Articles

Soil-transmitted helminth infection in South America: a systematic review and geostatistical meta-analysis

Frédérique Chammartin, Ronaldo G C Scholte, Luiz H Guimarães, Marcel Tanner, Jürg Utzinger, Penelope Vounatsou

Summary

Background The four common soil-transmitted helminth species—*Ascaris lumbricoides, Trichuris trichiura,* and the two hookworm species *Ancylostoma duodenale* and *Necator americanus*—are endemic in South America, but their distribution, infection prevalence, and regional burden are poorly understood. We aimed to estimate the risk and number of people infected with *A lumbricoides, T trichiura,* and hookworm across South America.

Methods We did a systematic review of reports on the prevalence of soil-transmitted helminth infection in South America published up to May 14, 2012. We extracted and georeferenced relevant survey data and did a meta-analysis of the data to assess the geographical distribution of the infection risk with Bayesian geostatistical models. We used advanced Bayesian variable selection to identify environmental determinants that govern the distribution of soil-transmitted helminth infections.

Findings We screened 4085 scientific papers and identified 174 articles containing relevant survey prevalence data. We georeferenced 6948 survey locations and entered the data into the open-access Global Neglected Tropical Diseases database. Survey data were sparse for the south of the continent and for the western coast, and we identified no relevant information for Uruguay and little data for smaller countries such as Suriname, Guyana, French Guiana, and Ecuador. Population-adjusted prevalence of infection with *A lumbricoides* was 15.6%, with *T trichiura* was 12.5%, and with hookworm was 11.9% from 2005 onwards. Risks of contracting soil-transmitted helminth infection have substantially reduced since 2005 (odds ratio 0.47 [95% Bayesian credible interval 0.46-0.47] for *A lumbricoides*, 0.54 [0.54-0.55] for *T trichiura*, and 0.58 [0.58-0.59] for hookworm infection).

Interpretation Our findings offer important baseline support for spatial targeting of soil-transmitted helminthiasis control, and suggest that more information about the prevalence of soil-transmitted helminth infection is needed, especially in countries in which we estimate prevalence of infection to be high but for which current data are scarce.

Funding UBS Optimus Foundation and Brazilian Swiss Joint Research Programme (BSJRP 011008).

Introduction

More than 5 billion people are at risk of soil-transmitted helminthiasis-parasitic worm infections caused by the roundworm Ascaris lumbricoides, the whipworm Trichuris trichiura, and the two hookworm species Ancylostoma duodenale and Necator americanus.1 More than 1 billion people worldwide are infected with one or several species of soil-transmitted helminths, with the highest prevalences reported in Africa, Asia, and Latin America.^{2,3} Chronicity, recurrence, and infections with several species are common in developing countries.^{4,5} Infections can cause diarrhoea, abdominal pain, weakness, and general ill-health. More serious long-term effects include malnutrition, physical and intellectual growth retardations in children, and reduced work productivity in adults.^{2,3,6,7} Soil-transmitted helminth infections are closely connected with poverty⁸ and are endemic in the whole of Latin America and the Caribbean.9 Preliminary estimates report that in this part of the world roughly 100 million people are infected with T trichiura, 84 million with A lumbricoides, and 50 million with hookworm.¹⁰

Preventive drug therapy and, whenever resources allow, improved access to clean water together with adequate sanitation and hygiene make up the global strategy to control soil-transmitted helminthiasis.¹¹ Spatially explicit risk maps at the appropriate resolution to plan interventions are needed for the most rational and costeffective targeting of control. Such maps need survey data and empirical models to predict risk areas, including uncertainty, at locations where actual data might be missing. Bayesian geostatistical models¹² are the most rigorous statistical approaches and such models are increasingly being used to estimate infection risk, number of people infected, and disease burden at high spatial resolutions.^{13,14} However, the shortage of readily available data is a serious impediment that has delayed mapping of soil-transmitted helminthiasis in Latin America.¹⁵

We aimed to produce high-resolution estimates of the risk and number of people infected with *A lumbricoides*, *T trichiura*, and hookworm across South America by doing a geostatistical meta-analysis of the compiled data using Bayesian approaches and advanced variable selection methods to identify the most important disease predictors.

Methods

Search strategy and selection criteria

We did a systematic review in accordance with the PRISMA (Preferred Reporting Items for Systematic



Lancet Infect Dis 2013; 13: 507–18

Published **Online** April 4, 2013 http://dx.doi.org/10.1016/ S1473-3099(13)70071-9

See **Comment** page 469

Department of Epidemiology and Public Health. Swiss Tropical and Public Health Institute, Basel, Switzerland (E Chammartin MSc. R G C Scholte PhD Prof M Tanner PhD, Prof J Utzinger PhD, P Vounatsou PhD). University of Basel, Basel, Switzerland (F Chammartin, R G C Scholte, M Tanner, I Utzinger, P Vounatsou); Centro de Pesquisas René Rachou, Fiocruz/MG, Barro Preto, Belo Horizonte, Brazil (R G C Scholte); and Immunology Service, Hospital **Edgard Santos**, Federal University of Bahia, Salvador, Bahia, Brazil (L H Guimarães MD)

Correspondence to:

Dr Penelope Vounatsou, Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, PO Box, CH-4002 Basel, Switzerland penelope.vounatsou@unibas.ch See Online for appendix

For more on the **GNTD database** see http://www.gntd.org/login. html

For **Google Maps** see https:// maps.google.com/

For more on **WorldClim** see http://www.worldclim.org/

For more on ISRIC World Soil Information see http://www. isric.org/

relevant publications pertaining to prevalence data on A lumbricoides, T trichiura, and hookworm infections in 13 South American countries (Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, French Guiana, Guyana, Paraguay, Peru, Suriname, Uruguay, and Venezuela). We searched PubMed and Web of Knowledge (covering all dates from the creation of each database up to May 14, 2012) with pertinent keywords related to parasite species and countries (appendix). We assessed titles and, if available, abstracts and examined relevant reports in full for soil-transmitted helminth prevalence survey data (for main exclusion criteria, see appendix). No restrictions were placed on date, study design, and language of publication. If surveys were done at the same location at different times, we made sure that they were separated by at least 12 months to avoid bias due to anthelmintic treatment outcomes. We obtained additional data from national ministry of health reports and from personal communication with the Pan American Health Organization (PAHO).

Reviews and Meta-Analyses) guidelines¹⁶ to identify all

Data extraction

We extracted prevalence data from reference sources in accordance with a standard protocol (appendix). We retrospectively georeferenced the data with online sources of information and entered them into the free open-access Global Neglected Tropical Diseases (GNTD) database so the data can be used by researchers and disease control managers.17 We assessed 30% of the publications identified through the systematic literature search for relevance (every third reference listed by author in alphabetical order) and assessed all relevant documents for quality of extraction. We double-checked all coordinates of survey locations in Google Maps to ensure that they referred to a human settlement. We carefully examined publications from the same investigators reporting survey data at the same location and period to avoid duplicate information.

Environmental and population data

We obtained 19 bioclimatic variables from WorldClim— Global Climate Data.¹⁸ These variables were derived from spatial interpolations of monthly average climate data from 1950 to 2000. Remotely sensed climatic proxies are not available before 1980. Hence, on the assumption that climate changes in South America were not severe enough to affect the parasites, we used WorldClim data, which cover similar periods to the disease data. We also extracted altitude data from the WorldClim database and variables about the soil acidity and soil moisture from ISRIC World Soil Information.¹⁹ The spatial distributions of the variables used in the final models are presented in the appendix. We obtained population densities for 2010 from Gridded Population of the World, version 3.²⁰

Geostatistical meta-analysis

We did a meta-analysis of the compiled survey data to develop predictive geostatistical logistical regression models estimating the risk of A lumbricoides, T trichiura, and hookworm infections at high spatial resolution. Environmental predictors were standardised or treated as categorical if they had a non-linear association with the infection outcome. We introduced a temporal trend as a binary variable, indicating whether a survey was done before or after 2005. Predictors were grouped together if they were highly correlated (ie, Pearson's correlation coefficient >0.9). We did Bayesian Gibbs variable selection²¹ to assess which were the most important of all 22 predictors. The procedure enabled several models to be fitted simultaneously. The models included all possible combinations of predictors, but only allowed a maximum of one predictor from each group of highly correlated predictors. We used the predictors included in the model with the highest posterior probability to fit the final geostatistical predictive model. Spatial correlation was regarded as an exponential function of distance between any pair of locations. The large number of survey locations gave rise to large correlation matrices, complicating model fit. To overcome this computational challenge we did predictive process approximations,²² estimating the spatial correlation parameters from a subset of 200 locations (knots). We used minimax space filling sampling to select the knots.^{23,24} Bayesian kriging²⁵ was done to predict the infection risk over a grid of 614044 pixels at 5×5 km spatial resolution covering South America. The models of A lumbricoides, T trichiura, and hookworm infections were fitted on a random subset of about 80% of the survey locations and validated on the remaining 20% by comparing the observed prevalence data with the model-based estimates. Based on experience, this sample is large enough for our purposes without compromising the amount of available data for model fit. Further details of the variable selection, model fit, and validation are given in the appendix.

Role of the funding source

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

Results

Our systematic review identified 4085 peer-reviewed reports. Together with ten additional sources of information from ministries of health and PAHO, 174 references had relevant soil-transmitted helminth infection prevalence data (figure 1). 86% of the survey locations that we identified were associated with survey data reported in grey literature only (ministries of health and PAHO).

An overview of the number of identified surveys with relevant soil-transmitted helminth infection prevalence data, stratified by country, soil-transmitted helminth species, survey period, and geographical unit (ie, municipality or specific location [point]), is presented in table 1. Most data were from Brazil. Survey data were sparse for the south of the continent, especially for Argentina and Paraguay, and for the western coast (ie, Chile and Peru; figures 2-4). We identified no relevant information for Uruguay. Smaller countries such as Suriname, Guyana, French Guiana, and Ecuador contributed few data, some dating back to 1963. Mean infection prevalences calculated from the observed survey data were 17.0% for A lumbricoides, 9.3% for T trichiura, and 9.4% for hookworm. Most (78%) of the surveys were done after 2000, and 98% were community based, with 95% using the WHO-recommended Kato-Katz technique for diagnosis (appendix).²⁶ A summary of the number of surveys with incomplete information, affecting the assessment of the observed prevalence, is provided in the appendix. Missing description of diagnostic methods (11%) was the most common reason for incomplete information.

Results of the variable selection to identify the most important environmental predictors of disease are given in table 2. The best models had high posterior probabilities of 78.9% for *A lumbricoides*, 98.7% for *T trichiura*, and 58.2% for hookworm infection. Model-based parameter estimates are summarised in table 3. Temporal analysis shows that risks of infection with each soil-transmitted helminth have substantially reduced since 2005 (odds ratio estimated to be 0.47 for *A lumbricoides*, 0.54 for *T trichiura*, and 0.58 for hookworm infection).

We noted a negative association between A lumbricoides infection and temperature variation measured by diurnal range and seasonality, and with high rainfall during the wettest season. Rainfall during the coldest quarter and acid soil with a pH between 5.4 and 5.8 were associated with an increased risk of infection. High temperatures during the warmest month and precipitation during the coldest quarter are associated with a higher risk of T trichiura infection. The higher the altitude and the temperature variation, the lower the infection risk. Furthermore, a negative association was estimated with rainfall during the driest quarter (table 3). With respect to hookworm infection, the risk increased with temperature. This risk is supported by a positive coefficient of minimum temperature during the coldest month and of the yearly temperature range after adjusting for the minimum temperature effect. Although precipitation during the wettest quarter increased the risk of hookworm infection, high soil moisture had a negative effect on the disease.

Figures 2–4 show model-based predictions of the geographical distribution of soil-transmitted helminth species-specific risk before and after 2005, and maps of the corresponding coefficient of variation of the predictive distribution and of the raw data. The three soil-transmitted



Figure 1: Study selection

Survey data were from 1952 to 2011; more than 80% of the data were obtained after 2000.

helminth infections show spatial patterns that are affected by the selected environmental predictors. Spatial correlations extended to distances ranging between $465 \cdot 7 \text{ km}$ and $905 \cdot 3 \text{ km}$ depending on the helminth species. The north of the subcontinent had a higher risk of infection compared with the south. Prediction uncertainty was more important for regions with sparse data, as shown in the maps of the coefficient of variation of the predictive distribution.

Population-adjusted prevalence estimates at country and subcontinental level for 2005 onwards are presented in table 4. The estimated *A lumbricoides* infection risk (15.6%) was higher than the risk of *T trichiura* (12.5%) and hookworm (11.9%) infection. On the assumption that risk of infection with the three soil-transmitted helminths was independent, we predicted an overall risk of infection with a soil-transmitted helminth of 27.1%. The countries at highest risk are French Guiana for *A lumbricoides* infection (25.1%) and hookworm infection (36.6%), and Venezuela for *T trichiura* infection (27.3%). French Guiana has the highest predicted risk for any soiltransmitted helminth (46.2%).

Model validation results are given in figure 5. The risks of infection are correctly predicted within a 95% CI for 98.6% of locations for *A lumbricoides*, 96.5% for *T trichiura*, and 97.8% for hookworm. The mean error based on the median of the posterior distribution was 0.3%, -3.4%, and -2.5% for the three species, suggesting that our models slightly underestimate the prevalence of *T trichiura* and hookworm infection. Table 5 presents the population at high (prevalence >50%) and low (prevalence 20–50%) infection risk, stratified by

	Identified reports*	Relevant papers	Survey l	ocation	cation Study level		Period Survey date			Mean prevalence
			Total	Unique	Municipality	Point		Before 2005	2005 onwards	
Ascaris lumbricoides	4022	159	2510	1682	2228	282	1952–2011	1456	1054	17.0%
Argentina	607	13	19	19		19	1993-2009	9	10	10.4%
Bolivia	70	7	49	49	7	42	1984–2006	28	21	27.6%
Brazil	1591	62	2219	1392	2180	39	2000-2009	1228	991	16.0%
Chile	554	14	28	28	2	26	1952-2007	27	1	14.2%
Colombia	133	18	19	19	1	18	1981-2008	10	9	17.1%
Ecuador	189	4	7	7		7	1989-2001	7		18.9%
French Guiana	137†	1	2	2		2	2000	2		14.4%
Guyana	137†	1	1	1		1	2002	1		18.8%
Paraguay	49	2	3	3		3	1996	3		4.3%
Peru	215	17	25	25	2	23	1986-2011	10	15	29.4%
Suriname	53	3	22	22	4	18	1963	22		30.5%
Uruguay	158	0	NA	NA	NA	NA	NA	NA	NA	NA
Venezuela	266	17	116	115	32	84	1984-2011	109	7	29.7%
Trichuris trichiura	4022	137	2175	1506	1928	248	1952–2011	1252	924	9.3%
Argentina	607	12	18	18		18	1993-2009	7	11	3.9%
Bolivia	70	7	49	49	7	42	1984-2006	28	21	16.6%
Brazil	1591	51	1909	1241	1881	28	1968-2011	1045	864	7.4%
Chile	554	14	19	19	2	17	1952-2007	18	1	22.9%
Colombia	133	14	14	14	1	13	1981-2008	8	6	19.6%
Ecuador	189	3	5	5		5	1989–2001	5		9.0%
French Guiana	137†	0	NA	NA	NA	NA	NA	NA	NA	NA
Guyana	137†	1	1	1		1	2002	1		14.1%
Paraguay	49	0	NA	NA	NA	NA	NA	NA	NA	NA
Peru	215	16	24	23	1	23	1986–2011	10	14	22-4%
Suriname	53	3	22	22	4	18	1963	22		10.2%
Uruguay	158	0	NA	NA	NA	NA	NA	NA	NA	NA
Venezuela	266	16	115	114	32	83	1984–2011	108	7	31.8%
Hookworm	4022	101	2263	1541	2048	215	1963–2011	1331	932	9.4%
Argentina	607	9	15	15		15	1968–2009	7	8	38.6%
Bolivia	70	6	47	47	7	40	1993-2006	26	21	15.8%
Brazil	1591	48	2037	1315	2008	29	2000-2009	1151	886	8.8%
Chile	554	0	NA	NA	NA	NA	NA	NA	NA	NA
Colombia	133	10	11	11	1	10	1981-2008	7	4	4.3%
Ecuador	189	3	5	5		5	1989–2001	5		10.8%
French Guiana	137†	1	2	2		2	2000	2		63.0%
Guyana	137†	1	1	1		1	2002	1		28.2%
Paraguay	49	2	3	3		3	1963	3		21.3%
Peru	215	9	18	18		18	1991–2011	7	11	11.6%
Suriname	53	3	21	21	4	17	1963	21		34.3%
Uruguay	158	0	NA	NA	NA	NA	NA	NA	NA	NA
Venezuela	266	9	103	103	28	75	1984-2011	101	2	8.2%

Data are number, timeframe, or %. --edata not found. NA=not applicable because there were no relevant papers for this country. *Number of identified reports per country, irrespective of species. †Number of identified reports of surveys done in either French Guiana or Guyana, or both.

Table 1: Overview of soil-transmitted helminth infection prevalence data in South America, by species and country

country and soil-transmitted helminth species. The numbers of people living in regions with risk greater than 20% are estimated to be 18.7 million for *A lumbricoides*, 30.4 million for *T trichiura*, and 13.3 million for hookworm infection.

Discussion

We present the first model-based estimates of soiltransmitted helminth infection risk and number of infected people at a detailed geographical scale for South America. Across the subcontinent, *A lumbricoides* infection

Articles



Figure 2: Ascaris lumbricoides infection risk in South America Infection risk estimated from surveys done before 2005 (A) and from 2005 onwards (B).

was most prevalent (61.5 million people were estimated to be infected; 15.6%), followed by *T trichiura* (49.3 million; 12.5%), and hookworm (46.9 million; 11.9%).

Mechanisms of interaction between the three soiltransmitted helminth species have yet to be fully elucidated. Co-infection with several helminths might impair the host's immune response to single parasites, and might increase susceptibility to clinical disease. Coinfection is probably high because the three helminths share similar climatic and socioeconomic ranges.¹⁶ Although interspecies associations in hosts with several infections have been suggested,²⁷ there is no evidence to



Figure 3: Trichuris trichiura infection risk in South America Infection risk estimated from surveys done before 2005 (A) and from 2005 onwards (B).

show that the three infections are heavily dependent. In our analysis, we assumed that at an individual level, the chances of being infected with any one helminth species were the same, irrespective of the presence of another species, and we estimated that the overall soil-transmitted helminthiasis risk is $27 \cdot 1\%$. Our geostatistical meta-analysis estimated transmission dynamics and broad-scale geographical patterns of soil-transmitted helminthiasis risk at continental and national levels in South America. However, our modelbased, high spatial resolution estimates should be interpreted cautiously, because our systematic review

Articles



Figure 4: Hookworm infection risk in South America Infection risk estimated from surveys done before 2005 (A) and from 2005 onwards (B).

showed that data were scarce and that national surveys are needed to obtain up-to-date information about infection risk. Brazil is the only country with a large number of soil-transmitted helminth surveys, which is partly explained by the establishment of a national schistosomiasis control programme in 1986.²⁸ As part of monitoring, evaluation, and surveillance of this programme, which repeatedly assesses the prevalence of *Schistosoma mansoni* with the Kato-Katz technique, stool samples were concurrently examined for soil-transmitted helminths.²⁹ Indeed, areas endemic for schistosomiasis had many survey locations, whereas other parts of the

	Ascaris lumbricoides	Trichuris trichiura	Hookworm
Group 1*			
Yearly mean temperature			
Maximum temperature of warmest month		Selected	
Minimum temperature of coldest month			Selected
Mean temperature of wettest quarter			
Mean temperature of driest quarter			
Mean temperature of warmest quarter			
Mean temperature of coldest quarter			
Group 2*			
Mean diurnal temperature range	Selected		
Yearly temperature range		Selected	Selected
Group 3*			
Isothermality			
Temperature seasonality	Selected	Selected	
Group 4*			
Yearly precipitation			
Precipitation in wettest month	Selected		
Precipitation in wettest quarter			Selected
Group 5*			
Precipitation in driest month			
Precipitation in driest quarter		Selected	
Variables moderately correlated			
Precipitation seasonality	Selected		
Precipitation in warmest quarter			
Precipitation in coldest quarter	Selected	Selected	
Altitude		Selected	
Soil pH	Selected		
Soil moisture			Selected
Posterior probability	78.9%	98.7%	58·2%

A maximum of one variable per species per variable group was allowed to be selected. *Variables are grouped with other variables with which they are highly correlated.

Table 2: Variables selected by a Gibbs variable selection procedure

country, especially the Amazon rainforest, had only very little information. No data were available for Uruguay, and we identified very few surveys for Argentina, Chile, Ecuador, French Guiana, Guyana, and Paraguay. Because of data scarcity, modelling risk at the unit of the country would not have been feasible. Our aim was to produce a map for the whole subcontinent and to obtain estimates in countries with little or no information. In regions with sparse or no data, our predictions are based on data available in neighbouring countries and on climatic factors identified to drive their spatial distribution. In the absence of control interventions, the assumption that infection risk is governed by climatic suitability is reasonable. Therefore, we believe that our predictions provide valuable information, although the results should be interpreted with caution, particularly in regions where data are sparse. New surveys should be done in southern countries such as Argentina and Uruguay to validate our model-based soil-transmitted helminth risk predictions of below 20%. However, we propose that first priority

	Rivariato non-	Multivariable		
	spatial, odds ratio (95% CI)	geostatistical, odds ratio (95% BCI)		
Ascaris lumbricoides				
Period				
<2005	1.00	1.00		
≥2005	0.52 (0.52-0.53)*	0.47 (0.46-0.47)*		
Mean diurnal temperature range	0.56 (0.56-0.56)*	0.81 (0.77–0.90)*		
Temperature seasonality	0.52 (0.52-0.52)*	0.92 (0.85–0.99)*		
Precipitation in wettest month	1.35 (1.34–1.35)*	0.97 (0.93–0.99)*		
Precipitation seasonality	0.87 (0.87-0.87)*	1.18 (1.11–1.25)*		
Soliph	1.00	1.00		
<5.4	1.00	1.00		
5.4-5.0	$0.73(0.72-0.73)^{\circ}$	$1.14(1.07-1.17)^{\circ}$		
≥5.8 Precipitation in coldest	0.80 (0.80–0.80)*	0.93 (0.83-1.02)		
<80	1.00	1.00		
<00 80.000	1.47/1.47.1.49*	1.12 (0.00, 1.20)		
<u>00−320</u> >200	1.4/ (1.4/-1.40)"	1.17 (0.22-1.30)		
≥320	4.04 (4.03-4.00)	2.00 (1.00-2.31)		
t" (non-spatial variance)		1.49 + (1.37 - 1.08)		
(spatial variance)		$2.59^{+}(1.05-3.77)$		
Range (km)		50/.87 (336.6-80/./)		
Tricnuris tricniura				
Period	1.00	1.00		
<2005				
≥2005 Maximum temperature of	0·59 (0·59=0·59)* 1·23 (1·22=1·23)*	0·54 (0·54=0·55)* 1·40 (1·21=1·47)*		
Precipitation in coldest				
	1.00	1.00		
80_225	2.24 (2.22-2.26)*	0.96 (0.91-1.02)		
~22E	6.84 (6.80, 6.88)*	1.24 (1.25 1.20)*		
<pre>>>>></pre>	0.04 (0.00-0.00)	1.24 (1.52–1.23)		
<200	1.00	1.00		
200 600	0.26 (0.26 0.26)*	0.80 (0.76, 0.87)*		
>600	0.12 (0.12 0.12)*	0.70 (0.62, 0.72)*		
Yearly temperature range	0.12 (0.12-0.12)	0.70 (0.02-0.73)		
<13	1.00	1.00		
13-17.5	0.26 (0.26-0.26)*	0.53 (0.51-0.57)*		
>17.5	0.13 (0.13-0.14)*	0.66 (0.60-0.74)*		
Temperature seasonality (°C)	(1 U U U U U U U U U U U U U U U U U U U	0 00 (0 00 074)		
<1.25	1.00	1.00		
1.25-1.65	 0.65 (0.65–0.66)*	0.84 (0.81-0.89)*		
>1.65	0.19 (0.19–0.19)*	0.79 (0.73-0.83)*		
Precipitation in driest quarter (mm)	2 1J (0.13-0.13)	0.02(0.02)		
<50	1.00	1.00		
- 50-100	1.19 (1.19–1.20)*	0.92 (0.85-0.99)*		
≥100	3.23 (3.22-3.25)*	0.81 (0.72–0.88)*		
τ ² (non-spatial variance)		1.44† (1.31–1.61)		
(Continues on next pag				

	Bivariate non- spatial, odds ratio (95% CI)	Multivariable geostatistical, odds ratio (95% BCI)				
(Continued from previous page)						
² (spatial variance)		4·21† (2·88–6·11)				
Range (km)		905·3† (591·4–1451·1)				
Hookworm						
Period						
<2005	1.00	1.00				
≥2005	0.62 (0.62–0.63)*	0.58 (0.58-0.59)*				
Minimum temperature of coldest month	2.02 (2.01–2.02)*	2.13 (1.99–2.18)*				
Yearly temperature range	0.64 (0.64-0.64)*	1.35 (1.33–1.41)*				
Precipitation in wettest quarter	1.47 (1.47–1.48)*	1.55 (1.44–1.69)*				
Soil moisture (%)						
<50	1.00	1.00				
50-80	0.99 (0.99–1.00)	0.59 (0.56–0.60)*				
≥80	0.65 (0.64-0.65)*	0.31 (0.26-0.41)*				
τ^2 (non-spatial variance)		2.09† (1.86–2.30)				
² (spatial variance)		2.68† (1.67–3.66)				
Range (km)		465·7† (292·8–683·1)				

	Ascaris Iumbricoides	Trichuris trichiura	Hookworm	All soil-transmitted helminth infections*
South America	15-6% (14-4–17-2)	12.5% (11.1–13.6)	11.9% (10.5–13.4)	27.1% (25.9–28.4)
Argentina	9.5% (6.9–13.8)	8.5% (6.3-11.6)	8.3% (6.6–10.3)	18.9% (16.4–23.0)
Bolivia	24.5% (18.4–29.8)	18.9% (14.5–24.9)	19·3% (15·2–23·5)	37.8% (33.2–41.6)
Brazil	14.3% (13.4–16.2)	10.1% (8.8–11.3)	12.3% (10.8–14.1)	25.5% (24.2–27.1)
Chile	16.8% (13.2–19.9)	11.7% (8.4–15.4)	7·2% (5·5–8·8)	24.7% (21.5–27.9)
Colombia	19.7% (16.9–24.0)	17.8% (14·4–21·7)	14.5% (10.3–17.5)	33·4% (30·7–37·6)
Ecuador	18.5% (14.9–24.9)	11.1% (8.4–15.1)	12.3% (8.1–15.7)	28.1% (23.8-33.3)
French Guiana	25.1% (15.3-33.0)	15.1% (7.4–29.9)	36.6% (28.8-44.3)	46·2% (38·4–56·1)
Guyana	23.6% (16.4–31.6)	11.1% (5.3–16.7)	25.0% (19.5–29.6)	37.4% (31.9–42.9)
Peru	17·3% (13·4–20·6)	10.8% (8.4–13.6)	8.7% (6.1–11.3)	25.0% (21.3–29.0)
Paraguay	8.3% (5.3–15.5)	7.1% (2.6–21.4)	18.3% (12.1–28.0)	26.7% (20.1–34.7)
Suriname	23.5% (15.9–34.8)	8.3% (3.5–16.6)	30.0% (20.3–41.3)	40.1% (30.2-51.1)
Uruguay	9.9% (6.9–16.1)	10.1% (7.3–15.1)	6.4% (4.2-9.2)	18.8% (14.7–24.7)
Venezuela	21.7% (17.9–25.4)	27.3% (25.0–29.8)	12·2% (9·8–15·6)	39.4% (36.3-42.5)

Data are population-adjusted prevalence (95% Bayesian credible interval) based on 2010 population estimates. *Calculated under the assumption that Ascaris lumbricoides, Trichuris trichiura, and hookworm infections are independent of one another.

Table 4: Population-adjusted prevalence of helminth infections from 2005 onwards, by country

CI=confidence interval. BCI=Bayesian credible interval. *Significant correlation based on 95% CI or BCI. \dagger Original scale instead of odds ratio.

Table 3: Logistic regression parameter estimates for Ascaris lumbricoides, Trichuris trichiura, and hookworm infection risk

should be given to surveys in countries such as French Guiana, Suriname, Venezuela, Bolivia, Guyana, Colombia, Ecuador, Paraguay, Peru, and Chile, for which our models predict that there are regions where prevalences are above 20%, and therefore need interventions according to PAHO recommendations.⁹ A soil-transmitted helminth infection prevalence survey has recently been done in five districts in Suriname. These data should be included in subsequent geostatistical analyses once they become available.

The Bayesian variable selection approach used in our analysis identified important predictors related to the biology, ecology, and epidemiology of soil-transmitted helminthiasis. The effect of some covariates changed after accounting for other covariates or spatial correlation. This issue emphasises the need to account for spatial correlation during analysis of geographical data. Warm and humid climatic conditions have been reported to be suitable for the development of parasite eggs and larvae.630 Our analyses confirm the positive association of T trichiura and hookworm infection risks with proxies related to temperature and precipitation, and of A lumbricoides with rainfall. Results of earlier studies provided temperature limits for the survival of the larvae of each soil-transmitted helminth species, and suggested that extreme temperatures might slow down or even stop their development.31 This effect is evident in the A lumbricoides and T trichiura models, which estimated a negative association between temperature variation and infection risks. The negative effect of altitude on T trichiura infection might arise as a result of lower temperature at higher altitudes. A lumbricoides infection is more prevalent in regions with acid soil. Similar results had been reported by Yaday,32 who considered different levels of soil acidity and reported that A lumbricoides egg development was accelerated in soils with a pH of 5.0 under specific moisture and temperature conditions. Our study estimated a negative effect of moist soil on hookworm risk after adjusting for precipitation during the wettest quarter. We also estimated a negative effect of rainfall on the risk of T trichiura during the driest quarter after adjusting for precipitation during the coldest guarter. These observations support earlier interpretations that high precipitation might wash out the helminth eggs and therefore reduce infection.^{33,34}

Our maps of the geographical distribution of soiltransmitted helminth infection risks present patterns coherent with recently released maps of the transmission limits of these infections.¹ More precisely, the estimated risk for any of the three soil-transmitted helminths is negligible in the northern part of Chile. The risk of infection with A lumbricoides and hookworm is low in Argentina. Hookworm risk is minor in the coastal regions of Peru and southern Chile. Although several regions were within the climatic suitability transmission limits provided by Pullan and Brooker,1 our models have identified additional regions where the estimated risk is of little importance (<5%, population-unadjusted)-ie, Uruguay, Paraguay, and parts of Brazil for A lumbricoides; Guyana, Suriname, and parts of Brazil for T trichiura; and coastal regions of Venezuela and parts of Brazil for hookworm. In South America, the population living in regions with a predicted risk greater than 20% is higher



Figure 5: Model validation results

Proportion of survey locations with prevalence of infection falling in the predicted highest posterior density intervals (bar plots) for Ascaris lumbricoides, Trichuris trichiura, and hookworm. The line plots show the corresponding width of the predicted highest density region.

	Total population (×1000)*	Population at low (20–50%) risk (×1000)†			Population at high (≥50%) risk (×1000)†		
		Ascaris Iumbricoides	Trichuris trichiura	Hookworm	Ascaris Iumbricoides	Trichuris trichiura	Hookworm
South America	394234	15923	28190	11702	2752	2169	1572
Argentina	47 417	0	0	1101	0	0	16
Bolivia	10 453	1510	2030	2201	927	0	594
Brazil	186 552	10681	8963	5853	1782	1597	290
Chile	19 435	258	345	0	0	0	0
Colombia	48 235	1131	4119	1258	0	0	671
Ecuador	14118	26	3	249	0	0	0
French Guiana	145	0	0	125	0	0	0
Guyana	629	1	0	79	0	0	0
Peru	27 832	828	347	62	42	547	1
Paraguay	7247	0	0	513	0	0	0
Suriname	407	0	0	51	0	0	0
Uruguay	3977	0	0	0	0	0	0
Venezuela	27786	1487	12382	209	0	26	0

*Estimates based on 2010 data from Gridded Population of the World, version $3.^{20}$ †Calculations were based on the median of the posterior distribution of the predicted risk from 2005 onwards.

Table 5: Estimated population at risk of soil-transmitted helminth infection, by country

for *T* trichiura (30.4 million) than for *A* lumbricoides (18.7 million) and hookworm (13.3 million), suggesting that *T* trichiura has a particularly high risk in densely populated regions. This result is in agreement with previous findings of a greater *T* trichiura risk in periurban, rather than rural, regions.¹

The surveys used different diagnostic approaches varying in sensitivity and specificity,³⁵⁻³⁷ which might have introduced bias into the data. Importantly though, the WHO-recommended Kato-Katz technique²⁶ was used in more than 95% of the surveys. Because of data sparsity, we did not exclude the remaining 5% of surveys, which used various techniques (appendix). Of the studies using the Kato-Katz technique, we noted that sampling efforts differed between surveys. Although most surveys prepared two slides, some used one Kato-Katz thick smear, or combined the Kato-Katz technique with other diagnostic techniques. Differences in sensitivity and specificity can be incorporated into our Bayesian models.³⁸ However, more than 10% of the surveys did not provide detailed information about diagnostic methods (including sampling efforts). Hence, any related assumption would be debatable and introduce additional bias. Additionally, assessment of prior information about the various sampling efforts would have been difficult.

Survey design also differs. Children aged 5–14 years are known to carry the heaviest burden of soil-transmitted helminthiasis,³⁹ but 98% of our survey locations were in the community. Of the remaining 2%, the surveys either screened children or did not provide any details of the population examined. We included surveys in the metaanalysis irrespective of the age profile, which might be sources of bias. Geostatistical models with age-alignment factors^{40,41} have been developed by calculating countryspecific alignment factors. In accordance with this approach, some countries would have had insufficient data to estimate the alignment factor. Furthermore, adjusting for age would have required some arbitrary assumptions about the unknown population and might have introduced even more bias.

We did not consider socioeconomic proxies when building our models. Because soil-transmitted helminth infections disproportionally affect poor people, such proxies might be related to infection risk. For some countries, measures of the proportion of households with sanitation are available from census data, but they often contain missing data and their spatial resolution is low. However, in previous studies, these poverty proxies did not explain small-scale spatial variation when diseases were modelled over large scales, which is intrinsically linked to the issue of pattern and scale.⁴² More efforts are needed to construct a socioeconomic index or to compile relevant socioeconomic predictors that can explain the socioeconomic disparities at high spatial resolution.

A temporal trend was estimated by a binary covariate indicating whether surveys had been done before or after 2005. We could not take into account spatiotemporal correlations because of the coarse temporal resolution of the data. Our analysis suggests that the risk of soiltransmitted helminth infection has decreased substantially in recent years in South America.¹⁰ We believe that this decrease is more related to the improvement of socioeconomic factors and ongoing control measures during the past decade than to climate change. *A lumbricoides* risk seems to have reduced more than that of the other soil-transmitted helminth infections. This risk reduction might be related to the higher efficacy of the available treatments against *A lumbricoides*,⁴³ leading to fewer eggs released into the environment and, consequently, a lower risk of reinfection.

South America has high climatic heterogeneity. Hence, a single logistic regression equation might not be able to describe variation of the effect of climatic factors on the disease risk across the subcontinent. A model estimating the climate-disease risk relation by ecological zone could be considered. However, this model would need better coverage of the ecological zones, with new survey data. Furthermore, we assumed a single spatial process over the whole of South America, which might not be true because of the region's large climatic diversity, socioeconomic disparities, and health system inequalities.44 Non-stationary models assuming a mixture of separate stationary processes within each agroecological zone have been applied to schistosomiasis and malaria risk mapping.45,46 A similar approach could be implemented and applied to a large dataset by approximating each spatial process on a subsample of locations.

Another limitation to consider is that people might have been infected before the survey period began. Even if seasonal dynamics in transmission occur, their overall effect on transmission dynamics is limited because of the lifespan of adult worms, which exceeds 1 year.³⁹ Therefore, we did not include interactions of climatic factors with seasons.

In conclusion, our study provides an open-access compilation of available survey data for soil-transmitted helminth infection prevalence, gives model-based georeferenced estimates of infection risk, and identifies regions with sparse or no data across South America. We believe that our estimates provide a valuable assessment of the national and subnational situation of soil-transmitted helminthiasis, and we hope that this first effort will contribute useful information to national control programmes for planning control and elimination strategies by indicating regions where survey data are urgently needed if risk prediction is to be improved. We will continue our efforts to further develop statistical models and update the GNTD database. We also invite researchers to assist these efforts by contributing their georeferenced data to the GNTD database so it can be further developed into a useful shared platform for research and control of soiltransmitted helminthiasis and other neglected tropical diseases.

Contributors

FC processed and analysed the data, interpreted the results, and wrote the manuscript. FC, RGCS, and LHG contributed to the systematic literature search and data extraction. FC, JU, and PV developed the protocol and search strategy for the systematic review. PV assisted in the meta-analysis. MT, JU, and PV conceptualised the project, revised the manuscript, and provided important intellectual content. All authors approved the final version of the manuscript.

Conflicts of interest

We declare that we have no conflicts of interest.

Acknowledgments

We thank the Pan American Health Organization Neglected Infectious Diseases Programme for their contribution to the data collection.

References

- Pullan RL, Brooker S. The global limits and population at risk of soil-transmitted helminth infections in 2010. *Parasit Vectors* 2012; 5: 81.
- 2 Bethony J, Brooker S, Albonico M, et al. Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. *Lancet* 2006; 367: 1521–32.
- 3 Knopp S, Steinmann P, Keiser J, Utzinger J. Nematode infections: soil-transmitted helminths and *Trichinella*. Infect Dis Clin North Am 2012; 26: 341–58.
- 4 Ezeamama AE, Friedman JF, Olveda RM, et al. Functional significance of low-intensity polyparasite helminth infections in anemia. J Infect Dis 2005; 192: 2160–70.
- 5 Steinmann P, Du ZW, Wang LB, et al. Extensive multiparasitism in a village of Yunnan province, People's Republic of China, revealed by a suite of diagnostic methods. *Am J Trop Med Hyg* 2008; 78: 760–69.
- 6 Brooker S, Clements ACA, Bundy DAP. Global epidemiology, ecology and control of soil-transmitted helminth infections. *Adv Parasitol* 2006; 62: 221–61.
- 7 Hotez PJ, Brindley PJ, Bethony JM, King CH, Pearce EJ, Jacobson J. Helminth infections: the great neglected tropical diseases. *J Clin Invest* 2008; **118**: 1311–21.
- 8 Hotez P. Hookworm and poverty. Ann N Y Acad Sci 2008; 1136: 38–44.
- 9 Pan American Health Organization, WHO. 61st session of the regional committee: elimination of neglected diseases and other poverty-related infections, resolution CD49.R19. Washington, DC: Pan American Health Organization, 2009. http://new.paho.org/hq/ dmdocuments/2009/CD49.R19%20(Eng.).pdf (accessed Jan 31, 2013).
- 10 de Silva NR, Brooker S, Hotez PJ, Montresor A, Engels D, Savioli L. Soil-transmitted helminth infections: updating the global picture. *Trends Parasitol* 2003; 19: 547–51.
- 11 WHO. Working to overcome the global impact of neglected tropical diseases. First WHO report on neglected tropical diseases (WHO/ HTM/NTD/2010.1). Geneva: World Health Organization, 2010. http://whqlibdoc.who.int/publications/2010/9789241564090_eng. pdf (accessed Jan 31, 2013).
- 2 Diggle PJ, Tawn JA, Moyeed RA. Model-based geostatistics. J R Stat Soc Ser C Appl Stat 1998; 47: 299–326.
- 13 Magalhães RJ, Clements ACA, Patil AP, Gething PW, Brooker S. The applications of model-based geostatistics in helminth epidemiology and control. *Adv Parasitol* 2011; 74: 267–96.
- 14 Schur N, Hürlimann E, Stensgaard AS, et al. Spatially explicit Schistosoma infection risk in eastern Africa using Bayesian geostatistical modelling. Acta Trop 2011; published online Oct 14. DOI:http://dx.doi.org/10.1016/j.actatropica.2011.10.006.
- 15 Inter-American Development Bank, Pan American Health Organization, Sabin Vaccine Institute. A call to action: addressing soil-transmitted helminths in Latin America and the Caribbean. http://new.paho.org/hq/index.php?option=com_docman&task=doc_ download&gid=13723&Itemid= (accessed Jan 31, 2013).
- 16 Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; **339**: b2535.
- 17 Hürlimann E, Schur N, Boutsika K, et al. Toward an open-access global database for mapping, control, and surveillance of neglected tropical diseases. *PLoS Negl Trop Dis* 2011; 5: e1404.

- 18 Hijmans RJ, Cameron SE, Parra JL, Jones PG, Jarvis A. Very high resolution interpolated climate surfaces for global land areas. Int J Climatol 2005; 25: 1965–78.
- Batjes NH. ISRIC-WISE derived soil properties on a 5 by 5 arcminutes global grid (version 1.1). Report 2006/02. Wageningen: ISRIC-World Soil Information, 2012.
- 20 Center for International Earth Science Information Network (CIESIN) Columbia University, UN Food and Agriculture Programme (FAO), Centro Internacional de Agricultura Tropical. Gridded population of the world: future estimates (GPWFE). Palisades, NY: Socioeconomic Data and Applications Center (SEDAC) Columbia University, 2005.
- 21 Dellaportas P, Forster JJ, Ntzoufras I. On Bayesian model and variable selection using MCMC. Stat Comput 2002; 12: 27–36.
- 22 Banerjee S, Gelfand AE, Finley AO, Sang H. Gaussian predictive process models for large spatial data sets.
- J R Stat Soc Ser B Stat Methodol 2008; 70: 825–48.
 Johnson ME, Moore LM, Ylvisaker D. Minimax and maximin distance designs. J Statist Plann Inference 1990; 26: 131–48.
- 24 Diggle PJ, Lophaven SÃ. Bayesian geostatistical design. Scand Stat Theory Appl 2006; **33**: 53–64.
- 25 Cressie N. The origins of kriging. Math Geol 1990; 22: 239–52.
- 26 Montresor A, Crompton DWT, Hall A, Bundy DAP. Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level (WHO/CDS/SIP/98.1). Geneva: World Health Organization, 1998.
- 27 Booth M, Bundy DAP, Albonico M, Chwaya HM. Associations among multiple geohelminth species infections in schoolchildren from Pemba Island. *Parasitology* 1998; 116: 85–93.
- 28 Ministerio da Saúde (Brasil). Programa Integrado de Esquistossomose da Fundação Oswaldo Cruz (PIDE). http://pide. cpqrr.fiocruz.br/index.php?pagina=3&PHPSESSID=f11d881b782237 9b490aeb4665c4c608 (accessed Jan 31, 2013).
- 29 Ministerio da Saúde (Brasil). Equistossomose mansônica. Document CID 10: B65. http://portal.saude.gov.br/portal/arquivos/ pdf/gve_7ed_web_atual_esquistissomose_mansonica.pdf (accessed Jan 31, 2013).
- 30 Spindler LA. The relation of moisture to the distribution of human Trichuris and Ascaris. Am J Epidemiol 1929; 10: 476–96.
- 31 Brooker S, Kabatereine NB, Tukahebwa EM, Kazibwe F. Spatial analysis of the distribution of intestinal nematode infections in Uganda. *Epidemiol Infect* 2004; 132: 1065–71.
- 32 Yadav AK. Development and survival of Ascaris lumbricoides eggs under the high rainfall and humid conditions prevailing in Meghalaya, India. Proc Zool Soc Calcutta 2003; 56: 109–12.

- 33 Brown HW. Studies on the rate of development and viability of the eggs of Ascaris lumbricoides and Trichuris trichiura under field conditions. J Parasitol 1927; 14: 1–15.
- 34 Gunawardena GS, Karunaweera ND, Ismail MM. Wet-days: are they better indicators of *Ascaris* infection levels? *J Helminthol* 2004; 78: 305–10.
- 35 Goodman D, Haji HJ, Bickle QD, et al. A comparison of methods for detecting the eggs of Ascaris, Trichuris, and hookworm in infant stool, and the epidemiology of infection in Zanzibari infants. Am J Trop Med Hyg 2007; 76: 725–31.
- 36 Knopp S, Mgeni AF, Khamis IS, et al. Diagnosis of soil-transmitted helminths in the era of preventive chemotherapy: effect of multiple stool sampling and use of different diagnostic techniques. *PLoS Negl Trop Dis* 2008; 2: e331.
- 37 Bergquist R, Johansen MV, Utzinger J. Diagnostic dilemmas in helminthology: what tools to use and when? *Trends Parasitol* 2009; 25: 151–56.
- 38 Wang XH, Zhou XN, Vounatsou P, et al. Bayesian spatio-temporal modeling of *Schistosoma japonicum* prevalence data in the absence of a diagnostic 'gold' standard. *PLoS Negl Trop Dis* 2008; 2: e250.
- 39 Anderson RM, May RM. Helminth infections of humans: mathematical models, population dynamics, and control. *Adv Parasitol* 1985; 24: 1–101.
- 40 Schur N, Hürlimann E, Garba A, et al. Geostatistical model-based estimates of schistosomiasis prevalence among individuals aged ≤20 years in West Africa. *PLoS Negl Trop Dis* 2011; **5**: e1194.
- 41 Magalhães RJ, Clements ACA. Mapping the risk of anaemia in preschool-age children: the contribution of malnutrition, malaria, and helminth infections in West Africa. PLoS Med 2011; 8: e1000438.
- 42 Levin SA. The problem of pattern and scale in ecology. *Ecology* 1992; 73: 1943–67.
- 43 Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. JAMA 2008; 299: 1937–48.
- 44 Belizán JM, Cafferata ML, Belizán M, Althabe F. Health inequality in Latin America. *Lancet* 2007; 370: 1599–600.
- 45 Raso G, Vounatsou P, Gosoniu L, Tanner M, N'Goran EK, Utzinger J. Risk factors and spatial patterns of hookworm infection among schoolchildren in a rural area of western Côte d'Ivoire. *Int J Parasitol* 2006; 36: 201–10.
- 46 Gosoniu L, Vounatsou P, Sogoba N, Maire N, Smith T. Mapping malaria risk in West Africa using a Bayesian nonparametric non-stationary model. *Computat Stat Data Anal* 2009; 53: 3358–71.