. Box 1254, Blantyre, Malawi. 3 Laboratory Department, Mangochi District Hospital, P.O. Box 42, Mangochi, Malawi. 4 Malawi Liverpool Wellcome Trust Programme of Clinical Tropical Research, Queen Elizabeth Central Hospital, College of Medicine, P.O. Box 30096, Blantyre, Malawi. 5 Ministry of Health, Qassim, Kingdom of Saudi Arabia. 6 National Schistosomiasis and STH Control Programme, Ministry of Health, Lilongwe, Malawi. 7 Department of Basic Medical Sciences, College of Medicine, University of Malawi, Blantyre, Malawi. 8 Research for Health Environment and Development, P.O. Box 345, Mangochi, Malawi.
References

1. Makaula P, Sadalaki JR, Muula AS, Kayuni S, Jemu S, Bloch P. Schistosomiasis in Malawi: A systematic review. Parasite Vector 2014; 7.

2. Kayuni S, Peeling R, Makaula P. Prevalence and distribution of *Schistosoma haematobium* infection among school children living in southwestern shores of Lake Malawi. Malawi Med J 2017; 29:16-23.

3. WHO. Schistosomiasis: Progress report 2001–2011 and strategic plan 2012–2020. World Health Organization, Geneva, 2013.

4. Bowie C, Purcell B, Shaba B, Makaula P, Perez M. A national survey of the prevalence of schistosomiasis and soil-transmitted helminths in Malawi. BMC Infect Dis 2004; 4.

5. Mtethiwa AHN, Nkwengulila G, Bakuza J, Sikawa D, Kazembe A. Extent of morbidity associated with schistosomiasis infection in Malawi: A review paper. Infect Dis Pov 2015; 4.

6. Alharbi MH, Condemine C, Christiansen R, LaCourse EJ, Makaula P, Stanton MC et al. *Biomphalaria pfeifferi* snails and intestinal schistosomiasis, Lake Malawi, Africa, 2017-2018. Emerg Infect Dis 2019; 25:613-5.

7. Bekana T, Hu W, Liang S, Erko B. Transmission of *Schistosoma mansoni* in Yachi areas, southwestern Ehtiopia: new foci. Infect Dis Pov 2019; 8:1.

8. Mari L, Casagrandi R, Rinaldo A, Gatto M. Epidemicity thresholds for water-borne and water-related diseases. J Theoret Biol. 2018 447:126-38.

9. Poole H, Terlouw DJ, Naunje A, Mzembe K, Stanton M, Betson M, et al. Schistosomiasis in pre-school-age children and their mothers in Chikhwawa district, Malawi with notes on the characterization of schistosomes and snails. Parasites Vector 2014; 7:153.

10. Stothard JR, Stanton MC, Bustinduy AL, Sousa-Figueiredo JC, Van Dam GJ, Betson M, et al. Diagnostics for schistosomiasis in Africa and Arabia: a review of present options in control and future needs for elimination. Parasitol 2014; 141:1947-1961.

11. Tchuente LAT, Rollinson D, Stothard JR, Molyneux D. Moving from control to elimination of schistosomiasis in sub-Saharan Africa: time to change and adapt strategies. Infect Dis Pov 2017;6:42.

12. Stothard JR, Campbell SJ, Osei-Atweneboana MY, Durant T, Stanton MC, Biritwum NK et al. Towards interruption of schistosomiasis in sub-Saharan Africa: developing an appropriate environmental surveillance framework to guide and to support ‘end game’ interventions. Infect Dis Pov 2017; 6:10.

13. Knopp S, Stothard JR, Rollinson D, Mohammed KA, Khamis IS, Marti H, et al. From morbidity control to transmission control: Time to change tactics against helminths on Unguja Island, Zanzibar. Acta Trop 2013; 128:412-22.

14. Toor J, Rollinson D, Turner HC, Gouvras A, King CH, Medley GF et al. Achieving elimination as a public health problem for *Schistosoma mansoni*and *S. haematobium*: When is community-wide treatment required? J Infect Dis 2020; corrected proof.

15. Kayuni SA, LaCourse EJ, Makaula P, Lampiao F, Juziwelo L, Fawcett J, et al. Case Report: Highlighting male genital schistosomiasis (MGS) in fishermen from the southwestern shoreline of Lake Malawi, Mangochi District. Am J Trop Med Hyg 2019; 101; 1331-1335.

16. Kayuni SA, Corstjens PLAM, LaCourse EJ, Bartlett KE, Fawcett J, Shaw A, et al. How can schistosome
circulating antigen assays be best applied for diagnosing male genital schistosomiasis (MGS): an appraisal using exemplar MGS cases from a longitudinal cohort study among fishermen on the south shoreline of Lake Malawi. Parasitol 2019:146;1785-1795.

22. Campbell SJ, Biritwum NK, Woods G, Velleman Y, Fleming F, Stothard JR. Tailoring Water, Sanitation, and Hygiene (WASH) targets for soil-transmitted helminthiasis and schistosomiasis control. Trends Parasitol 2018; 34:53-63.

Figures
Figure 1

Schematic map showing the prevalence of intestinal schistosomiasis in June 2019, by sampled school, by urine CCA-dipsticks. Freshwater sites inspected for B. pfeifferi over the November 2017 – December 2019 period are also shown [Note that schools denoted with a flag represent locations where ova-patent S. mansoni infection was observed, and the schools associated with each objectives(1-3). The black arrow labelled ‘A’ denotes the bay area as shown in the Figure 3 where the shoreline has changed during the 2005-2016 most likely due to lowering lake levels and local sedimentation, where numerous B. pfeifferi (n≥10) have been consistently found].
Figure 2

The year-on-year increase of prevalence of urogenital (by urine filtration) and intestinal (by urine CCA-dipsticks) schistosomiasis despite annual MDA across the two schools Mchoka and Samama as sampled in 2018 and 2019. Error bars indicate 95% confidence intervals.
A. Composite satellite map, modified from GoogleEarth imagery, that illustrates the changing shoreline of the lake in 2005, 2012, 2013 and 2016. The featured area is the bay indicated by the black arrow labelled ‘A’ in Figure 1. The green circle ‘M12’ denotes the sampling location where numerus Biomphalaria have been found.
during all malacological inspections from November 2017 to December 2019. The changing shoreline is most likely resultant from lowering lake levels, see 3B, as well as, upon influx of sediments from the seasonal river in the bottom part of this image. B. Annual changes in the lake level during 1992 – 2019 period (see https://ipad.fas.usda.gov/cropexplorer/global_reservoir/gr_regional_chart.aspx?regionid=eafrica&reservoir_name=Malawi), as detected by remote altimetry, denoting two particularly low-level periods, in 1996-1998 and 2017-2019, which helps explain the changing shoreline shown in 3A as the lake recedes.