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Shrinking risk profiles after deworming of children in Port Elizabeth, South Africa, with special reference to *Ascaris lumbricoides* and *Trichuris trichiura*

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Abstract

Risk maps facilitate discussion among different stakeholders and provide a tool for spatial targeting of health interventions. We present maps documenting shrinking risk profiles after deworming with respect to soil-transmitted helminthiasis among schoolchildren from disadvantaged neighbourhoods in Port Elizabeth, South Africa. Children were examined for soil-transmitted helminth infections using duplicate Kato-Katz thick smears in March 2015, October 2015 and May 2016, and subsequently treated with albendazole after each survey. The mean infection intensities for *Ascaris lumbricoides* were 9,554 eggs per gram of stool (EPG) in March 2015, 4,317 EPG in October 2015 and 1,684 EPG in March 2016. The corresponding figures for *Trichuris trichiura* were 664 EPG, 331 EPG and 87 EPG. Repeated deworming shrank the risk of soil-transmitted helminthiasis, but should be complemented by other public health measures.

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Introduction

Soil-transmitted helminths (STH), such as *Ascaris lumbricoides*, hookworm and *Trichuris trichiura* are among the most common parasite infections in humans (Bethony *et al.*, 2006). Indeed, more than 4 billion people are at risk of infection globally and more than a billion are infected (Pullan *et al.*, 2014). STH infections are most prevalent in poor communities in low- and middle-income countries, where these parasitic worms are of direct public health relevance because of their negative impact on children's health and development. The highest prevalence and intensity of STH infections are typically observed in school-aged children (Woolhouse, 1998). However, hookworm infection might peak in older age groups (Bethony *et al.*, 2006). Morbidity due to STH infections can be prevented through periodic administration of anthelminthic drugs – a strategy known as *preventive chemotherapy* (WHO, 2006). School-aged children, and increasingly also preschool-aged children and women of reproductive age, are the key target groups for preventive chemotherapy. The school platform has been shown to be a cost-effective approach for regular deworming, as it offers a readily available, extensive and sustained infrastructure with a skilled workforce that is in close contact with the target age group, the community and authorities alike (Lo *et al.*, 2015).

South Africa has a moderate burden of soil-transmitted helminthiasis (Karagiannis-Voules *et al.*, 2015). Yet, there is a paucity of quality data on the risk of STH infections in school-aged children. At the national level, there is a concentration of data coming from Western Cape province, *i.e.* around Cape Town, and the KwaZulu-Natal province, *i.e.* around Durban (GAHI, 2017), whilst there is a lack of data from the southern part of Eastern Cape, *i.e.* around Port Elizabeth. Precise estimates of the number of people with STH infections are important as they are needed to guide treatment campaigns (Scholte *et al.*, 2013). Of particular utility in this regard are spatially explicit risk maps that facilitate targeted interventions. Indeed, the development and use of risk maps is being recommended by the World Health Organization (WHO) to support planning and implementation of preventive chemotherapy (WHO, 2006). Risk maps must, however, be updated over time to reflect changing risk profiles resulting from treatment interventions and other public health measures, such as water, sanitation and hygiene (WASH) approaches and information, education and communication (IEC).

Methods

The Disease, Activity and Schoolchildren's Health (DASH) study is focusing on schoolchildren from deprived neighbourhoods in Port Elizabeth (geographical coordinates: 34°07′54″ to 33°57′29″ S latitude and 25°36′00″ to 25°55′49″ E longitude) in South Africa (Gall *et al.*, 2017; Müller *et al.*, 2016; Yap *et al.*, 2015). Within the frame of this 3-year investigation, a longitudinal study was implemented to document spatial and temporal changes in the distribution of STH infections as a result of repeated anthelminthic treatment among schoolchildren from Port Elizabeth.

A baseline cross-sectional survey carried out in March 2015 constituted the time point 1 data assessment (T1), a mid-line survey seven months later in October 2015 was designated T2 and an end-line survey after another seven months in May 2016 marked point T3 (Müller *et al.*, 2016; Yap *et al.*, 2015). Grade-4 schoolchildren aged 9-12 years from eight Quintile-3 schools were included in the study. Note that South African schools are divided into Quintiles reflecting the socioeconomic status of the community in which the school is located (Quintile-1 schools are the poorest and Quintile-5 schools are the least underprivileged). Preparation of the study, including identification of schools, commenced in September 2014. Eight schools were selected based on: i) sufficiently large Grade-4 classes (n>100 children); ii) geographical location (accessibility); iii) representation of the various target communities; and iv) commitment to support the project activities over the duration of the 14-month study. The study population consisted of coloured children, *i.e.* of mixed-race ancestry (generally Afrikaans-speaking) and black Africans children (largely Xhosa-speaking). The schools are situated in areas colloquially known as the *northern areas* (for coloured people: four schools) and townships (for black African people: four schools). These areas are considered to be adversely affected by high unemployment rates and low levels of educational attainment and socioeconomic status as well as criminality.

We informed school principals, teaching staff, schoolchildren and their parents/guardians about the purpose, procedures and potential risks and benefits of the study. Purposes of the documentation and risk maps were: i) to visualise the spatial and temporal changes in the STH infection risk profile patterns among school-aged children between March 2015 and May 2016 in the light of three rounds of deworming; ii) to facilitate access to this information for a broad range of stakeholders (staff of the project schools, parents/guardians, epidemiologists and health specialists) in Port Elizabeth, as well as public health policy makers and the Departments of Health and Education in South Africa.

Written informed consent was obtained from the parents/guardians. Assenting children were provided with uniquely identifiable empty stool containers and invited to return them the next day filled with a fresh morning stool specimen. Duplicate 41.7 mg Kato-Katz thick smears were prepared on glass slides from each stool sample (Yap *et al.*, 2012) and subsequently independently examined by experienced microscopists. We multiplied species-specific helminth egg counts by 24 to obtain an approximation of the infection intensity that was expressed in eggs per gram of stool (EPG) (Leuenberger *et al.*, 2016). At the end of each of the three cross-sectional surveys, a single 400 mg oral dose of albendazole (INRESA; Bartenheim, France) was administered to children tested positive for STH. All children were treated regardless of infection status in schools where the infection prevalence was equal to or larger than 50%, according to national and international treatment guidelines (WHO, 2006). Ingestion of albendazole was monitored by health staff and children remained under medical supervision for 24 hours.

Data were double-entered and cross-checked using EpiData version 3.1 (EpiData Association; Odense, Denmark). Children with complete data records, *i.e.* duplicate Kato-Katz thick smears at each of the three cross-sectional surveys were included in the final analysis. Spatially explicit risk maps were created using ArcGIS version 10.2.1 (ESRI; Redlands, CA, USA). Statistical analysis [χ^2-tests, average calculations, computations of minima and maxima as well as standard deviations (SD)] was done using STATA version 13.0 (STATA Corp.; College Station, TX, USA). For a simple interpolation of georeferenced data (obtained from coordinates of the children's homes), the inverse distance weighting (IDW) method was employed to obtain smoothed values of infection intensity. The IDW is based on the assumption that two geographically close sites are more similar than two locations further apart. It should be noted that IDW is a univariate approach, and hence does not consider individual and environmental risk factors. Further applied software packages were: Microsoft Power Point 2013 (Microsoft Corporation; Redmond, WA, USA); and Camtasia Studio 9 (TechSmith Corporation; Okemos, MI, USA).

Results

Complete data records were available for 638 children in the eight surveyed schools. Interestingly, no hookworm infections were found. Infections with *A. lumbricoides* and *T. trichiura* showed spatial clustering. At the baseline cross-sectional survey in March 2015, the prevalence of *T. trichiura* and *A. lumbricoides* at school A in Helenvale was 65% and 72%, respectively, while in school B in Hillcrest, the corresponding prevalence values were 65% and 60%. Compared to the other six schools, these prevalence levels were significantly higher, both for *T. trichiura* [χ^2=592.5, degree of freedom (df)=7, P<0.001] and *A. lumbricoides* (χ^2=475.3, df=7, P<0.001). Similarly, infection intensities were highest in schools A and B (red area in Figure 1) both for *T. trichiura* (χ^2=185.4, df=7, P<0.001) and *A. lumbricoides* (χ^2=166.7, df=7, P<0.001). At the mid-line (October 2015) and end-line surveys (May 2016), the reduction of infection intensity for both types of STH was significant as shown by the considerably larger green area in Figure 1, both for *T. trichiura* ($F_{(7,631)}$=94.6, P<0.001) and *A. lumbricoides* ($F_{(7, 631)}$=92.2, P<0.001).

At baseline, we recorded a mean *A. lumbricoides* infection intensity among infected schoolchildren of 9,554 EPG (SD=26,245 EPG) (Table 1). Seven months after a first round of deworming, the mean infection intensity of *A. lumbricoides* was more than halved to 4,317 EPG (SD=15,665 EPG). Another seven months later, at the end-line survey in May 2016, the mean infec-

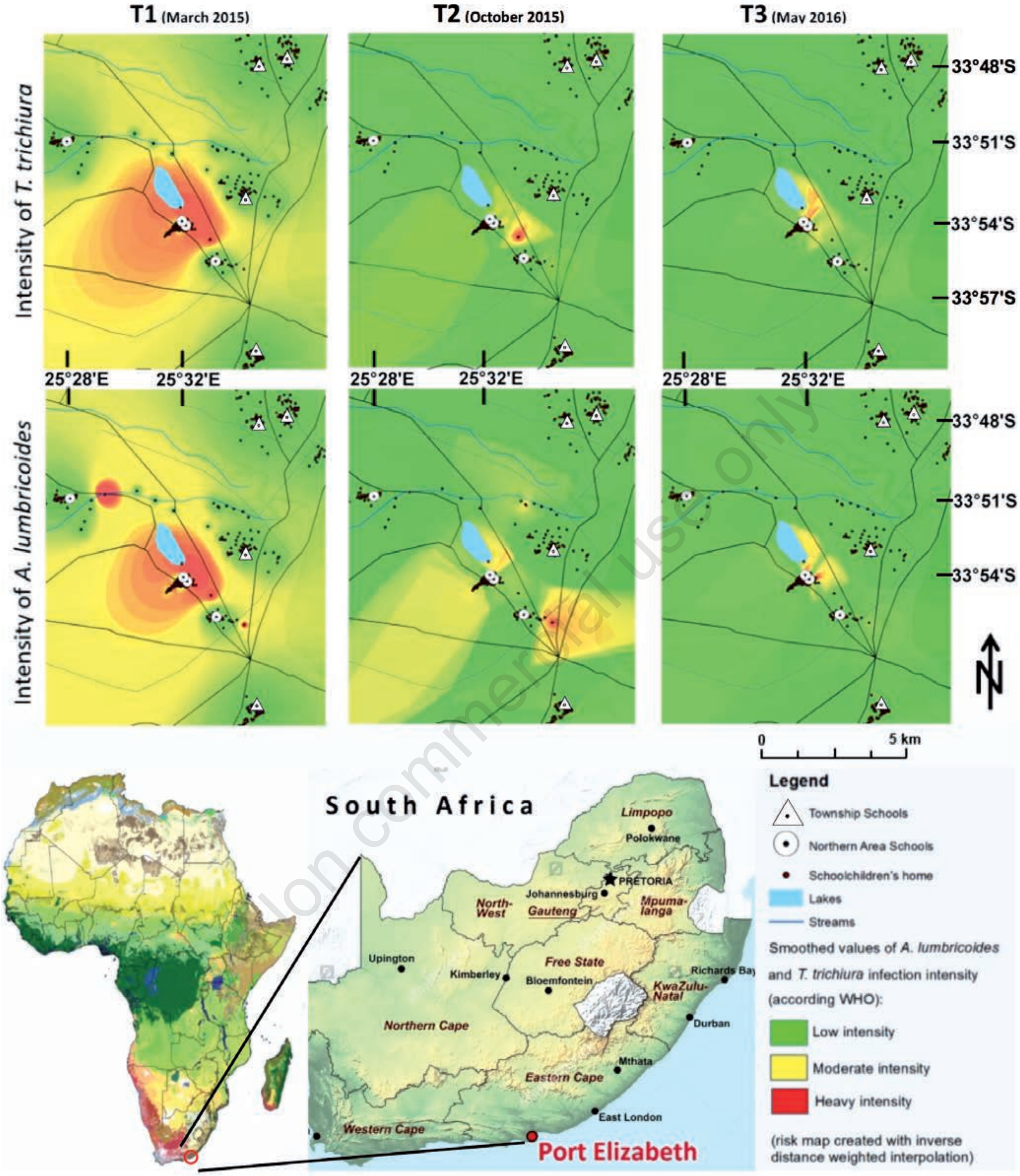

Figure 1. ***Ascaris lumbricoides*** **and** ***Trichuris trichiura*** **infection intensities, stratified according to World Health Organization guidelines. The study was carried out in the northern part of Port Elizabeth, South Africa, between March 2015 and May 2016. Smoothed maps based on 638 geographical coordinates of schoolchildren's homes are given. Low intensity of infection:** ***A. lumbricoides*****, 1-4,999 eggs per gram of stool (EPG);** ***T. trichiura*****, 1-999 EPG; Moderate intensity of infection:** ***A. lumbricoides*****, 5,000-49,999 EPG;** ***T. trichiura*****, 1,000-9,999 EPG; High intensity of infection:** ***A. lumbricoides*****, ≥50,000 EPG;** ***T. trichiura*****, ≥10,000 EPG.**

Table 1. Change of infection intensities of *Ascaris lumbricoides* and *Trichuris trichiura* among 638 schoolchildren from disadvantaged communities in Port Elizabeth, South Africa over the 14-month study period.

Intensity of infection		Observations (n)	Mean°	IQR	Minimum	Maximum
A. lumbricoides	EPG T1	638	9,554	324	0	217,608
	EPG T2	638	4,317	0	0	118,728
	EPG T3	638	1,684	0	0	100,956
T. trichiura	EPG T1	638	664	0	0	33,900
	EPG T2	638	331	0	0	17,892
	EPG T3	638	87	0	0	6,108

EPG, eggs per gram of stool; IQR, interquartile range (difference between 75th and 25th percentiles). °Calculated among infected children only.

tion intensity was further reduced to 1,684 EPG (SD=8,082 EPG). With regard to *T. trichiura* infections, the mean infection intensities among infected schoolchildren were 664 EPG (SD=2,787 EPG) at baseline, halved to 331 EPG (SD=1,457 EPG) at mid-line and reduced to 87 EPG (SD=382 EPG) at the end. The highest *A. lumbricoides* egg count was 217,608 EPG, while the highest *T. trichiura* egg count was 33,900 EPG, both observed during the baseline cross-sectional survey.

Outlook

Specific public health interventions are warranted in our study area given the high prevalence and intensity of two of the three STH species, *i.e. A. lumbricoides* and *T. trichiura*, observed during a baseline cross-sectional survey among children in two out of eight schools located in poor neighbourhoods. Discussions with local health and education authorities revealed that preventive chemotherapy (with either albendazole or mebendazole) against STH has been neglected in recent years. Our data confirm that multiple rounds of deworming targeting school-aged children are an effective approach to reduce infection intensity. Following national and international guidelines, we recommend the following treatment strategies: i) individual testing and treatment of infected children are indicated if the STH prevalence is below 20% (seen in five of the schools); ii) annual deworming if the prevalence ranges between 20% and 50% (seen in one school); and iii) biannual treatment of all children if the prevalence exceeds 50% (seen in two schools). The high spatial heterogeneity suggests that data from additional schools in different neighbourhoods will be needed to determine a locally appropriate intervention strategy, which ideally should not only be carried out by the school community but cover the entire local population at risk. Lastly, such activities should be complemented by efforts to strengthen hygiene awareness and to improve related behaviour such as hand washing with soap along with improved water and sanitation infrastructure – collectively known as WASH interventions – in schools and households alike (Strunz *et al.*, 2014).

Conclusions

Our findings should be interpreted in the light of several limitations. First, only a single stool sample was collected before each round of deworming, and subjected to duplicate Kato-Katz thick smear testing. Hence, some STH infections, particularly those of light intensity, were missed (Steinmann *et al.*, 2008). It follows that the *true* infection prevalence is likely to be even higher than reported in our study. Second, we focussed only on Grade-4 children attending disadvantaged Quintile-3 schools. Generalisability of our findings to a broader population is thus not possible. Third, we employed an IDW method for risk mapping. This univariate approach has shortcomings, as it does not consider individual and environmental risk factors. Hence, a Bayesian-based geostatistical approach should be considered, ideally using zero-inflated models to account for the excess number of children without STH infections in six of the eight surveyed schools (Vounatsou *et al.*, 2009). Fourth, the current risk maps do not deal with the uncertainty in the estimates including variation in risk due to child-specific traits (*e.g.* behavioural and genetic characteristics), as described, for example, by Diggle *et al.* (2007). Finally, the reduction in STH infection intensities cannot be attributed solely to deworming interventions, since the complex temporal interaction between host and parasite can only be displayed to a limited extent in the mathematical model presented here.

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