Published in final edited form as:
*Trans R Soc Trop Med Hyg*. 2011 February ; 105(2): 68–73. doi:10.1016/j.trstmh.2010.11.003.

# Moderate and high endemicity of schistosomiasis is a predictor of the endemicity of soil-transmitted helminthiasis - Systematic review

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## Abstract

The authors conducted a systematic literature review with the following aims: (i) to investigate how frequently soil-transmitted helminthiasis (STH) infections are endemic where schistosomiasis is present; and (ii) to assess the correlation between the risk level of schistosomiasis and that of STH. Among 155 sites on which data were collected and analyzed, schistosomiasis was present in 130 sites, all of which were also co-endemic for STH, whereas 25 sites were endemic only for STH. Out of 83 sites where at least one biannual round of preventive chemotherapy (PC) for schistosomiasis is recommended, 94% were also eligible for at least a yearly round of PC against STH. And among 21 sites where PC for schistosomiasis is recommended once a year, 81% were also eligible for at least a yearly round of PC for STH. This fact provides managers of control programmes with the operationally important indication that use of available information on endemicity of schistosomiasis is a valid tool to predict the presence of STH in the same geographical area as well as to estimate the need of PC for STH. The implementation of this tool is expected to save financial and human resources and help accelerate the scale-up of PC throughout the world.

### Keywords

Soil transmitted helminthiasis; schistosomiasis; co-endemicity; preventive chemotherapy

## 1 Introduction

Schistosomiasis (infection with *Schistosoma haematobium*, *S. intercalatum, S. japonicum*, *S. mansoni*, *S. mekongi*) and soil-transmitted helminthiasis (STH) (caused by *Ascaris lumbricoides*, *Trichuris trichiura* and hookworms) are among the most prevalent neglected tropical diseases (NTDs) caused by helminths, and affect a significant proportion of the global human population, especially in developing countries1. But they are also among the "tool-ready" diseases for which safe and effective single-dose medicines are available.1

**Authors' contributions:** AY and AM conceived and designed the study and conducted the data extraction and analysis; AY prepared the draft that was critically reviewed and finalized by AM, AG and DE. AY is the guarantor of the paper.

**Conflicts of interest:** None declared.

**Ethical Approval:** Not required.


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Preventive chemotherapy (PC), which is the population-based distribution of anthelminthic drugs at regular intervals, is the World Health Organization (WHO)-recommended strategy for both diseases and represents an effective tool for public health control of their associated morbidity.2 In May 2001, the World Health Assembly passed Resolution 54.19, which urged endemic countries to regularly treat at least 75% of school-age children at-risk of morbidity due to schistosomiasis and STH.3 Since then, coverage of PC has gradually expanded.4,5 However, significant gaps in access to treatment are still existent.4,5 Such gaps find their principal cause in the limited availability of resources for the implementation of disease control interventions.

Another factor limiting expansion of PC is the lack of information on the geographical distribution of the target diseases. Geographical overlapping among different helminth infections is however frequent6: in such situations, integrated implementation of PC for the simultaneous control of morbidity and reduction of transmission of two or more of the four diseases eligible for PC (in addition to schistosomiasis and STH, also lymphatic filariasis and onchocerciasis) using the same drug distribution channels is recommended as the most cost-effective approach.7

STH is most prevalent in humid, tropical and sub-tropical regions of the developing countries where adequate sanitation is lacking and the soil is sufficiently moist to allow survival of worm eggs or larvae,8 thereby allowing humans to come in contact with them either through soil or contaminated food. The distribution pattern of schistosomiasis, on the other hand, is determined not only by the lack of adequate sanitation but also by the presence of freshwater bodies near human settlements and of an adequate climate suitable for survival of intermediate host (snails) so that the biological cycle of the infection can be completed, and cercariae can develop and come in contact with human skin.

Based on the above considerations, we can conclude that the environmental characteristics of the areas where schistosomiasis is transmitted also allow transmission of STH; the opposite is not true, as schistosomiasis requires the additional conditions mentioned before. We can therefore assume that the occurrence of schistosomiasis in a given area might suggest a high possibility of the presence of STH in the same area.

This consideration might be of no practical use should detailed information on distribution of both infections be available. However, this is not the case. While a relatively good amount of current or historical data exists on the distribution of schistosomiasis, as exemplified, for example, by the Atlas of Global Distribution of Schistosomiasis,9 information on global distribution of STH remains poorly defined.8

This raises one question: can occurrence of schistosomiasis be used as a proxy for occurrence of STH? To answer this question, we need to assess how common endemicity of STH is where schistosomiasis is also present. The present study was conducted with the aim to provide indication to managers of control programmes on the possibility of using the existing data on distribution of schistosomiasis as a predictor for estimating the need of PC for STH. Should this hypothesis be confirmed, the result would be a substantial saving in time and resources for design and implementation of PC interventions.

## 2 Methods

### Systematic literature search

A systematic literature search was carried out with the aim to identify all relevant publications reporting on the simultaneous collection of data on prevalence of schistosomiasis and STH. The search engines used were PubMed and the Cochrane Controlled Trials Register. The combination of the following keywords: "schistosomiasis" and ("helminth" or "hookworm" or "ascaris" or "trichuris") and "prevalence", was used in order to identify the articles that investigated the occurrence of the two diseases in a given area. As our primary aim was to see how common the co-endemicity of schistosomiasis and STH is at subnational level throughout the world, we only included articles that reported data by first-level or second-level administrative units (province and districts, respectively), and excluded those that reported only national prevalence figures. For the same reason, those reporting data collected among hospital patients and nomadic communities were also excluded as the prevalence in such a sample is unlikely to be representative for a specific geographical location. In principle, we included only publications reporting pre-treatment data, either presented as a result of a baseline survey or in the form of “baseline data” in the context of an evaluation survey. The temporal limit of 1990 to present (February 2009) was set. In case more than two articles reporting on the same administrative unit were identified, we selected those with the most recent data, with the largest study population size, or those most likely to represent the local population (for instance, those sampling the entire village population rather than pregnant women only). The number of sites where co-endemicity of the two diseases was reported was then counted.

### Statistical analysis

From all the articles obtained through the systematic literature search, we extracted those which reported numerical values of prevalence of both schistosomiasis and STH, and entered the relevant data into Microsoft Excel. The raw, extracted dataset thus included prevalence data of schistosomiasis and STH among different target groups in different locations: in case more than a single *Schistosoma* species was present in a specific site, the highest species-specific prevalence value was taken as the representative of overall schistosomiasis prevalence, while in case only individual prevalence of STH species was available, cumulative prevalence of STH infections (i.e. prevalence of infection with any one of the STH) was calculated for each site, based on the assumption that the probability of infection with one species was independent of infection with another species, according to de Silva and Hall.10 The equation used was as follows:

$$P_{ath}=a+t+h-(a\times t+a\times h+t\times h)+a\times t\times h$$

Where:

$P_{ath}$ = the combined proportion infected with *Ascaris*, *Trichuris* and hookworms (cumulative prevalence of infection)

$a$ = proportion infected with *Ascaris*;

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$t$ = proportion infected with *Trichuris*;

$h$ = proportion infected with hookworms.

The WHO7 classifies communities according to risk of schistosomiasis based on the following prevalence thresholds (as detected by parasitological surveys): a high-risk community where prevalence of infection is equal to or over 50%; a moderate-risk community where prevalence is equal to or over 10% but below 50%; and a low-risk community where prevalence is below 10%. Equally, communities are classified for STH risk as follows: a high-risk community where prevalence of any STH is equal to or above 50%, a low-risk community where the prevalence is equal to or above 20% and below 50%, and a very-low risk community where prevalence is below 20% According to the risk level, a different frequency of treatment is recommended for each community (Table 1). In reference to the said threshold prevalences, risk levels for schistosomiasis and STH were determined for each element of the dataset (i.e. each site), and the whole dataset was divided into 4 groups: high-, moderate-, low- and no-risk (i.e. where no cases of schistosomiasis were reported) according to prevalence of schistosomiasis. The first three groups were further divided into high-, low-, and very low/no-risk according to prevalence of STH. The Spearman rank correlation was then calculated to assess the correlation between the risk level of schistosomiasis (high-, moderate-, and low-risk) and that of STH (high-, low-risk, and very-low/no risk). The statistical analysis was conducted using STATA version 11 (Statacorp, TX). The statistical significance of 5% was applied where appropriate.

## 3 Results

### Systematic literature review

Figure 1 shows the decision tree adopted by the systematic literature search. The search identified 179 articles that met all the inclusion criteria, i.e. to have investigated and reported on the co-endemicity of schistosomiasis and STH in the same province or district. After exclusion of overlapping data from the same administrative units, prevalence data were available from 156 sites, of which 155 presented numerical values of disease prevalence and were therefore included in the review, while the one that presented non-numerical values, was excluded. The exhaustive list of all the sites is shown in Supplemental Table 1. Articles included in the review reported data from 14 countries in the African region, 3 in the Eastern Mediterranean Region, 4 in the Western Pacific Region, 1 in the Americas Region and 1 in the European Region, according to the WHO regional classification. Figure 2 presents the schematic diagram of endemicity and co-endemicity of schistosomiasis and STH. Out of 155 sites for which prevalence figures were available for either or both diseases, 130 sites were endemic for schistosomiasis, all of which were also co-endemic for STH. There was no site where schistosomiasis was present but STH were not, while 25 sites were endemic only for STH.

### Association between the risk level of schistosomiasis and STH

Table 2 summarizes the association between the eligibility for PC interventions against schistosomiasis and STH based on the prevalence of each disease in all the sites included in

the systematic review. Out of 130 sites eligible for PC against schistosomiasis, 117 (90%) were also eligible for PC against STH. Among 83 sites where at least one biannual round of PC against schistosomiasis is recommended, 78 (94%) were eligible for at least a yearly round of PC against STH. Similarly, 17 sites out of 21 that are eligible for a yearly round of PC against schistosomiasis (81%) were also eligible for at least a yearly round against STH infection. The Spearman rank correlation showed that the risk levels of schistosomiasis were correlated with those of STH ($P$=0.045).

## 4 Discussion

Prior to implementation of PC interventions against helminth infections, an initial assessment is required to identify communities at which the interventions need to be targeted, as well as the appropriate frequency of treatment. Where data are lacking, the most common approach is to conduct epidemiological surveys. Considering that the 'gold' standard for community diagnosis of schistosomiasis and STH is light microscopy of stool and urine samples to detect eggs11, these surveys are costly to carry out as they require significant logistics and manpower; besides, technical personnel as well as equipment supplies are often not readily available in developing countries12; in addition, the need to carry out surveys is often responsible for delays in the implementation of disease control interventions. Therefore, rapid and low-cost mapping methods to identify communities that require treatment are clearly beneficial.13

The distribution of STH is assumed to be geographically more homogeneous than that of other NTDs.14,15 Consequently, the rapid assessment approach recommended by the WHO for STH is to divide the entire national territory of a country in ecologically homogenous areas, to choose 5 to 10 schools (according to size) in each area where prevalence of STH is suspected, and then to conduct stool examination on 50 children from each of the selected schools for STH eggs using the Kato-Katz thick smear method.7 The geographical distribution of schistosomiasis, on the other hand, is rather focal. Its transmission is commonly found near freshwater bodies such as lakes, ponds, streams and irrigation canals where infected people and snails come together.16 Accordingly, for identification of transmission sites, a more focal screening of communities near freshwater bodies is needed. While, as mentioned, stool examination for eggs is the recommended tool in the case of intestinal schistosomiasis, questionnaire screening for visible haematuria, urine dipsticks for microhaematuria or the urine filtration method for eggs is the recommended investigation tools for urinary schistosomiasis.7 In whichever cases, review of available data, including historical reports and publications, as well as consultation with local health service staff usually provides important information for identification of communities and areas at risk.

The present study shows the high chance of co-endemicity for schistosomiasis and STH in areas where schistosomiasis is prevalent, and in particular, that 90% of the areas eligible for PC against schistosomiasis are also eligible for PC against STH. Besides, we demonstrate that 94% of the areas where at least a biannual round of PC is recommended against schistosomiasis are also eligible for at least a yearly round of PC against STH, and 81% of the areas where a yearly round of PC against schistosomiasis is recommended are also eligible for at least the same frequency of PC against STH. These facts allow concluding that

where interventions distributing praziquantel for the control of schistosomiasis are implemented, albendazole or mebendazole for the control of STH should constantly be associated. This concept was further confirmed by the statistically significant correlation between the risk levels of schistosomiasis and those of STH.

The use of schistosomiasis data to predict the need for control of STH has important operational implications in planning and implementation of PC interventions because it would allow avoiding the implementation of parasitological surveys for STH and consequently, accelerate the implementation and the scaling-up of PC.

Commitments have been increasingly made by a number of pharmaceutical companies to continuous donations of drugs for lymphatic filariasis, onchocerciasis, trachoma and fascioliasis.17,18 However, drug donation for STH is currently limited to that of mebendazole by Johnson & Johnson7,19. Praziquantel for schistosomiasis control is also donated in limited quantities by Merck19. Co-administration of praziquantel for schistosomiasis and albendazole (or mebendazole) for STH is safe and recommended by WHO.21,22,23,24 As such, in terms of policy, inclusion of either albendazole or mebendazole in large-scale interventions delivering praziquantel based on the review of existing schistosomiasis data rather than on a new detailed parasitological survey for STH is, in our opinion, justified.

The limitations of our study include several potential sources of false negative data. First of all, scientists are likely to investigate both diseases only when their co-endemicity is expected. In sites where this is not the case, only the expected disease would be investigated and reported. This could underestimate the proportion of sites where STH and schistosomiasis are co-endemic yet, in our opinion, will not affect the validity of our key finding that the presence of schistosomiasis can be used as a predictor of the presence of STH. Besides, the chances of exclusion of the sites where only STH is investigated and the sites where only schistosomiasis is investigated are presumed to be more or less equal. Secondly, when both diseases are investigated and only one disease is found to be endemic, there might be chances that only the endemic disease is reported. Such cases, which would lead to overestimate the number of mono-endemic sites of either STH or schistosomiasis, are however believed to be only few since these findings would conflict with the initial expectation of the investigators and thus even the absent disease would likely be reported. Thirdly, while we attempted to include only the publications that reported baseline data, some of them might have failed to report the past implementation of deworming and might therefore have been included in our review. In such cases, the prevalence of the diseases could significantly be reduced from the baseline level. Nonetheless, we believe that such exceptional cases are negligible. The authors are also aware of the possible presence of other environmental, biological and socioeconomic determinants for distribution of these infections, such as duration of annual dry period, vegetation, soil type25, presence of other host reservoirs26, acquired immunity level of the population,27 occupation and behaviours28. However, once again, we believe that - overall - our findings are valid and of significant importance for operational purposes.

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In conclusion, we consider the use of available information on endemicity of schistosomiasis as an indicator of the presence of STH in the same geographical area as a valid tool to accelerate the cost-effective scale-up of deworming programmes. This is also likely to save financial and human resources, which can be effectively utilized for further scale-up of the programme in other areas.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

We are indebted to all the investigators and the individuals who were involved in the studies included in the review. They eventually allowed us to generate the conclusions and the recommendations presented in this paper.

**Funding:** None declared.

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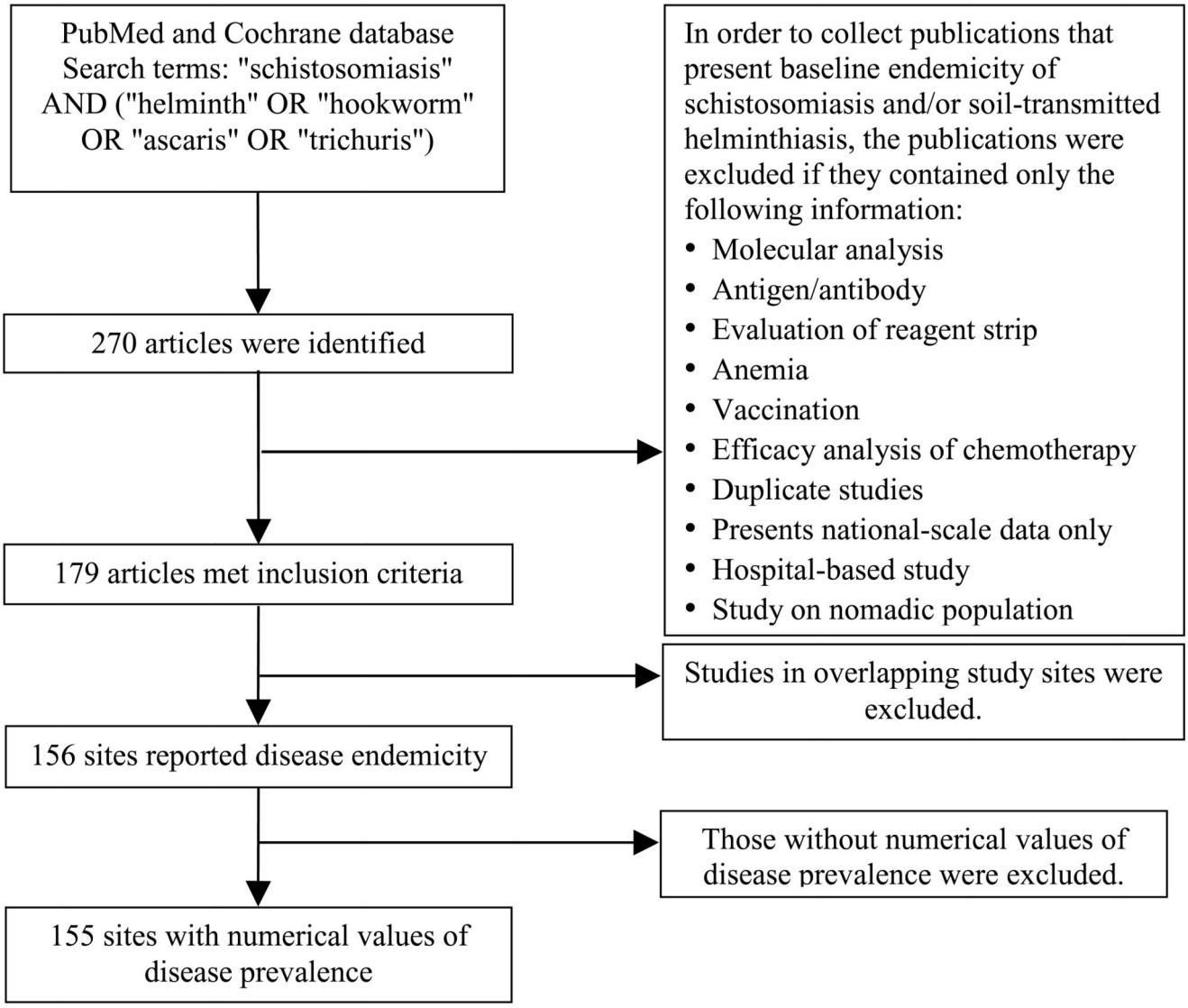


**Figure 1.**
Decision tree showing the inclusion and exclusion criteria of the studies on geographical co-endemicity of schistosomiasis and soil-transmitted helminth infection.

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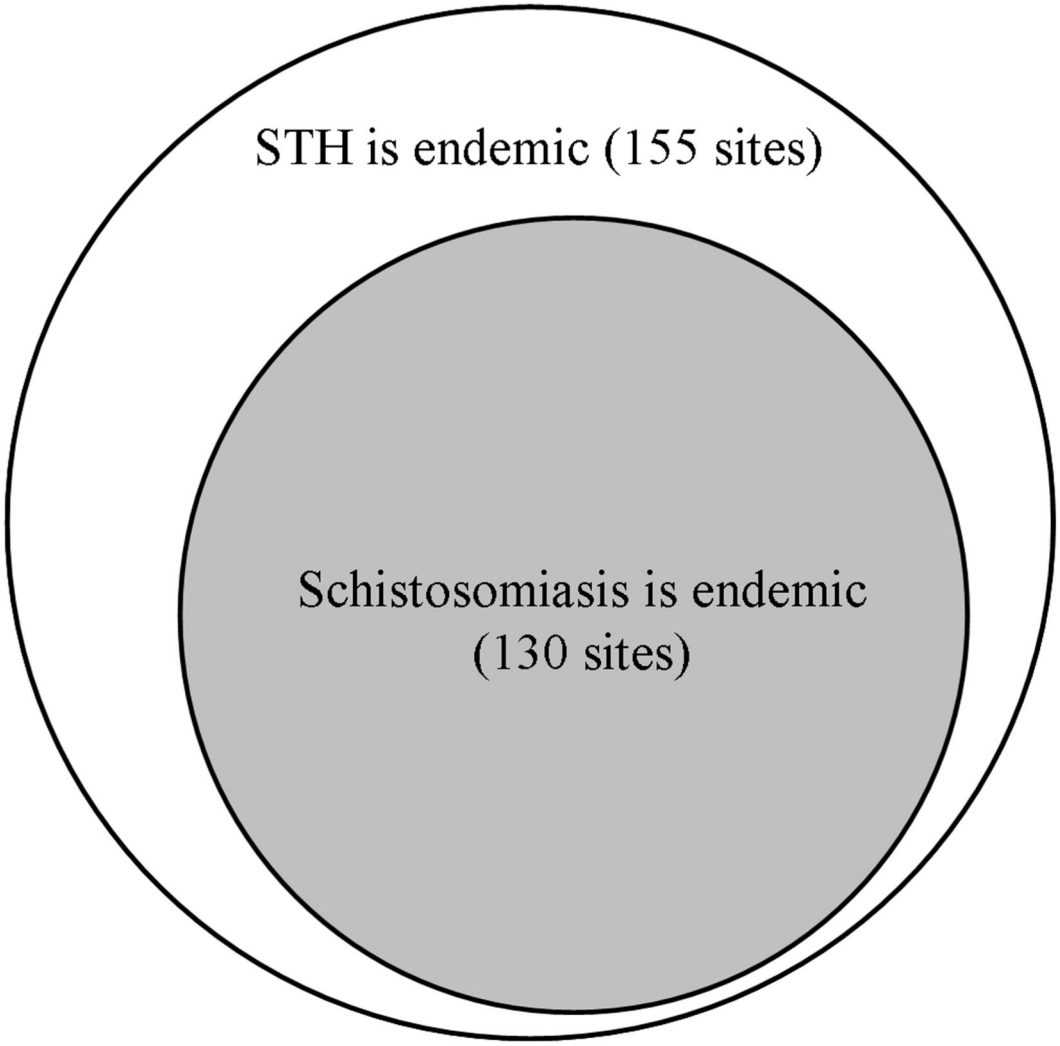


STH and schistosomiasis are co-endemic = 130 sites
Only STH is endemic = 25 sites
Only schistosomiasis is endemic = 0 sites

**Figure 2.**
Schematic diagram showing endemicity and co-endemicity of soil-transmitted helminthiasis (STH) and schistosomiasis among the 155 sites (i.e. datasets) collected through systematic review

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**Table 1**

Recommended treatment strategy for soil-transmitted helminthiasis and schistosomiasis in preventive chemotherapy (adapted from WHO6)

| Disease | Category | Prevalence of infection among school-aged children | Recommended intervention | | |
|---|---|---|---|---|---|
| | | | Type | Frequency | Target population |
| **Soil-transmitted helminthiasis** | High-risk community | ≥50% | PC | Twice each year | All school-aged children, preschool children, women of child-bearing age (including pregnant women in the 2nd and 3rd trimesters and lactating women, and adults at high risk in certain occupations (ex. tea pickers and miners) |
| | Low-risk community | ≥20% and <50% | | Once a year | |
| | Very low-risk | >0% and <20% | Affected individuals should be treated on a case-by-case basis | | |
| | No risk | 0% | None | | |
| **Schistosomiasis** | High-risk community | ≥50% [a] | PC | Once a year | All school-aged children, preschool children and adults at risk [*] |
| | Moderate-risk community | ≥10% and <50% [b] | | Once every 2 years | |
| | Low-risk community | >0% and <10% [c] | | Twice during their primary schooling age (ex. once on entry and once on exit) | All school-aged children |
| | No risk | 0% | None | | |

[a] By parasitological methods for intestinal and urinary schistosomiasis. Or ≥30% by questionnaire for visible heamaturia for urinary schistosomiasis.

[b] By parasitological methods for intestinal and urinary schistosomiasis. Or <30% by questionnaire for visible heamaturia for urinary schistosomiasis.

[c] By parasitological methods for intestinal and urinary schistosomiasis.

[*] Adults considered to be at risk are from special groups (pregnant and lactating women, people with occupation involving contact with infested water such as fishermen, farmers, irrigation workers, or women in their domestic tasks) to entire communities living in endemic areas.

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## Table 2

Association between the recommended preventive chemotherapy (PC) interventions for soil-transmitted helminthiasis (STH) and schistosomiasis among the 130 sites where numerical prevalence values for both diseases were available

| Recommended interventions for schistosomiasis | No. Sites (% of total) | | |
|---|---|---|---|
| | Total | PC for STH is recommended | |
| | | (i) At least once a year | (ii) Twice each year |
| **PC for schistosomiasis is recommended** | 130 | 117 (90%) | 72 (55%) |
| **(i) At least once every 2 years** | 83 | 78 (94%) | 53 (64%) |
| **(ii) Once a year** | 21 | 17 (81%) | 10 (48%) |