Global feasibility assessment of interrupting the transmission of soil-transmitted helminths: a statistical modelling study

Simon J Brooker, Birgit Nikolay, Dina Balabanova, Rachel L Pullan

Summary

Background Emphasis is being given to the control of neglected tropical diseases, including the possibility of interrupting the transmission of soil-transmitted helminths (STH). We evaluated the feasibility by country of achieving interruption of the transmission of STH.

Methods Based on a conceptual framework for the identification of the characteristics of a successful STH control programme, we assembled spatial data for a range of epidemiological, institutional, economic, and political factors. Using four different statistical methods, we developed a composite score of the feasibility of interrupting STH transmission and undertook a sensitivity analysis of the data and methods.

Findings The most important determining factors in the analysis were underlying intensity of STH transmission, current implementation of control programmes for neglected tropical diseases, and whether countries receive large-scale external funding and have strong health systems. The composite scores suggested that interrupting STH transmission is most feasible in countries in the Americas and parts of Asia (eg, Argentina [range of composite feasibility scores, depending on scoring method, 9·4–10·0], Brazil [8·7–9·7], Chile [8·84–10·0], and Thailand [9·1–10·0]; there was perfect agreement between the four methods), and least feasible in countries in sub-Saharan Africa (eg, Congo [0·4–2·7] and Guinea [2·0–5·6]; there was full agreement between methods), but there were important exceptions to these trends (eg, Ghana [7·4–10·0]; there was agreement between three methods). Agreement was highest between the scores derived with the expert opinion and principal component analysis weighting schemes (Pearson correlation coefficient, r=0·98). The largest disagreement was between benefit-of-the-doubt-derived and principal-component-analysis-derived weighting schemes (r=0·74).

Interpretation The interruption of STH transmission is feasible, especially in countries with low intensity of transmission, supportive household environments, strong health systems, and the availability of suitable delivery platforms and in-country funds, but to achieve local elimination of STH an intersectoral approach to STH control will be needed.

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Introduction

In the past decade, commitment has been increasing to the control and elimination of neglected tropical diseases, which affect more than 1 billion of the poorest people worldwide. In 2012, WHO identified a set of goals, which included the global elimination of lymphatic filariasis and blinding trachoma and the regional or country elimination of onchocerciasis and schistosomiasis by 2020. The goal for soil-transmitted helminths (STH; *Ascaris lumbricoides*, *Trichuris trichiura*, and hookworms) was defined as 75% coverage of mass chemotherapy for at-risk preschool (typically aged 2-4 years) and school-aged populations (typically aged 5–14 years) by 2020.[1] Recently, however, new emphasis has been given to the potential interruption of STH transmission, with experts questioning whether mass chemotherapy alone can interrupt transmission, and, if yes, what coverage and frequency of treatment is needed to reduce transmission to a level where parasites cannot persist.[2,3]

History shows that the interruption of STH transmission is possible. STH were highly prevalent in the southern states of the USA, Japan, South Korea, and Taiwan, but sustained control efforts led to elimination in these countries.[4–6] A key component of these programmes was mass chemotherapy or selective chemotherapy of infected schoolchildren identified during periodic mass screening campaigns, supported by legislative measures and strong intersectoral collaboration.[4,5] There were also concomitant improvements in socioeconomic status and access to water and sanitation, which undoubtedly contributed to the success of the programmes. These early experiences show that elimination of STH is feasible if specific technical, operational, and policy factors are addressed. Building on these successes and recent modelling results,[2,3] in 2014, a group of partners, including the Bill & Melinda Gates Foundation (USA) and the Children's Investment Fund Foundation (UK), pledged funding for developing new methods and strategies for interrupting STH transmission.[7] However, there are no clear, evidence-based criteria to help define where elimination of these helminths might be possible.

Evaluating the feasibility of disease elimination is not new. The International Task Force for Disease Eradication identified several criteria for assessing the potential for the global eradication or local elimination of infectious diseases, including the epidemiological factors reducing the transmission of the disease (eg, lack of an animal reservoir and restricted duration of infectiousness), availability of an effective, practical intervention, and demonstrated feasibility of elimination.[8] The Global Malaria Eradication Programme of the 1950–60s recommended that countries undertake an analysis of the technical, operational, and socioeconomic conditions before embarking on a malaria elimination programme;[9] more recently, a framework has been developed for the assessment of the technical and operational feasibility for malaria elimination.[10]

Here, we develop and use a framework for evaluating the feasibility of interrupting the transmission of STH and assemble spatial data for a range of distal and proximal determinants to provide an ordinal ranking of countries for the feasibility of achieving and maintaining interruption of STH transmission.

Methods

Conceptual framework

We first developed a conceptual framework, drawing on a range of existing health systems frameworks,[11,12] work on neglected tropical diseases and health systems,[13,14] and discussions with neglected tropical diseases control programme staff and policy makers. This framework (figure 1) was used to identify the factors associated with a successful STH control programme, including political and economic context, health and education systems, inputs and outputs of STH control programmes, and the underlying epidemiology of infection. We define the interruption of transmission (elimination) as the effective implementation of interventions leading to a sustained interruption of transmission in a defined geographical area, such that interventions can be stopped but actions to prevent recrudescence might be needed.

Our key study question is what determines the feasibility of interrupting transmission of STH? In addressing this question, we identified three main domains that affect this feasibility: STH epidemiology (made up of three components: intensity of transmission, household environment, and current control measures); capacity to deliver STH interventions (comprised of health systems, education systems, delivery platforms, and availability of external funding); and political and financial feasibility (logistics and infrastructure, governance, and economy; panel 1).

The underlying transmission potential of STH, as for other helminth species, is best measured with the basic reproductive number (R_0).[31] The size of R_0 determines prevalence and intensity of STH infection in a locality and is a key determinant of the success of intervention and the rate of reinfection after treatment. Reinfection rates are determined by the coverage and frequency of mass treatment and the efficacy of treatment. Therefore, if the intensity of transmission is high before large-scale control, then the coverage and frequency of mass treatment must also be high to interrupt transmission and vice versa. The results of mathematical modelling studies[2,3] show that in all but low transmission settings the treatment of school-aged children is unlikely to reduce transmission to a level where the parasites cannot persist and that additional treatment of adults and pre-schoolchildren is needed for mass treatment to reduce parasite populations to below a breakpoint under which transmission is interrupted. The underlying intensity of STH transmission is also affected by the levels of access to clean water and adequate sanitation and hygiene[32] and individual and sociocultural factors that affect the rate of exposure to STH infective stages.

The ability to achieve successful and sustained treatment is dependent on the capacity of national control programmes for neglected tropical diseases, specifically for STH. The effectiveness of such programmes and health systems as a whole[12] depends on long-term financing, clear policies, effective leadership and long-term vision, and functioning institutions. Equally important are the capabilities of the wider health and education systems to meet the technical requirements of a STH control programme. Mass treatment can be delivered through schools or communities, and as such, strong school systems and community health structures are necessary to support effective programmes. Also, it is important that populations have access to programmes and this depends on the accessibility of populations and ability of the health or education systems to promote access to and distribute drugs.

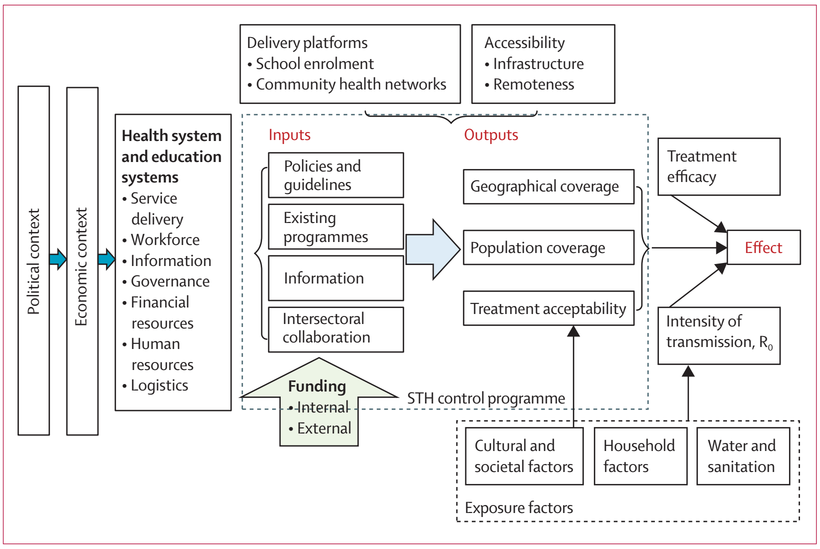

Figure 1: **Conceptual framework used to assess the feasibility of interrupting transmission of STH**
STH=soil-transmitted helminths.

Panel 1: Indicators of the feasibility of interrupting transmission of STH

STH epidemiology

We estimated STH transmission intensity using an approximation of the relation between prevalence and reproductive number (R_0)[3] as follows: 70% (high, R_0=4·0), 50% (medium, R_0=1·7), and 20% (low, R_0=1·1; appendix). To capture population-at-risk and within-country heterogeneity, two measures were compiled for each country: population-weighted mean prevalence and the proportion of the population exceeding the STH prevalence thresholds indicated above. Population-weighted prevalence estimates were based on work[15] that was previously used to define the global burden of STH.[16] The proportion of the population exceeding each threshold was generated by overlaying the subnational prevalence dataset on a gridded population density map for 2015.[17] We subsequently stratified countries into five categories of transmission based on a combination of both these components.

To estimate exposure rates we used country-level data on access to improved water and sanitation facilities and used maternal education as a proxy for hygiene-related behaviour and health knowledge. Estimates for the proportion of rural households with access to improved or unimproved sanitation and piped water were obtained from the WHO-UNICEF Joint Monitoring Programme for Water Supply and Sanitation.[18] Data for female educational achievement, expressed as the final grade of primary school, were obtained from the UNESCO Institute for Statistics.[19]

Capacity to deliver

Previous progress of STH treatment programmes provides a good indication of how successful programmes will be in the near future. The percentage of school-aged children needing and receiving treatment were abstracted from the WHO preventive chemotherapy and transmission control databank[20] for 2007–11 and countries were stratified by the constancy of achieving greater than 75% coverage.

The strength of health and educations systems in a country is integral to the successful implementation of an STH control programme. A well funded health system with good infrastructure suggests political commitment to health-care delivery and the goal of disease elimination. Data for per-person health expenditure (as a percentage of government spending) were obtained from the WHO National Health Account database[21] and the number of beds per 1000 population from the World Bank data bank.[22] Countries that have implemented successful community-based health programmes are most likely to deliver high and sustained coverage of STH treatment. We therefore included the percentage of pregnant women receiving qualified antenatal care at least once during their pregnancy from the World Bank data bank[23] and the percentage of patients with tuberculosis completing a full course of directly observed therapy from the WHO Global Health Observatory[24] because these are likely to represent the availability of community-based health personnel and essential care and require a sustained access to community health services by the population. Also, we included the mortality rate in children younger than 5 years as an indication of overall health system effectiveness.[25]

A similar approach was used to characterise education systems, including data for educational expenditure (as a percentage of government spending); ratio of primary school teachers to the number of pupils enrolled in primary school; primary school completion rate (total number of new entrants in the final grade of primary education as a percentage of the total population of theoretical entrance age to the final grade); and youth literacy rates (percentage of young people aged 15–24 years who can read and write a short simple statement).[19]

Three components were chosen to describe available delivery platforms, such as schools of community health systems. The effective delivery of school-based deworming depends on the school enrolment rate. As countries look to increase programmatic coverage to other age groups they might choose to use a community-wide delivery model. Data for immunisation coverage (the proportion of 1-year-old children given the third dose of diphtheria and tetanus toxoid with pertussis vaccine, the measles-containing vaccine, and the third dose of polio vaccine[26]) were used as a proxy indicator of the health system to deliver essential services to populations. As an indication of the ability to deliver large-scale community-based programmes, information about the existence and performance of lymphatic filariasis treatment programmes was extracted from WHO.[20]

To capture whether sufficient resources are available for the required lifetime of the STH control programme, we relied on stratifying countries as having a gross domestic product (GDP) of less than US$5000 per person but no external partner support, no external partner support but a GDP of more than $5000 per person, and external partner support (irrespective of GDP).

Operational and financial feasibility

Political commitment and good governance are essential for the well functioning of health systems,[12] including effective neglected tropical disease control programmes. To generate a general governance index, we compiled data from two sources, the World Bank worldwide governance indicators (government effectiveness and control of corruption),[27] and the fragile states index.[28] The performance of an STH control programme will also be affected by the country's capacity to sustain supply chains for treatment delivery. As indication of the country's logistical performance, we used the World Bank logistics performance index for 2014[29] (combining information about efficiency of customs and quality of transport infrastructure). Remoteness of at risk-populations will make the delivery of treatment more difficult; therefore, we used a global accessibility map.[30] We used GDP per person as an indicator of overall financial capacity that will affect the level of the public sector provision.

STH=soil-transmitted helminths.

See Online for appendix

		Epidemiology			Capacity to deliver				Political and financial			
	Country	Transmission intensity	Home environment	Current control	Health systems	Education systems	Delivery platforms	Funding partners	Logistics and infrastructure	Governance	Economy	Agreement
Most feasible (best scoring quintile)	Argentina	10·0	9·2	2·5	9·6	9·6	9·4	5·0	9·6	9·6	7·5	4
	Belize	10·0	7·5	7·5	6·3	9·7	8·2	0·0	1·1	9·2	2·8	4
	Brazil	10·0	9·5	2·5	9·5	7·8	6·6	5·0	9·6	9·5	7·3	4
	Cambodia	7·5	0·7	7·5	2·9	1·2	9·8	10·0	8·3	2·2	0·5	2b
	Chile	7·5	9·9	0·0	9·6	9·3	9·5	5·0	9·0	9·9	10·0	4
	China	5·0	9·7	2·5	9·7	9·7	9·8	5·0	9·6	7·9	3·9	2a
	Costa Rica	7·5	9·5	0·0	9·5	9·8	5·9	5·0	5·4	9·8	6·0	2a
	Dominican Republic	10·0	5·4	10·0	1·9	1·7	2·1	5·0	9·4	9·5	3·6	3
	Egypt	10·0	9·9	2·5	6·2	5·0	9·8	0·0	9·9	3·7	1·9	2a
	Ghana	10·0	1·6	7·5	8·4	9·7	2·0	10·0	6·7	9·2	0·9	3
	Indonesia	10·0	2·0	2·5	0·4	9·3	3·1	10·0	9·1	6·7	2·2	2a
	Lebanon	10·0	9·7	0·0	8·3	1·6	5·2	5·0	9·6	4·5	6·3	2a
	Malaysia	5·0	9·9	2·5	3·3	9·8	8·0	5·0	9·9	9·8	6·7	3
	Mexico	10·0	9·3	7·5	5·0	9·4	9·2	5·0	9·8	9·1	6·3	4
	Nicaragua	10·0	2·6	10·0	8·6	9·3	9·0	0·0	7·3	4·5	1·0	3
	Panama	10·0	8·9	2·5	9·6	7·3	7·7	5·0	8·7	9·5	6·1	3
	Peru	7·5	5·5	5·0	6·0	8·7	7·0	5·0	6·9	8·2	4·2	2b
	Thailand	10·0	9·2	2·5	9·5	9·8	9·8	5·0	9·3	8·9	3·5	4
	Tunisia	10·0	8·7	0·0	9·7	9·3	9·8	0·0	7·9	8·7	2·6	2b
	Turkey	10·0	9·6	0·0	9·8	9·4	9·6	5·0	9·9	9·2	6·9	4
	Uruguay	10·0	9·7	0·0	9·7	9·8	9·7	5·0	7·4	9·9	9·4	4
Feasible	Algeria	10·0	7·2	0·0	1·2	9·3	8·2	5·0	6·9	6·3	3·4	2b
	Armenia	10·0	9·7	0·0	9·0	8·0	6·1	0·0	7·7	8·6	2·0	3
	Azerbaijan	10·0	9·1	2·5	5·0	6·6	2·3	5·0	6·3	3·8	4·6	2b
	Colombia	5·0	7·3	2·5	8·4	9·6	3·9	5·0	5·6	7·6	5·0	2a
	Cuba	10·0	8·9	0·0	9·6	9·8	9·5	0·0	6·1	9·1	2·3	3
	Ecuador	5·0	7·4	5·0	0·5	9·6	9·8	5·0	7·6	6·2	3·4	4
	El Salvador	7·5	9·5	5·0	8·7	5·2	6·5	0·0	9·8	8·6	2·3	4
	Georgia	10·0	8·7	0·0	9·2	6·6	8·4	0·0	5·2	9·5	2·2	2b
	Iran	10·0	9·6	0·0	8·7	8·9	9·9	5·0	5·2	4·1	3·6	3
	Jordan	7·5	9·9	0·0	9·8	9·3	8·2	0·0	9·7	8·9	3·1	3
	Kazakhstan	5·0	9·9	0·0	9·5	9·5	8·7	5·0	5·2	7·7	7·8	4
	Kenya	10·0	2·5	2·5	2·2	1·7	1·7	10·0	6·6	1·8	0·4	2a
	Kyrgyzstan	5·0	9·5	7·5	9·7	9·8	6·3	0·0	0·9	3·2	0·6	2a
	Libya	10·0	7·7	0·0	9·5	9·3	8·9	5·0	7·8	0·1	5·0	2b
	Senegal	10·0	2·5	2·5	0·4	5·0	0·8	10·0	6·5	7·2	0·5	2a
	Suriname	10·0	9·4	0·0	3·3	8·0	5·4	5·0	5·8	9·1	5·7	2b
	Turkmenistan	10·0	8·3	0·0	9·4	9·5	8·2	5·0	0·6	1·1	4·1	2b
	Uzbekistan	10·0	9·5	5·0	9·5	8·7	9·2	0·0	7·5	1·4	1·0	3
	Venezuela	5·0	8·7	2·5	7·1	9·8	4·8	5·0	8·4	2·3	8·3	2b
	Vietnam	2·5	5·8	5·0	7·9	9·4	9·1	10·0	9·9	7·7	0·9	2b
Less feasible	Bhutan	10·0	8·8	0·0	8·0	2·1	5·9	0·0	0·3	9·6	1·4	2a
	Bolivia	10·0	6·8	2·5	0·3	9·4	3·6	0·0	2·0	5·8	1·5	2a
	Burma	5·0	1·5	10·0	1·3	6·3	9·0	5·0	1·5	0·2	3·8	3
	Guatemala	5·0	7·5	5·0	2·7	8·0	6·8	0·0	7·1	5·3	2·1	3
	Honduras	5·0	7·4	5·0	7·2	9·2	9·5	0·0	8·2	4·6	1·3	2b
	India	10·0	0·6	2·5	2·3	0·8	2·0	10·0	9·9	7·3	0·8	2b
	Iraq	10·0	8·5	0·0	7·5	5·4	2·9	5·0	2·5	0·6	4·1	2a
	Mongolia	10·0	3·6	0·0	9·4	8·9	9·6	0·0	0·6	8·9	2·3	4
	Morocco	10·0	6·6	0·0	3·6	9·7	8·8	0·0	6·0	8·3	1·8	2a
	Namibia	7·5	1·7	0·0	3·3	8·0	2·7	10·0	1·5	9·4	3·6	3
	Rwanda	5·0	0·2	7·5	9·3	3·3	9·3	10·0	6·4	8·5	0·2	2b
	South Africa	5·0	6·9	0·0	6·2	8·4	2·1	5·0	9·9	9·3	4·8	3
	Sri Lanka	10·0	9·8	2·5	9·1	6·5	9·5	0·0	8·4	5·9	1·8	2a
	Tajikistan	10·0	9·5	2·5	6·6	9·4	8·8	0·0	4·0	2·0	0·4	2b
	Tanzania	5·0	1·8	2·5	7·5	2·3	6·5	10·0	1·4	4·6	0·2	2a
	Zambia	5·0	1·0	2·5	9·5	1·7	6·2	10·0	1·7	6·6	0·8	2a
Unfeasible	Bangladesh	2·5	3·0	2·5	0·3	1·3	2·8	10·0	8·9	2·2	0·3	2a
	Benin	10·0	0·2	2·5	0·2	5·0	2·7	10·0	5·2	5·0	0·3	3
	Burkina Faso	10·0	0·2	7·5	1·3	0·2	5·8	0·0	4·3	4·7	0·3	3
	Burundi	5·0	1·9	7·5	3·7	8·2	6·1	10·0	5·7	0·0	0·0	2b
	Cameroon	5·0	2·7	5·0	0·8	1·1	1·4	10·0	1·6	0·8	0·6	3
	Côte d'Ivoire	7·5	2·5	5·0	0·2	5·4	0·0	10·0	6·4	1·0	0·7	3
	Equatorial Guinea	5·0	0·4	2·5	0·5	0·6	0·1	5·0	0·8	0·1	10·0	2b
	Ethiopia	10·0	0·4	2·5	5·0	2·4	0·2	10·0	1·7	3·1	0·1	4
	Gabon	5·0	3·3	0·0	7·1	0·6	0·4	5·0	0·7	6·7	7·4	2a
	Gambia	10·0	5·3	5·0	5·4	4·4	2·2	0·0	0·6	5·4	0·2	2b
	Haiti	7·5	1·6	5·0	1·5	5·7	0·5	10·0	4·6	0·0	0·3	3
	Laos	5·0	1·9	5·0	0·8	2·7	4·6	10·0	1·2	2·9	0·8	3
	Mali	10·0	1·6	7·5	0·2	0·2	0·2	10·0	2·9	2·7	0·3	4
	Nepal	5·0	0·4	2·5	8·0	9·5	0·9	10·0	4·0	2·3	0·3	4
	Nigeria	5·0	0·1	2·5	0·5	2·1	0·0	10·0	7·8	1·0	0·9	2a
	Papua New Guinea	0·0	3·5	2·5	8·9	5·4	1·5	10·0	0·5	3·3	1·3	2a
	Philippines	2·5	4·1	2·5	4·5	4·6	1·5	10·0	8·8	7·3	1·5	2b
	Togo	10·0	0·0	2·5	1·2	1·1	1·7	10·0	2·5	1·0	0·2	3
	Uganda	10·0	0·1	5·0	4·6	0·8	3·3	10·0	8·4	2·1	0·2	2b
	Yemen	7·5	1·6	2·5	0·5	1·8	0·8	10·0	0·1	0·2	0·8	2a
	Zimbabwe	5·0	1·6	0·0	1·6	0·3	5·7	10·0	2·3	0·1	0·4	3
Highly unfeasible (worst scoring quintile)	Afghanistan	5·0	1·3	5·0	0·1	1·2	1·2	0·0	0·2	0·0	0·2	4
	Chad	10·0	0·0	0·0	0·1	0·0	0·1	0·0	1·1	0·0	0·4	4
	Congo	5·0	2·5	0·0	0·2	0·1	6·0	0·0	0·2	1·0	1·9	4
	Djibouti	5·0	3·8	2·5	8·2	5·5	0·3	0·0	0·8	4·7	0·7	3
	Eritrea	10·0	0·1	0·0	4·4	1·0	1·3	0·0	0·4	0·3	0·2	4
	Guinea	5·0	1·0	2·5	0·2	0·1	1·0	10·0	3·2	0·5	0·2	4
	Guinea Bissau	10·0	0·2	2·5	0·3	1·0	0·5	0·0	1·8	0·5	0·2	4
	Lesotho	2·5	2·2	0·0	7·6	7·3	2·3	0·0	0·3	8·7	0·6	4
	Liberia	5·0	0·0	2·5	3·7	0·4	0·1	10·0	2·2	2·3	0·1	4
	Madagascar	5·0	0·0	5·0	1·5	2·4	1·3	0·0	2·5	3·6	0·1	4
	Mauritania	7·5	0·9	0·0	0·4	0·8	1·5	0·0	0·1	2·6	0·6	4
	Mozambique	5·0	0·0	2·5	2·6	1·3	1·3	10·0	1·1	4·6	0·2	4
	Niger	10·0	0·1	2·5	0·4	0·8	0·2	10·0	2·5	2·3	0·1	3
	Pakistan	10·0	1·0	2·5	2·9	0·1	1·4	0·0	8·2	0·7	0·7	3
	Paraguay	7·5	8·2	0·0	6·6	3·3	3·6	0·0	1·2	5·8	2·4	2b
	Sierra Leone	5·0	0·2	5·0	1·2	0·7	0·7	10·0	0·7	1·5	0·3	3
	Syria	7·5	9·4	0·0	8·7	9·7	4·1	0·0	2·8	0·5	2·0	2b
	Timor Leste	10·0	2·1	2·5	3·3	0·1	0·8	0·0	0·0	1·4	0·5	4
Unscored	Angola	10·0	0·1	0·0	0·1	0·1	3·6	10·0	1·2	0·5	3·5	n/a
	Botswana	5·0	6·9	0·0	8·2	6·2	5·9	5·0	2·9	9·7	4·6	n/a
	Guyana	7·5	8·1	5·0	9·6	1·7	2·5	0·0	0·8	8·1	2·2	n/a
	Malawi	10·0	1·0	5·0	9·5	0·4	9·7	10·0	7·5	5·1	0·0	n/a

***Figure 2*: National ranking of the feasibility of interrupting the transmission of STH and indicator scores**
Countries are ordered alphabetically within quintiles of STH elimination feasibility scores. For illustrative purposes, partially ordered sets (posets) rank scores are shown for each indicator, shaded to indicate value, ranging from blue (highest percentile, best scoring) to red (lowest percentile, poorest scoring). The strength of agreement between scoring methods is shown as 4=allocated to the same quintile with four methods, 3=allocation to the same quintile with three methods; 2a=allocation to the same quintile with two methods with a maximum range of one quintile; 2b=allocation to the same quintile with two methods with a maximum range of two quintiles.

Analysis overview

The main steps in the evaluation of the feasibility of interrupting transmission of STH within our analytical framework are outlined in the appendix. First, we developed a set of inclusion and exclusion criteria to identify countries to be included in the analysis. Second, we identified suitable and comparable indicator data for each of the three domains identified in our conceptual framework. Many of the included indicators are composites of several measures, which we term components. Third, we combined the different indicators to provide a composite score of the feasibility of interrupting transmission of STH for each country included in the analysis. Since there is no universally accepted approach for the construction of composite measures, we used four commonly applied methods. For each of the above steps, the data, detailed methods, and sample sensitivity analyses are provided in the appendix.

Countries

Globally, 166 countries are potentially endemic for STH.[15] However, some countries would not regard interruption of STH transmission as a public health priority and therefore were excluded a priori from our analysis (see appendix for countries excluded on the basis of different criteria). The first set of countries excluded were those defined as very high alert in the 2014 fragile state index[28] and which are subject to internal conflict and unable to provide reasonable public services (ie, Central African Republic, Democratic Republic of the Congo, Somalia, South Sudan, and Sudan). The second set of exclusions were countries for which STH elimination through mass intervention would not be a political priority since, although STH are endemic, rapid ongoing socioeconomic development means that transmission will become negligible. An example would be Saudi Arabia, where STH occurs only at low levels in small isolated foci and is regarded as a minor public health issue that will disappear of its own accord. The third set of countries were small island states (defined as <2000 km²), where interruption of transmission is potentially feasible but the specific settings are not generalisable (49 countries). Last, countries were also excluded if there were insufficient data for the range of core indicators, defined as more than 50% of the indicators (Guyana, occupied Palestinian territory, South Korea, and Western Sahara were excluded on this basis). These criteria resulted in the inclusion of 100 countries, representing 96% of the global population at risk of STH.

Indicators and data sources

We identified three domains and ten indicators to represent our conceptual framework (panel 1). The indicators were either single components or composites of multiple components (appendix). Such a nested structure was chosen to prevent one area of the conceptual framework from dominating the final scores and help calculate weights across different indicators. Components were chosen on the basis of relevance and interpretability, accuracy, timeliness, and availability. To meet these criteria, component data had to be reliably measured across countries using standardised methods, be representative of a year since 2009, and be available for at least 80 included countries. For countries with missing data, the regional average was used. In total, 18 countries had fully complete component data, 78 were missing four or fewer component data sources, and two were missing ten or more. In total, 25 components were included in the final analysis. To ensure comparability, component and indicator data were normalised to the 0–10 scale before aggregation: for data presented as a percentage, normalisation was achieved by dividing by ten; for rates and other measures maximum–minimum normalisation was used; ordinal categorical data were rescaled to cover the full range with equal distances. To avoid outliers dominating component scores, data were checked for skewness and outliers were removed before any maximum–minimum calculation. Full details of included component data and the combining and standardisation of data are provided in the appendix.

Developing a composite feasibility score

There are several methods by which components can be combined into a single statistic or score,[33] with each approach inevitably involving some degree of judgment about the importance of included indicators. To avoid a methodological bias in ordinal rankings, we used four alternative methods to combine component and indicator data: weightings based on an expert opinion survey, principal component analysis,[34] benefit of the doubt weightings estimated with data envelopment analysis,[35] and the partly ordered sets (posets) discrete ordinal method.[36]

Details of each approach are described in the appendix. Briefly, in the expert opinion survey, 29 STH experts were asked to assign a value from one to five for each of the ten different indicators, using an online survey at a dedicated URL between June 7, and July 20, 2014. In the principal component analysis, indicator weights were generated according to the proportion of the indicator's variance attributed to the principal component it was associated with, multiplied by the proportion of variation in the dataset attributed to this principal component. Final weightings were scaled to unity, and composite scores were generated with standardised components or indicators. The benefit of the doubt approach generates weighting that maximises scores and allows weights to vary across indicators and countries. With this approach, component weights are restricted to non-negative, are summed so that no country has a composite value larger than 1 when optimal weights are applied, have a minimum weight set to half that of the associated equal weight, and have a maximum weight of 0·5. The posets method explores the partly ordered structure of the data, assigning countries to ranked sets only when there is sufficient information. An algorithm based on a local part model outlined by Bruggemann and colleagues[37] was used to generate all possible ranked sets based on the indicator data and average country rankings were used to derive one composite score.

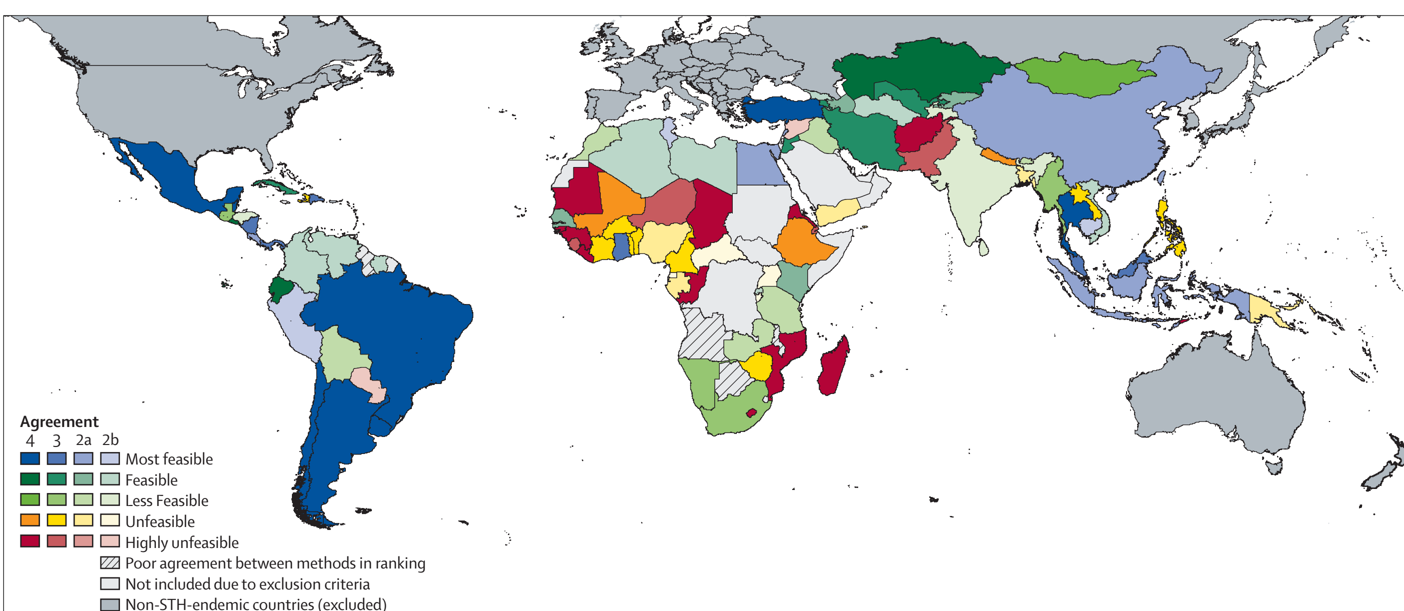

Figure 3: **Quintiles of relative elimination feasibility scores between STH-endemic countries**
The strength of agreement between scoring methods is shown as 4=allocated to the same quintile with four methods, 3=allocation to the same quintile with three methods, 2a=allocation to the same quintile with two methods with a maximum range of one quintile; 2b=allocation to the same quintile with two methods with a maximum range of two quintiles. STH=soil-transmitted helminths.

Indicators consisting of components were first combined by use of the principal component analysis, benefit of the doubt, and poset and by equal weighting for expert opinion. The indicator scores were normalised to a 0–10 scale (using maximum–minimum normalisation for expert opinion, principal component analysis, and benefit of the doubt analyses and dividing the average rank by 10 for poset analysis) and used to derive the final feasibility scores by each method. These scores were normalised to a 0–10 scale and countries were stratified into quintiles. Final country groupings were based on the mode quintile across the four methods. Agreement between the four methods were graded from excellent (country allocated to the same quintile by all four methods), to poor (countries allocated to the same quintile by two methods, with a maximum range not greater than two quintiles). Final results are presented in a heat map (figure 2) and a global map (figure 3). The effects of different indicators on the overall score are presented in a radar chart (figure 4).

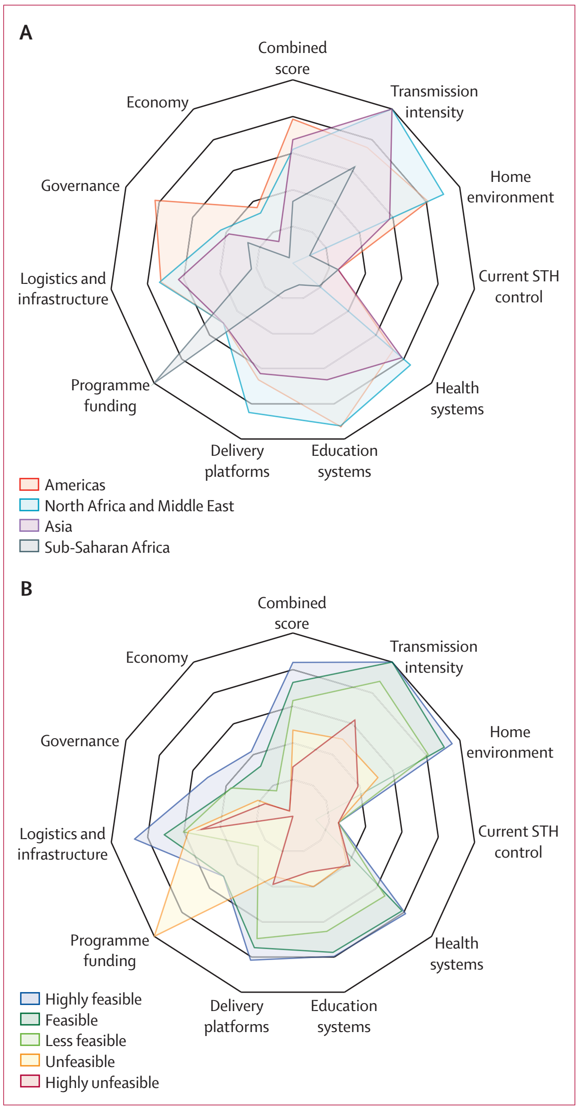

Figure 4: **Radar chart showing the median indicator scores and overall feasibility by geographic region (A) and feasibility quintile (B)**
For all composite indicators, median partially ordered sets (posets) rankings are shown.

Since the final ranking and scores are by definition sensitive to the set of components or indicators included, we did an extensive sensitivity analysis to assess the robustness of all derived composite indicators and scores (appendix).

Role of the funding source

The funder of the study had no role in the study design, data gathering, analysis, and interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The table shows the associated weights assigned to each indicator generated with the three alternative weighting schemes and the poset sensitivity scores. Generally, differences between the three weighting approaches were small, but the range in weights was greatest for the benefit of the doubt method. All three methods gave high weights to the intensity of STH transmission (table). By contrast, household environment and current STH control were weighted more strongly in both the expert opinion and principal component analysis schemes, whereas the benefit of the doubt scheme gave the highest weighting to the programme external partner funding (ie, whether countries received large-scale external funding). The upper range of the country-specific weights generated with the benefit of the doubt analysis suggest that for several countries, external partner funding, intensity of transmission, and health systems performance, and programme funding are important indicators and thus have much higher weightings. Sensitivity scores for the poset analysis (table) also suggest that intensity of transmission, current STH control programme implementation, and programme funding are important. Taken together, these results emphasise four key indicators as being the most important in determining country feasibility scores: intensity of transmission, household environment, existing control programmes, and external partner funding. Specifically, a high level of feasibility is associated with low intensity of transmission, reduced exposure in the household environment, the existence of ongoing control that provides high STH treatment coverage to school children, and less reliance on external funding (see appendix for the components of these indicators).

Overall, agreement between scores derived with each approach was reasonable, and was highest between the expert-opinion-derived and principal-component-analysis-derived weighting schemes (Pearson correlation coefficient, $r=0 \cdot 98$); the largest disparity was noted between benefit-of-the-doubt-derived and principal-component-analysis-derived weighting schemes (r=0·74). Agreement between quintile allocation was therefore high: 31 of 100 included countries were allocated to the same quintile with all methods, 26 countries were allocated to the same quintile with three methods, 20 countries were allocated to the same quintile twice with a maximum range of only one quintile, and 23 to the same quintile twice with a maximum range of two quintiles. Four countries (Angola, Botswana, Guyana, and Malawi) showed poor agreement between quintile allocation and thus were not scored.

Figure 2 shows the feasibility ranking (mode quintile from the four methods) for each country, with indicator scores based on the poset approach and an indication of the degree of agreement between the four methods. Figure 3 maps countries by feasibility ranking (mode quintile) and shows the degree of agreement between methods. Final rankings based on each of the methods are presented in the appendix. The combination of low transmission intensity with good health systems performance, available delivery platforms, and high overall operational and financial capacity result in much of Latin America being scored as being more feasible for STH elimination than are other endemic countries, but there are notable exceptions. China, Malaysia, Indonesia, and Burma also scored highly. The countries where interruption of STH transmission is least feasible are mainly in east, central, and west sub-Saharan Africa, where capacity to deliver is much lower than elsewhere. Exceptions to this trend are Ghana and Kenya (figure 2).

Figure 4A shows the broad regional differences and low scores across all four domains for sub-Saharan Africa, but high scores for other world regions. In sub-Saharan Africa, the low scores are associated with an over-reliance on external funding. Comparison of median indicator scores across quintiles (figure 4B) suggests a good performance in all four domains in the higher scoring countries, with no indicator dominating. However, three domains consistently scored poorly across all quintiles and regions: coverage of existing STH control, programme partner funding, and economic capacity (figure 4B).

	Indicator weightings			Sensitivity: partially ordered sets
	Expert opinion	Principal component analysis	Benefit of the doubt*	
Transmission intensity	0·12	0·11	0·12 (0·05–0·50)	151
Household environment	0·12	0·11	0·05 (0·05–0·11)	34
Current STH control	0·12	0·10	0·05 (0·05–0·09)	184
Health systems	0·10	0·08	0·05 (0·05–0·20)	52
Education systems	0·07	0·09	0·05 (0·05–0·05)	34
Delivery platforms	0·10	0·08	0·05 (0·05–0·11)	29
Programme funding	0·10	0·09	0·18 (0·05–0·45)	239
Logistics and infrastructure	0·10	0·06	0·05 (0·05–0·12)	30
Governance	0·10	0·07	0·05 (0·05–0·05)	51
Economy	0·10	0·09	0·05 (0·05–0·05)	67

All weights were scaled so that the total equalled 1. STH=soil-transmitted helminths. *Data for the benefit of the doubt method are median (IQR) of derived country-specific weights.

Table: **Indicator weightings generated with three weighting schemes, and sensitivity scores for poset analysis**

Panel 2: Research in context

Systematic review

We searched PubMed for any article published before Jan 23, 2015, with the terms "soil-transmitted helminths" (STH), "hookworm", "*Ascaris lumbricoides*", or "*Trichuris trichiura*" and "elimination", "eradication", or "interruption of transmission". We were unable to identify any previous global assessment of the feasibility of interrupting the transmission of STH. We were aware, however, that the International Task Force for Disease Eradication, in 1990, identified hookworm as not eradicable at the time and listed the lack of national and international commitment and monitoring systems as the main obstacles to eradication.[8,38] An email survey of 365 experts in neglected tropical diseases noted that up to 21% of respondents thought the goal of STH programmes should be elimination or eradication and that mass drug administrations, other non-medication health measures, and education were more important for local elimination than the development of a new method or the presence of a secular trend.[39] Specific circumstances that would favour STH elimination in Sri Lanka are discussed elsewhere.[40]

Interpretation

Our study is the first global assessment of the feasibility of interrupting the transmission of STH on a country by country basis. Our results suggest that interruption of STH transmission is feasible, especially in countries with a low intensity of transmission, supportive household environments, and strong delivery platforms and health systems. With the recent new emphasis given by donors and partners to the possibility of interrupting the transmission of STH in selected foci, our analysis provides a theory-based, non-subjective, and comparable approach for identifying priority countries. The approach could also be applied to other neglected tropical diseases.

Discussion

The results of our analyses emphasise the important role of the underlying intensity of STH transmission, household environments, effectiveness of current control programmes for neglected tropical diseases, and whether countries receive large-scale external funding through financial resources. Our analysis also provides the first quantitative assessment of the potential for interrupting the transmission of STH (panel 2), and for identifying the crucial factors that might lend support to or hamper this process. In 1990, the International Task Force for Disease Eradication identified hookworm as not eradicable at the time and listed the lack of national and international commitment and monitoring systems as the main reasons preventing eradication.[8,38] Such obstacles have, partly, been overcome in recent years, through the commitments made at the London Declaration to support the control and elimination targets of the WHO roadmap on neglected tropical diseases.[1] These commitments were strengthened further in April, 2014, when several partners pledged support for the implementation of systemic approaches to STH control with the aim to break transmission in selected countries. Although strengthened leadership is an important first step in this process, here we have shown that it needs to be supported by other key interventions and systems.

National ordinal rankings can be used to identify countries that are in the best position to implement strategies targeting elimination, and elsewhere can help identify sectors that need targeted policies to achieve improvement to move towards elimination (figure 4). Our findings suggest that countries in the Americas have the greatest potential for interrupting transmission of STH; half the countries where interruption of transmission was most feasible were in South and Central America. This high degree of feasibility indicates a combination of the low intensity of transmission, strong health systems, availability of delivery platforms, and high overall operational and financial capacity. There are nonetheless exceptions to this trend, with Paraguay, Bolivia, Guatemala, and Honduras all scoring fairly low, due in part to weak delivery platforms and lack of funding. The countries where interruption of transmission is not feasible and highly unfeasible are mostly in sub-Saharan Africa where intensity of transmission is high and there are deficiencies in health systems, delivery platforms, and in-county funding. There are exceptions to this rule such as Ghana, where there is substantial capacity to deliver programmes, and in Kenya, where low transmission intensity is coupled with improved home environment and good logistics and infrastructure.

Experience in the control of other neglected tropical diseases shows that local elimination is indeed feasible. For instance, the two regional onchocerciasis control programmes, the Onchocerciasis Elimination Program for the Americas and the African Programme for Onchocerciasis Control, have successfully interrupted transmission in previously intense transmission areas[41,42] and put these regions on track to eliminate the disease from all endemic countries within the next 15 years. The success of these programmes is due to strong public–private partnerships coupled with long-term political commitment and funding. In the case of lymphatic filariasis, a previous expert review of national control programmes identified prominent factors associated with successful programmes, including precontrol intensity of transmission, vectorial capacity of mosquito species, drug efficacy, and treatment compliance;[43] compliance is enhanced when programmes are tailored to local diseases.[44] The importance of intervention coverage and frequency has been shown for other neglected tropical diseases[2,45] and vaccine-preventable diseases.[46] Our analysis additionally shows the effect of non-epidemiological factors, and shows the role of a strong and intersectoral collaborative effort to achieve local interruption of STH transmission.

The strength of our work is the conceptual, theory-based approach to developing a feasibility framework. It encompasses targeted programmes to address STH, infrastructure, funds, and policies and locating them within broader health and education systems. Moreover, the framework enables the recognition of the huge complexity of the operation of health systems and the role of context, thus enabling us to capture the hierarchy of factors that affect outcomes and their interaction. Additionally, we sought to assemble comparable spatial data and use a range of methods to derive a composite score. Each method comes, however, with its own advantages and disadvantages. The use of expert opinion can help to emphasise indicators that are deemed more influential, thus better indicating stakeholder priorities and providing a consensus viewpoint, but can deliver contradictory results. However, weighting based only on statistical approaches can be associated with estimation problems, especially when there is little correlation in the indicator data. Poset rankings, by contrast, are highly sensitive to deviant indicators. We have attempted to address these variations by undertaking sensitivity analyses of the effects of using different methods and the effects of alternative component and indicator data (appendix).

Our epidemiological data are based on those recently used to inform the 2010 Global Burden of Disease study,[15] thereby providing a standardised information base that is also available for other diseases.[16] Future work can update these data, using information from additional sources.[47] With our inclusion and exclusion criteria, we sought to provide an objective analysis. However, we recognise that some countries prioritised for control of neglected tropical diseases have been excluded. For example, our use of the fragile state index resulted in the exclusion of the Democratic Republic of the Congo, a country regarded by WHO as one of the big five countries for control of neglected tropical diseases. However, the emphasis of our work is on the feasibility of interrupting transmission of STH, rather than providing a basis for implementing control efforts for neglected tropical diseases. In view of the key role of governance for effective health systems,[11] we analysed the governance dimension of STH control through the use of world governance indicators, widely used as a composite measure of a country's governance. However, there is much debate over their ability to capture fundamental aspects of governance and particularly the tendency to oversimplify multifaceted issues.[48] Despite limitations in operationalising each dimension, the indicators used in this analysis are widely used proxies that can be further refined or substituted as new data sources become available.

The results are not intended to be prescriptive, rather a first step, and we encourage national programmes and partners to undertake national and regional feasibility analyses. In such work, there is a need to obtain improved estimates of the spatial variation in STH transmission intensity, especially after the advent of control activities, and to link these maps with mathematical modelling[2,3] and estimates of treatment coverage to better predict the effect of the interventions. Furthermore, although we have attempted to capture proxy indicators of policy and health system environment and political commitment to programmes within countries, it was not possible to evaluate the contribution of national policies or financial commitment to STH control. The epidemiological, programmatic, and demographic variation between and within countries will require locally tailored strategies for reducing transmission as a step towards the goal of local elimination. For example, different treatment strategies might be needed in different settings, and this is an important research issue that currently needs addressing.

Efforts to control neglected tropical diseases reached a turning point in 2012, when WHO launched its roadmap and partners met in London, UK, and pledged to work together to control and eliminate ten neglected tropical diseases by 2020.[49] Building on this momentum, a new collaboration was announced in Paris, France, in April, 2014, to scale-up deworming efforts and develop new methods and strategies for interrupting transmission of STH. The decision of where to attempt the interruption of transmission needs to be based on comparable data and objective methods and the current work seeks to provide a theory-based, non-subjective, and comparable approach to identifying priority countries. The framework developed here can be readily applied to a range of other neglected tropical diseases.

Contributors

SJB and RLP conceived the idea for the study and all authors were involved in the study design. BN and RLP assembled the data and did the statistical analysis. SJB wrote the first draft and all authors contributed to further drafts and approved the final manuscript.

Declaration of interests

We declare no competing interests.

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