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**DATES:**

**Received:** 25 Aug. 2016

**Revised:** 17 Oct. 2016

**Accepted:** 19 Oct. 2016

**KEYWORDS:**

urogenital schistosomiasis; KwaZulu-Natal; *Ascaris lumbricoides*; *Trichuris trichiura*; schoolchildren

**HOW TO CITE:**

Molvik M, Helland E, Zulu SG, Kleppa E, Lillebo K, Gundersen SG, et al. Co-infection with *Schistosoma haematobium* and soil-transmitted helminths in rural South Africa. *S Afr J Sci.* 2017;113(3/4), Art. #2016-0251, 6 pages. <http://dx.doi.org/10.17159/sajs.2017/20160251>

**ARTICLE INCLUDES:**

- × Supplementary material
- × Data set

**FUNDING:**

Norwegian Centre for Imported and Tropical Diseases, Oslo University Hospital Ullevaal (VIRUUS); S.G. Sønneland Foundation; Shipowner Tom Wilhelmsen Foundation

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# Co-infection with *Schistosoma haematobium* and soil-transmitted helminths in rural South Africa

Schistosomiasis and soil-transmitted helminthiasis are among the most prevalent neglected tropical diseases and may lead to severe consequences. We assessed the extent of co-infection between *Schistosoma haematobium* and the soil-transmitted helminths (STHs) *Ascaris lumbricoides* and *Trichuris trichiura* in schoolgirls in the rural areas of KwaZulu-Natal, South Africa. We also explored if *S. haematobium* can serve as a predictor for soil-transmitted helminths in this area. From 15 selected schools, 726 primary schoolgirls aged 10–12 years provided both urine and stool samples. The samples were examined for the presence of eggs using the urine sedimentation technique for *S. haematobium* and the Kato Katz technique for STHs. Pearson's chi-square test was used to calculate the association and Spearman's rank correlation was used for the correlation analysis. There was a highly significant correlation between *S. haematobium* and STHs at a school level (Spearman's correlation coefficient = 0.93;  $p < 0.001$ ). The prevalences were found to be 36.9% and 38.8% for *S. haematobium* and STHs, respectively. A significant association was found between *S. haematobium* and STHs (odds ratio = 2.05; confidence interval = 1.58–2.93;  $p < 0.001$ ). Indirect indicators of urogenital schistosomiasis (e.g. water contact and haematuria) were significantly associated with *A. lumbricoides* and *T. trichiura* infection. We have demonstrated a highly significant correlation and overall association between urogenital schistosomiasis and *A. lumbricoides* and *T. trichiura*. We cautiously suggest that all *S. haematobium* endemic areas should be treated for STH infections.

**Significance:**

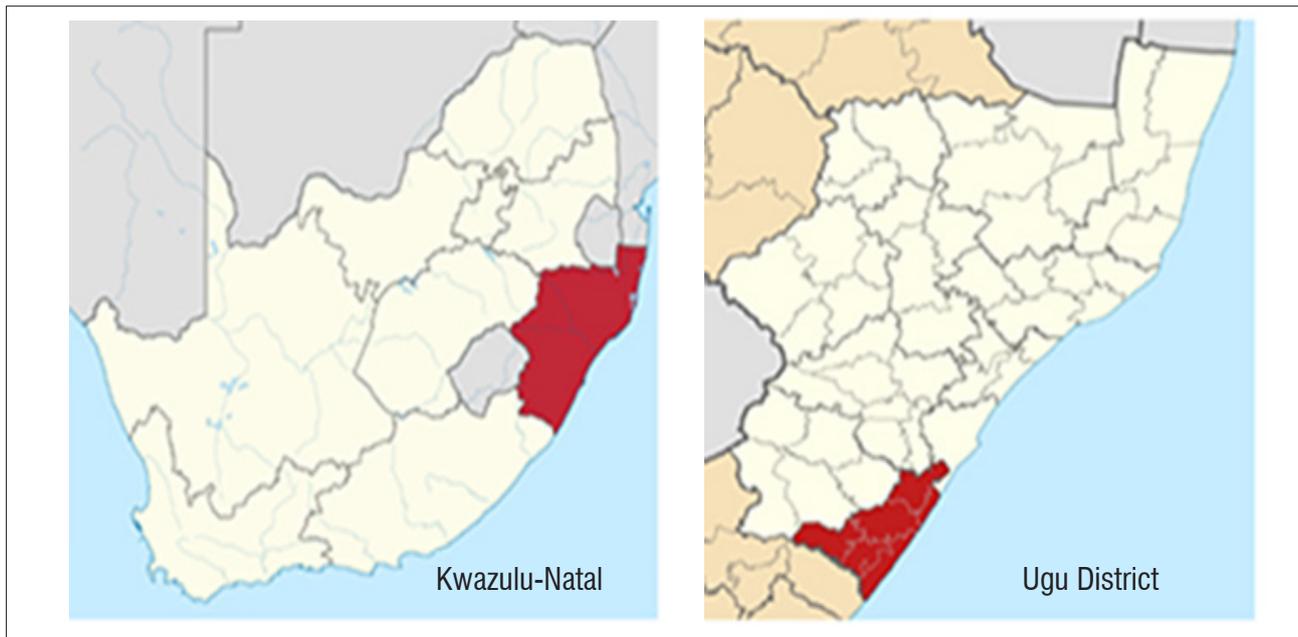
- The prevalences of urogenital schistosomiasis and soil-transmitted helminth infections were highly significantly correlated.
- More than half (60%) of the investigated schools are in need of annual treatment for *S. haematobium* infection.
- Almost half of the infected schoolgirls had a heavy intensity of *S. haematobium* infection.
- Nearly all the schools investigated require treatment for soil-transmitted helminthiasis once or even twice per year.
- This study can contribute to the epidemiological planning process of the deworming programme.

## Introduction

Schistosomiasis and soil-transmitted helminthiasis represent the most common neglected tropical diseases and may cause acute and chronic illness.<sup>1</sup> The most prevalent schistosome species in South Africa is *Schistosoma haematobium*, which causes urogenital schistosomiasis.<sup>2</sup> It is estimated that 5.2 million people in South Africa are infected with *S. haematobium*.<sup>3</sup> The total number of people infected with soil-transmitted helminths (STHs) in South Africa is unknown, but according to the World Health Organization (WHO) approximately 3.2 million children require treatment in South Africa.<sup>4</sup> These helminth infections may have serious consequences in children, which could lead to decreased growth and stunting, decreased cognitive development and school performance and increased school absenteeism.<sup>5,6</sup> Furthermore, infection with STHs is associated with anaemia and malnutrition<sup>5,7</sup> and urogenital schistosomiasis may also lead to anaemia, dysuria, haematuria, infertility and, in some instances, bladder cancer<sup>8</sup> and may increase the risk of HIV infection in women<sup>6,9,10</sup>. The diseases may be controlled by periodic treatment with so-called preventive chemotherapy.<sup>11</sup>

Studies have demonstrated that deworming programmes significantly improve learning, growth and school attendance among schoolchildren<sup>1,12</sup> and mass treatment programmes integrated with other health services have been found to be the most cost-effective approach to combat the helminth infections<sup>11</sup>.

Previous studies have shown that areas endemic for schistosomiasis are often also endemic for soil-transmitted helminthiasis.<sup>13</sup> *S. haematobium* is transmitted to humans through infested fresh water and STHs are transmitted from contaminated soil in areas that lack adequate sanitation, as eggs are excreted in human urine and faeces, respectively.<sup>1</sup> Improvements in water, sanitation and hygiene are important to prevent all helminth infections<sup>14</sup> and in South Africa, sanitation programmes have been rolled out but have not yet reached all areas<sup>15</sup>. In KwaZulu-Natal, 14% of households have never had access to potable water.<sup>15</sup> Furthermore, even people who have access to taps providing potable water must often use the river because of irregular water supply and/or long queues for drinking water at the communal taps.<sup>16</sup>



**Figure 1:** Map showing KwaZulu-Natal Province and Ugu District within KwaZulu-Natal, South Africa.

Soil-transmitted helminthiasis is most commonly diagnosed by stool collection and microscopy, requiring willing patients and trained laboratory staff.<sup>1</sup> *S. haematobium* prevalence may be assessed in children by detecting macro- or microscopic haematuria through a questionnaire or by urine dipstick. The latter technique has demonstrated to be quick, easy to perform, and highly sensitive and specific in children<sup>17-19</sup>, although final diagnosis must be confirmed by microscopy or more advanced methods<sup>20</sup>.

The Integrated School Health Programme's policy in South Africa recommends treatment for all children in areas endemic for schistosomiasis and soil-transmitted helminthiasis, but this recommendation has still to be implemented<sup>21</sup>; and these areas have still to be identified<sup>22</sup>. In order to make decisions on where to treat, countrywide mapping of helminth infections is needed.

In this study, we aimed to explore the burden of water- and soil-transmitted helminth infections in a middle-income country like South Africa and to determine if infection with *S. haematobium* could serve as a predictor for STHs.

## Methods

### Study area

The study was conducted between September 2009 and November 2010 in Ugu District in the KwaZulu-Natal Province of South Africa (Figure 1). The study site is endemic for *S. haematobium* and STHs.<sup>23-26</sup> The total population of the District is 709 918; over 50% are female and 33% are under the age of 14.<sup>27</sup>

### Study population

Of the 309 primary schools in the area, 18 schools in rural Ugu were randomly selected for inclusion. All girls between the ages of 10 and 12 were invited to participate, and a total of 1057 girls participated in the study. In three of the schools, fewer than 10 girls provided urine and stool samples, and the schools were therefore excluded from the calculations. From the 15 included schools, 726 individuals submitted both stool and urine samples. Girls who did not provide at least one urine and one stool sample were excluded. No mass treatment had been conducted in this cohort of children before the data collection.

### Parasitological examination

Urine specimens were collected for three consecutive days between 10:00 and 14:00. Samples were transported to the laboratory in dark cooler boxes. After arrival, 1 mL of 2% tincture of merthiolate in 5% formalin solution was added to each 10-mL urine sample for preservation. Two samples from each participant (labelled A and B) were registered daily (six samples in total per girl). Within the same week, the samples were centrifuged and microscopically investigated for *S. haematobium* eggs. The egg counts were based on the 10 mL of urine and each slide was read independently by two technicians. One stool sample was provided by each girl and the stool samples were kept at 4 °C until they were processed within 24 h after collection. The Kato-Katz technique was used for diagnosing STHs.<sup>28,29</sup> The stool sample was divided into two (A and B) and each sample of 41.9 mg was prepared on a slide and investigated by microscope by two laboratory technicians. Because of the duration between sampling and preservation, it was not possible to identify hookworm eggs in the stool samples.

### Ethical considerations and treatment

Three ethics committees granted permission to undertake this study. The Biomedical Research Ethics Committee of the University of KwaZulu-Natal (reference BF029/07), the KwaZulu-Natal Department of Health (Pietermaritzburg, 3 February 2009, reference HRKM010-08) and the Regional Norwegian Ethics Committee gave ethical clearance (reference 469-07066a1.2007.535). Further, both the Departments of Health and Basic Education in Ugu District gave permission. Prior to the study, information meetings were held for the parents, principals, school governing bodies and teachers. Assent was given by each girl, and informed consent forms were signed by parents/guardians. Treatment with a single dose of praziquantel (40 mg/kg) for schistosomiasis was offered to all by the Department of Health and information about possible side effects was given. Treatment for STH was offered at the local clinics.

### Data analysis

If at least one egg was found in the urine or stool sample, the person was registered as positive. Schools were categorised into risk groups according to WHO guidelines.<sup>1</sup> Intensity of *S. haematobium* was expressed as eggs per 10 mL of urine, based on the maximum egg count of the three urine samples provided. 'Light infection' is defined as 1–50 eggs per 10 mL of urine and 'heavy infection' as more than 50 eggs per 10 mL of urine.<sup>1</sup> The median egg count of the study population

was calculated for *S. haematobium*. The egg counts for the STHs were stopped at 500 eggs per slide and so it was not possible to calculate median or intensity of egg excretion in the high excretors and therefore for the STHs.

### Interviews

Research assistants interviewed each girl in the local language (isiZulu) using a pre-designed questionnaire, the results of which are described elsewhere.<sup>25</sup> Interviews included questions on water contact and urogenital symptoms such as pain when urinating and having observed red urine.

### Statistical analysis

Data were entered into MS Excel spreadsheets and exported to SPSS Statistics (IBM SPSS Version 22). When the data did not have a normal distribution, a non-parametric statistical test was used. A *p*-value lower than 0.05 was considered statistically significant. Pearson's chi-square test and odds ratios were used to calculate the association between the helminth species. Pearson's chi-square and Mann-Whitney U tests were used for comparison of age or household size and categorical data of included and excluded cases. The helminth prevalences found in each school were compared using Spearman's rank correlation.

## Results

Table 1 shows the descriptive characteristics of the study population. Over a third (37%; 268/726) of the girls was infected with schistosomiasis and the prevalence of STHs (either *A. lumbricoides* or *T. trichiura*) was 38.8% (282/726). The egg counts for *S. haematobium* ranged from 1 to 624 eggs per 10 mL (with a median of 21). Heavy intensity of *S. haematobium* was found in 47.8% (128/268) of the girls positive for this infection. Infection with *S. haematobium* was not only significantly associated with STH infection (either ascariasis or trichuriasis) (odds ratio = 2.15; 95% confidence interval = 1.58–2.93; *p* < 0.001), but also with each of the species (Table 1). Red urine, dysuria, washing blankets in the river and swimming in the river were associated with *S. haematobium* (data not shown). These variables were also investigated as a predictor for STHs and found to be significantly associated (Table 1). Age did not influence any of the associations. The included (*n* = 726) and excluded (*n* = 297) cases had similar exposures to risk water and similar family structures as those shown in Table 2.

### School-level analysis

The prevalence of *S. haematobium* found in each investigated school ranged between 8.8% and 70.0% (median 50.0%) and the prevalence of STHs in the schools ranged between 0 and 63.0% (median 37.5%).

**Table 1:** Descriptive characteristics of the study population, prevalence of *Schistosoma haematobium*, *Ascaris lumbricoides*, *Trichuris trichiura*, and association with soil-transmitted helminth (STH) infection

Category	Prevalence	Association with STH infection
<i>Schistosoma haematobium</i>	36.9% (268/726)	OR = 2.15, 95% CI = 1.58–2.93, <i>p</i> < 0.001
<i>Ascaris lumbricoides</i>	25.6% (184/726)	OR = 1.62, 95% CI = 1.15–2.28, <i>p</i> = 0.005
<i>Trichuris trichiura</i>	28.0% (203/726)	OR = 2.33, 95% CI = 1.67–3.24, <i>p</i> < 0.001
Access to water from communal tap (mean)	73.3% (530/723)	No association
Have an indoor tap	22.3% (161/723)	No association
Use river as a source for drinking water	1.7% (12/723)	No association
Swim in river/dam	32.4% (235/726)	Adjusted OR = 1.38, 95% CI = 1.00–1.89, <i>p</i> = 0.05
Wash blankets in river	26.2% (190/726)	Adjusted OR = 1.80, 95% CI = 1.28–2.52, <i>p</i> < 0.001
Red urine	17.6% (127/723)	Adjusted OR = 1.44, 95% CI = 1.14–1.83, <i>p</i> = 0.002
Dysuria	21.5% (155/721)	Adjusted OR = 1.55, 95% CI = 1.19–2.03, <i>p</i> = 0.001

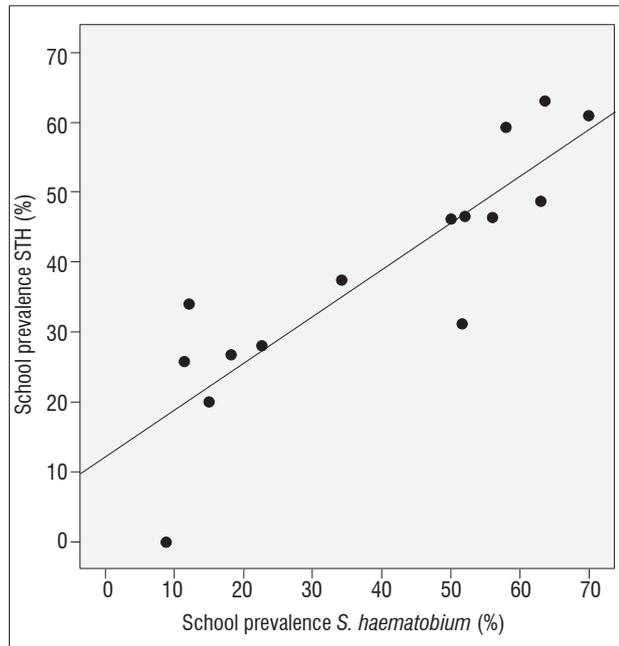
OR, odds ratio; CI, confidence interval

**Table 2:** Comparison of characteristics of included cases (stool, urine and questionnaire provided) and excluded cases

Category	Included ( <i>n</i> = 726)	Excluded ( <i>n</i> = 297)	<i>p</i> -value
Median age in years (range)	11 (9–13)	11 (9–13)	0.98 <sup>†</sup>
Median household size	6 (2–19)	6 (2–19)	0.51 <sup>†</sup>
Access to piped/potable water (mean)	97.0% (700/722)	96.6% (287/297)	0.79 <sup>†</sup>
Swim in river/dam	32.4% (235/726)	29.6% (98/331)	0.37 <sup>†</sup>
Ever lived in city	6.6% (47/710)	7.4% (22/297)	0.65 <sup>†</sup>
Median employed people in household	1 (0–8)	1 (0–9)	0.66 <sup>†</sup>
Mother as main caregiver	65.3% (473/724)	64.5% (193/299)	0.81 <sup>†</sup>
Mothers highest education is high school or higher	63.3% (386/610)	64.4% (159/247)	0.76 <sup>†</sup>

<sup>†</sup>Mann-Whitney U test, <sup>†</sup>chi-square test

Figure 2 shows the correlation between *S. haematobium* and STHs based on school prevalences. The correlation coefficient was found to be 0.93 ( $p < 0.001$ ). Of the investigated schools in Ugu District, 60% (9/15) were found to have a prevalence of urogenital schistosomiasis above 50% and the same applied for 20% (3/15) of the schools for soil-transmitted helminthiasis. Just above 70% (11/15) of the schools had a prevalence of STH infection between 20% and 50%.



**Figure 2:** Significant correlation (Spearman's correlation coefficient = 0.93;  $p < 0.001$ ) between prevalence of *Schistosoma haematobium* and soil-transmitted helminths (*Ascaris lumbricoides* and *Trichuris trichiura*) in schoolchildren.

## Discussion

At a school level, the prevalence of urogenital schistosomiasis and STH infections were highly significantly correlated. Overall prevalence of infection with *S. haematobium* and STHs was significantly associated. In addition, indirect indicators of urogenital schistosomiasis were significantly associated with *A. lumbricoides* and *T. trichiura* infection. Based on the WHO recommendations, this study shows that 60% of the investigated schools are in need of annual treatment for *S. haematobium* because they show a prevalence in excess of 50%.<sup>1</sup> For soil-transmitted helminthiasis, the recommendation is treatment once per year if the school is classified as low risk (a prevalence of 20–50%) and twice a year if classified as high risk (a prevalence greater than 50%).<sup>1</sup> Nearly all the schools investigated require treatment for soil-transmitted helminthiasis once or even twice per year. Almost half of the infected school girls showed a heavy intensity of *S. haematobium* infection.

The observed associations are consistent with previous studies<sup>13,30</sup> and contribute to the evidence showing that co-infection occurs in areas endemic for *S. haematobium*. This present study shows that the prevalence of *S. haematobium*, *A. lumbricoides* and *T. trichiura* was within the same range as reported previously in the area.<sup>23,24,31</sup> Our study only included participants who provided both urine and stool samples, but there was no difference between the included and excluded girls in terms of household size, water contact and age.

Intensity of infection has been shown to be positively correlated with morbidity, and measuring intensity allows quantification of the proportion of individuals with high intensity of infection who may suffer serious consequences.<sup>1</sup> However, previous studies have shown that the majority of infected children harbour light infections and relatively few people suffer severe morbidity.<sup>32</sup> The WHO recommends calculating the intensity of infection at community level to estimate the morbidity rate

in the same area.<sup>1</sup> This calculation can be done by estimation of the mean intensity, or more comprehensively by classes of intensity,<sup>33</sup> as done in this paper. Our results showed that almost 50% of the girls had a heavy intensity *S. haematobium* infection (egg counts above 500). We did not investigate the intensity of STH infection. However, persons with a heavy intensity of one helminth species have been found to be more likely to harbour a heavy intensity of the other helminth species.<sup>34</sup> It has been hypothesised that overdispersion may be explained by a predisposition of some individuals to helminth infections, although the underlying reasons remain poorly understood.<sup>32,35</sup> Possible factors are differences in susceptibility and immunity against infection.<sup>32</sup> Another possibility is that because of poor sanitation in general, infestation in only a few latrines can lead to contamination of the water and soil by these helminths, as there is often limited access to clean water. Jinabhai et al.<sup>31</sup> reported this pattern of intensity for *S. haematobium* and *T. trichiura* in southern KwaZulu-Natal.

Saathoff et al.<sup>36</sup> found that amongst 10- to 12-year-old pupils, the boys had about 10% lower prevalence of *S. haematobium* than the girls and the prevalence of *A. lumbricoides*, but not *T. trichiura*, also differed significantly between boys and girls. On the other hand, the opposite tendency was found among schoolchildren in Zanzibar: boys were slightly more affected by *S. haematobium*, both regarding prevalence and intensity, and significantly more heavily infected with *T. trichiura* than the girls.<sup>30</sup> Hence, the results from this study on schoolgirls cannot be extrapolated to different populations because local gender-related habits can differ.

Low socio-economic status is intimately related to the presence of helminth infections.<sup>37</sup> Members of poorer families are found to be more frequently infected with *A. lumbricoides* and *T. trichiura* and more likely to have both schistosomiasis and soil-transmitted helminthiasis.<sup>37</sup> Poor economic growth has been shown to maintain high prevalences of STH infections.<sup>38</sup> However, the connection between poverty and STHs is complex, because STH prevalence in turn is a contributing factor to poor economic growth and the anaemia caused by soil-transmitted helminthiasis is associated with reduced work output.<sup>38</sup> It has been shown that children from poorer families are more likely to drop out of school.<sup>39</sup> There is an 85% school enrolment in South Africa.<sup>40</sup> This study only included enrolled schoolgirls and those present at the days of sample collections. Schoolgirls may be absent as a result of sickness caused by urogenital schistosomiasis or soil-transmitted helminthiasis or other health issues, or may stay home for family reasons. Hence, these prevalences and intensities of infection may be underestimated.

Different activities involving water contact are highly associated with *S. haematobium* infection,<sup>41</sup> and washing hands with soap after defecation and before eating is protective against STHs (except hookworm) by limiting the faeco-oral route of infection.<sup>37</sup> Access to clean fresh water has been associated with a significant reduction in STH infection.<sup>30</sup> Furthermore, not using a tap as the source for drinking water is positively associated with urogenital schistosomiasis.<sup>37</sup> The Ugu District Municipality Integrated Development Plan confirmed that constructions of sanitary facilities and water sources have taken place in the area in recent years, but improvements have not reached all areas.<sup>27</sup> The prevalence of the helminth infections in the schools varied from 8.8% to 70.0% for *S. haematobium* and 0 to 63% for STHs. In order to explain the differences between schools, more background information about the socio-economic status of the participants and their community, their access to water and sanitation facilities and local risk factors is needed.<sup>14,37,39,41</sup>

Because of both time and resource constraints, only one faecal sample was collected from each participant in this study, although three faecal samples on three consecutive days markedly raises the sensitivity.<sup>29,42</sup> Because egg excretion has a day-to-day variation, there may have been an under- or overestimation of both prevalence and intensity of infection.<sup>42</sup> Hookworm was not investigated, because of logistical constraints, although it would have been desirable as part of the total examination for STHs.

The difference in transmission patterns of *S. haematobium* and STHs is essential when it comes to prevention and control. Although the helminth

infections have many of the same risk factors, the transmission cycle of *S. haematobium* requires fresh water with snails as the intermediate host.<sup>2</sup> The distribution and transmission of schistosomiasis is therefore known to be highly focal – depending on different factors such as presence of water and local environmental conditions – whereas STHs are more widely distributed.<sup>1</sup> In the southern part of South Africa, schistosomiasis is not found more than 300 m above sea level, and often not in urban areas. STHs, however, are found in the Cape Peninsula and in urban slums.<sup>43</sup> However, because of the great burden of helminth infections, WHO recommends coordinated interventions to secure a joint and synergic control of the diseases.<sup>11</sup> South Africa's first school-based helminth control programme in KwaZulu-Natal, from 1997 to 2000<sup>23</sup>, showed a decrease in prevalence for all the helminths investigated (*S. haematobium*, *A. lumbricoides*, *T. trichiura* and hookworms) after treating the schoolchildren with chemotherapy.<sup>44</sup> Despite the successful results, the programme was discontinued and it has been suggested that this discontinuation was a result of a shift in funding priorities consequent to the massive burden of HIV and tuberculosis.<sup>43</sup> Newer studies have shown that patients with urogenital schistosomiasis may be at higher risk for HIV acquisition, which should be considered of importance for control of the helminth infection.<sup>45</sup> The South African health authorities have recently launched an initiative to combat helminth infections in endemic areas and this study can contribute to the epidemiological planning process of the deworming programme.

Considering the significant correlation and association between urogenital schistosomiasis and STH infection shown in this study, using *S. haematobium* as a predictor for STHs, at least in rural parts of districts where urogenital schistosomiasis is endemic, may facilitate the processes of planning interventions.<sup>1</sup> Stool sampling and analyses are laborious and the faecal collection may be challenging as a result of age and cultural differences of the study participants.<sup>1</sup> Despite the fact that the investigated helminth infections have different transmission patterns and require different treatment interventions, this study shows that simple urine analyses, or possibly even water contact information, may indicate which persons and rural schools need intervention for both urogenital schistosomiasis and soil-transmitted helminthiasis. However, because of the focal nature of schistosomiasis transmission, ultimately, both stool and urine prevalence surveys should be done countrywide with a view of mapping disease distribution.

## Acknowledgements

We warmly thank the schoolgirls who participated in this study and their carers. We are grateful for the help from the BRIGHT clinical staff for sample collection and laboratory work – this study could not have been done without their hard work and effort. We thank R.F. Manyaira for able assistance, S.D. Holmen for SPSS support and P.D. Ndhlovu, H.N. Galappaththi-Arachchige and I. Lindstroem for valuable feedback. We also thank the Norwegian Centre for Imported and Tropical Diseases, Oslo University Hospital Ullevaal (VIRUUS), Shipowner Tom Wilhelmsen Foundation, S.G. Sønneland Foundation and General Travel Scholarships for funding. The funders had no role in data collection, study design and analysis, decision to publish, or preparation of the manuscript.

## Authors' contributions

M.M. and E.H. worked on the original report, analysed the data and conceptualised the paper together with E.F.K. and B.J.V.; S.G.Z. and E.F.K. contributed to data collection. All authors contributed to the editing of the manuscript.

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