Ecological and Economic Modeling of Hookworm Burden Under Climate Change

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Ecological and Economic Modeling of Hookworm Burden under Climate Change

Gordon C. McCord, PhD¹ and Karl Rubio, MA²

Abstract

Background The disease burden of hookworm is disproportionately borne by tropical and sub-tropical regions because hookworm thrives in warm surroundings with moist soil. Climate change will alter the ecological strength of transmission, affecting the spatial extent and intensity of hookworm burden.

Methods This paper explains the relationship between hookworm transmission strength and geographic factors, and constructs a global hookworm ecological index (HEI) at a 0.5-degree spatial resolution. We test the HEI against spatial variation in hookworm prevalence, and then use three climate models to estimate the change in the spatial extent of ecological suitability for hookworm. Finally, we estimate the impact of climate change on public health costs and human capital loss due to hookworm.

Results The models predict that East Asia, Latin America and the Middle East will experience increases in hookworm prevalence while South Asia and Sub-Saharan Africa will experience decreases. Our estimates suggest that if climate change occurred now, public health costs to avert DALYs from hookworm would rise by \$680 million, 72-268 thousand fewer children would enroll in school, up to 165 thousand fewer children would attain literacy, and incomes would decrease for people across much of the developing world.

Conclusion This paper represents the first assessment of the global effect of climate change on the population at risk and economic burden of hookworm infections.

Keywords: Soil-transmitted helminths, Hookworm, Transmission limits, Climate change, Population at risk

I. Background

In 2015, there were approximately 430 million cases of hookworm infection around the world [1]. Hookworm primarily causes malnutrition and iron-deficiency anemia, particularly in pregnant women and children given their lower iron stores. Infection has been shown to lead to

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lower school attendance, literacy, and worker productivity, thus decreasing incomes and economic growth [2].

Parasitic nematodes thrive in warm and humid environments. We construct a hookworm ecology index (HEI) as a function of how temperature, rainfall, relative humidity, and soil texture dictate the reproductive and survival rate of hookworm. Climate change will alter the ecological strength of transmission, affecting the spatial extent and intensity of hookworm burden. The use of GIS to construct suitability maps for prediction has been demonstrated for other diseases [3–5], and the applicability for climate change has been shown in the case of malaria [6]. We measure the effect of the HEI on spatial variation in hookworm prevalence rates, and then predict prevalence under different climate futures. Since hookworm prevalence rates are also dependent on other non-climate factors (such as availability of medical treatment), our exercise measures the effect of climate change assuming no change in current-day public health efforts or the spatial distribution of the human population.

a. The Ecology of Hookworm

The most common species of hookworm that infects humans are *Ancylostoma duodenale* and *Necator americanus*. These nematodes live and reproduce in the upper section of the human small intestine. Eggs are transferred in the stool and, under favorable conditions, embryonate within one to two days. The first larvae form lasts for five to ten days; this is followed by a three to four week infective stage during which the larvae must find a human host to prevent dessication [4]. Human infections can occur at any stage of the hookworm's life cycle in which it lives in the external environment. Infections can occur either through accidental ingestion of

the eggs (i.e., open defecation near vegetation), or the larvae can easily penetrate the skin.

However, infection rates highly depend on the rate at which hookworms eggs/larvae develop and survive.

The endemicity of hookworm infection is determined by the reproductive number (the lifetime number of surviving offspring a hookworm in a particular host produces in the absence of density dependent constraints) [7]. The reproductive number of hookworm independent of age and population density is:

$$(1) \quad R_0 = \frac{\lambda}{\mu}$$

where λ is the fecundity rate and μ is the mortality rate. The fecundity rate is the number of eggs produced by a female hookworm in a day while the mortality rate is the number of eggs surviving. The Hookworm Ecology Index (HEI) models the effect of the climate on the mortality rate.

Under adequate moisture, hookworm development and survival is strongly influenced by the surrounding temperature. We fit the following function from data on the percentage of *Ancylostoma tubaeforme* (cat hookworm) eggs developing to the infective stage at different temperatures [8]:

$$(2) \quad d(T) = -0.0028T^2 + 0.1348T - 0.7244$$

Figure 1 shows the data fitted using a quadratic function. Larvae cease to develop below 10 degree Celsius or above 40 degree Celsius.

Relative humidity and rainfall also influence hookworm development. Ova of soil-transmitted helminthes generally do not embryonate below relative humidity of 50 percent [4]. Hookworms are more susceptible to desiccation than other soil-transmitted helminthes. A rainfall annual average of more than 40 inches (or 1,016 millimeters) is almost required for ova to develop to the first larvae stage and for the larvae to develop to the infective stage [9]. Increased precipitation prevents egg and larvae from drying up, but excessive rainfall could also potentially reduce the hatch rate [10].

Although weather data is available at monthly or even daily temporal resolution, we note that long-term average rainfall is the relevant ecological driver for hookworm endemicity. Although a location might have months where the basic reproduction number is below unity, the long life-span of adult hookworm (typically 1-10 years) maintains overall endemicity as long as the basic reproduction number is on average above one over longer periods [4]. The HEI is therefore constructed for every month using the required yearly rainfall divided by twelve months. The monthly HEI is then aggregated to the yearly level.

The final environmental variable we incorporate is soil texture. Hookworms thrive in moist, sandy soil, and transmission is facilitated when porous soil allows them to easily migrate to the surface [11]. When the soil is high in clay content, hookworm larvae are restricted in movement and tend to desiccate. The soils of coarser texture are more effective for eggs to develop towards

the larvae stage (although very coarse sands produce drier conditions because of high permeability). Efficiency decreases rapidly as soil becomes less granulated (increase in fineness). We incorporate the effect of soil type into the HEI using data from an experiment on hookworm development using ova in feces under different soil types, documenting the relation of soil texture to hookworm development [12]. Table 1 reports the percentage of ova that develops under different soil types.

II. Methods

The Hookworm Ecology Index takes the following value for every grid cell i in month m :

$$(3) \quad HEI_{i,m} = d(T_{i,m}) * f(s_i)$$

$d(T_{i,m})$ is the percentage of eggs developing to the infective larval stage as a function of temperature in equation (2), and $f(s_i)$ is the probability of eggs developing towards the larvae stage as a function of soil texture. The value calculated in equation (3) can range from 0 to 1.

The HEI is further modified by the following constraints:

1. HEI takes on a value of zero if relative humidity falls below 50 percent.
2. HEI takes on a value of zero if temperature is less than 10 degree Celsius or greater than 40 degree Celsius.
3. An annual precipitation of 40 inches (1,016 millimeters) is required for hookworm to survive. Since the HEI is constructed at the monthly level, 1,016 is divided by 12. The HEI for a given month is equal to zero if precipitation is less than 85 millimeters.

The HEI is calculated using gridded data on temperature, precipitation, relative humidity, and soil content. Historical simulations and future projections are generated by three global climate models from the Coupled Model Intercomparison Project Phase 5 (CMIP5) [13]. CCSM4, CESM1-CAM5, and HadGEM2-AO each have outputs for four representative concentration pathways (RCP) scenarios and historical simulations. We use RCP 4.5 and RCP 8.5 to give a plausible range of the change in hookworm burden. Three variables are obtained for each model: (1) near-surface air temperature which is the temperature reported at the 2-meter height, (2) relative humidity expressed as a percentage (ratio of current absolute humidity to the highest absolute humidity), and (3) precipitation in millimeters per day. Each variable is obtained at a monthly-year level, downscaled to 0.5 decimal degree (around 50km at the equator) in the case of temperature and precipitation [14]. Monthly relative humidity projections were available at a coarser resolution (0.9424° latitude $\times$ 1.25° longitude under CCSM4 and CESM1-CAM5, 1.25° latitude $\times$ 1.875° longitude under HadGEM2-AO). Historical simulations have climate data starting from 1860 up to 2005. Each RCP output for CCSM4 and CESM1-CAM5 has climate variables from 2006 to 2100, while HadGEM2-AO has them from 2006 to 2099.

Clay, silt, and sand content of topsoil (expressed as a percent of total soil content) are available at a 0.5-degree spatial resolution [15]. Since relative humidity was available at a coarser resolution, the centroids of the downscaled temperature and precipitation were spatially joined with relative humidity centroids using ArcGIS. The HEI is then constructed at the monthly level at a 0.5-degree spatial resolution.

The HEI was validated using available hookworm prevalence data both at the country and village level. Country-level validation was conducted by regressing country prevalence rates (provinces in the case of China, and states in India) [16] on 10-year HEI average (1993-2003); we use the 10-year average as the appropriate comparison given that the adult hookworm's lifespan within a host is 1-10 years. Village-level validation was conducted using prevalence rates obtained from survey data in the Global Atlas of Helminth Infections (GAHI) [17]. Data range from 1975 to 2013 and span 17 countries, most in sub-Saharan Africa. We regressed prevalence rates on a 30-year HEI average (1975-2005) and note that results are robust to using average HEI during the 1950 to 1974 pre-period. For locations with observed prevalence rates in more than one year, we use the average (results are unchanged when using the prevalence rate from the first available year instead).

We then calculated the expected change in population at risk by computing the HEI in each grid cell in the year 2100 under both RCPs for the three climate models. Using the estimates from the regression of prevalence on HEI, we calculate the expected value of the change in prevalence in each grid cell under the future HEI, and aggregate to the country and region. Results are presented in ranges to reflect the estimates from both country-level and village-level regressions. To estimate the economic consequences of climate change through changes in hookworm prevalence, a literature review was conducted to identify studies that quantify the economic and human capital effects of hookworm infection and eradication.

III. Results

The average Hookworm Ecology Index during 1996-2005 is mapped in Figure 2. The index is highest in central Africa, the northwestern Amazon, and the southeastern United States. The map also outlines countries with nonzero hookworm prevalence as of 2003 [16], as well as the location of subnational data on prevalence rates used for validation of the index.

Table 2 shows the results from regressing the country/province prevalence rates on the 10-year HEI average for each climate model. The magnitude of the association is consistent across the three climate models and statistically significant at 1 percent levels. A one-standard deviation higher level in HEI of 0.02 translates into a 10% higher level of prevalence.

Table 3 runs the analysis at the village level, and shows that the association between the HEI and village prevalence rates is statistically significant and consistent across climate models, whether or not a country fixed effect is included to absorb all unobserved country-level variables that might confound the estimated effect of HEI on prevalence. Figure 3 graphically shows the within-country relationship between hookworm prevalence and the HEI (in this case constructed using climate data from the Hadley model), clearly showing the strength of the association.

Using the mean of the three coefficients in the model with country fixed effects, a within-country one standard deviation higher HEI of 0.014 translates into a 4 percentage point higher hookworm prevalence rate (0.2 standard deviations). Note that the HEI index explains around 25% of the variation in hookworm prevalence within a country, underlining the important role of ecology in disease prevalence while leaving a large part of variation explained by socioeconomic and public health system factors not in our model.

a. Estimating disease burden

We use the results in Tables 2 and 3 combined with gridded population data for the year 2000 in urban and rural areas [18] and national age distribution data [19] in order to estimate the number of children between ages 0-14 with hookworm infection. At the global level, we estimate 266-342 million children suffer from hookworm infection in the year 2000, of which 96-154 million are in urban areas and 169-188 million are in rural areas. The global estimate is larger than some estimates of around 156 million infections in children ages 0-14 in 2003 [16], though not inconsistent with other global estimates of population at risk of 576 million [2]. Moreover, our estimate of 62-109 million infected children in sub-Saharan Africa is consistent with previous estimates of around 90 million [4].

The HEI can map where hookworm burden will expand geographically, increase in intensity, or disappear as climate change proceeds. The change in hookworm burden will be a nonlinear function of temperature and precipitation: increases in temperature facilitate hookworm transmission below 24 degrees Celsius, while the opposite is true above that threshold. Changes in the hydrological cycle also affect hookworm by facilitating transmission as precipitation levels increase, while reducing transmission at both drought and flooding extremes.

Figure 4 shows the growth in HEI and hookworm expansion under one climate change scenario (RCP 4.5 in the HadGEM2-AO model). An important implication of the model is spatial variation in the direction of the effect of climate change on hookworm. Whereas the model predicts an expansion of the range of ecologically suitable areas for hookworm at high latitudes,

in the western U.S., western China, and parts of the Middle East, the model also predicts an elimination of suitable habitat in the Sahel, the Amazon basin, most of Australia, and much of Europe. Meanwhile, areas where public health consequences might be greatest are those where hookworm is currently endemic and climate change will improve ecological conditions for transmission. These include the horn of Africa, southern Africa, the central Andes, and eastern China.

Table 5 shows the projected change in the number of hookworm infections by region, and climate model, for both RCP 4.5 and 8.5 scenarios, using the current population count and spatial distribution. Averaging across the three climate models, the increase in population infected with hookworm under the RCP 4.5 scenario is 0.77-1.6 million people in urban areas and 0.43-1.22 million people in rural areas. East Asia, Latin America and the Middle East would experience increases in infections, while South Asia would experience a decrease in infections due to changing precipitation patterns. Sub-Saharan Africa would experience a small decrease in infections in urban areas, and a small increase in rural areas. Under the RCP 8.5 scenario, there is an overall decrease in the number of people who would be infected (-0.81 — 2.02 million in urban areas, -2.69 — 6.6 million in urban areas), with both South Asia and sub-Saharan Africa experiencing decreases in prevalence.

b. Health and economic burden due to climate change

Hookworm infection rarely leads to death, however heavy infection leads to lethargy, anemia, growth stunting, and weaker immunological response to other infections. The documented social consequences of hookworm infection include school absenteeism and reduced educational

attainment in children, leading to adverse outcomes as adults in terms of labor force productivity [20].

One way to measure the direct cost of a disease is by modeling cost of treatment. In terms of hookworm, mass drug treatments are conducted by distributing deworming pills, usually in school-based treatment programs. Soil-transmitted helminth infections are treated with ivermectin, albendazole, azithromycin, or praziquantel. These drugs can cost \$0.46 to \$0.90 per patient if economies of scale are achieved by commitment of pharmaceuticals to provide free drugs, synergizing delivery modes, and commitments of communities and schools to distribute the drugs [21]. Table 6 details how public health costs to treat all children infected with hookworm would change under RCP 4.5 and RCP 8.5 scenarios. Assuming that each child receives treatment yearly for 10 years in school, the RCP 4.5 scenario generates an increase of 5.5-25.3 million dollars in treatment costs, while the RCP 8.5 scenario suggests a decrease of 16.2-77.8 million dollars in treatment costs. Public health costs can also be calculated using cost per disability-adjusted life years (DALYs) averted. Using previous estimates of \$2 - \$11 per DALY averted to treat intestinal worms [21], our estimates suggest an increase of up to \$680 million to avert DALYs from hookworm under the RCP 4.5 scenario, and a decrease of up to \$2 billion under the RCP 8.5 scenario. Note that even if global health costs decrease under the RCP 8.5 scenario, East Asia, North Africa and the Middle East will experience increased hookworm burden.

Since most infections occur in childhood age, the economic burden of hookworm occurs through adversely affecting educational outcomes. Estimates from the successful eradication of

hookworm in the American South in 1910 suggest that enrollment, attendance, and literacy increased by 8%, 16%, and 5% respectively in areas where hookworm prevalence was 100 percent [22]. Economic benefits from deworming are also realized later in life with increased income. One estimate suggests that deworming increases the net present value of wages by over \$40 per treated person [21]. An experiment in Kenya measured the positive effects of school-based deworming on health, education, and labor market outcomes and found that a decade after the deworming, moderate to heavy infections decreased by 17%, total years enrolled in school increased by around 0.3 years, and time spent working among men increased by around 17% or 3.49 hours a week [20]. We use these estimates together with the changes in HEI to estimate the change in hookworm's economic burden due to climate change. Table 7 presents the results by region and scenario, showing that under RCP 4.5 changes in hookworm ecology would result in 72-268 thousand fewer children enrolled in school around the world, up to 165 thousand fewer children attaining literacy, and lower incomes for people across East Asia, Latin America, the Middle East and sub-Saharan Africa.

c. Sensitivity Analyses

We analyzed the sensitivity of the results by presenting both RCP 4.5 and 8.5 scenarios from three climate models, and present ranges on our estimates of children at risk, public health costs and human capital losses for both rural and urban areas. These ranges result from the two regression estimates of the association between HEI and hookworm prevalence (the first using country-level data and the second using village-level data) as reported in Tables 2 and 3.

IV. Discussion

The Hookworm Ecology Index method leads to estimates of hookworm prevalence at global level which are consistent with other research. The HEI-based estimate of 266-342 million children suffer from hookworm infection in the year 2000, of which 96-154 million are in urban areas and 169-188 million are in rural areas, is larger than some estimates of around 156 million infections in children ages 0-14 in 2003 [16], though not inconsistent with other global estimates of population at risk of 576 million [2]. Moreover, our estimate of 62-109 million infected children in sub-Saharan Africa is consistent with previous estimates of around 90 million. The forward-looking

The true burden of hookworm decades in the future will, of course, depend on much more than changes in the ecological drivers of transmission. By 2100, factors such as internal and international human migration, economic growth, increased expenditure on infrastructure and public health, increases in social expenditure on education, and technological change will all affect disease burden. While all those factors are difficult to predict and beyond the scope of this paper, this exercise nevertheless serves to provide a magnitude of the impact that climate change-induced ecological change will have on the underlying strength of transmission, holding other factors constant.

V. Conclusion

This paper represents the first assessment of the global effect of climate change on the population at risk and economic burden of hookworm infections. Results suggest that climate change will lead to an intensification of hookworm burden in some regions, and the opposite in

other regions where the optimal temperature threshold is surpassed or changes in precipitation patterns reduce the ecological suitability for hookworm. Understanding the prevalence and spatial distribution of hookworm infections under climate change scenarios contributes to measuring the overall social impact of climate change as well as focusing cost-effective health interventions to areas of greatest need.

Figures and Tables

Figure 1: Data from Nwosu (1978) on the proportion of *Ancylostoma tubaeforme* eggs developing to infective stage as a function of temperature.

Figure 2: Hookworm Ecology Index average from 1998-2005 calculated using the Hadley model. Map created in ArcGIS 10.3. Country boundaries are from gadm.org. Data displayed are authors' calculations.

Figure 3: Within-country relationship between Hookworm Ecology Index and Hookworm Prevalence Rate. Graph shows local polynomial plot with 95% confidence intervals and density of within-country deviation of HEI data values.

Figure 4: Percent change in Hookworm Ecology Index from the 1998-2005 average to the 2099 HEI calculated from the Hadley model. Map created in ArcGIS 10.3. Country boundaries are from gadm.org. Data displayed are authors' calculations.

Table 1: Soil Texture and Hookworm Larva Development

Soil Texture	Total no. of ova per gram	Total no. of larvae per gram	Percent development
Fine sand	56,700	23,195	0.39
Sandy loam	64,700	24,475	0.38
Fine sandy loam	90,200	20,076	0.22
Shale loam	265,550	23,897	0.09
Silt loam	159,200	11,114	0.07
Clay loam	82,300	4,470	0.05
Silty clay loam	36,000	2,045	0.06
Clay	530,900	14,980	0.03

Data from Augustine and Smillie (1926)

Table 2: HEI validation using country-level prevalence data

Dependent Variable: Hookworm Prevalence (%) in 2003			
	(1)	(2)	(3)
HEI	554.5*** (80.90)	545.0*** (81.46)	556.2*** (81.02)
Constant	2.567 (2.590)	3.149 (2.566)	2.892 (2.548)
Climate Model	CCSM4	CESM1-CAM5	HadGEM2-AO
Observations	147	147	147
R-squared	0.245	0.236	0.245

Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Table 3. HEI validation using village-level prevalence data

Independent Variable: 1975-2005 HEI average	Dependent Variable: Hookworm Prevalence (%)					
	CCSM4		CESM1-CAM5		HadGEM2-AO	
	(1)	(2)	(3)	(4)	(5)	(6)
HEI	253.5 (155.1)	251.4** (116.7)	279.3* (151.7)	294.7** (132.1)	323.3* (154.6)	306.1** (137.2)
Constant	15.08*** (3.290)	10.54** (4.116)	14.44*** (3.064)	9.020* (4.656)	13.25*** (3.026)	8.855* (4.730)
Country fixed effect	No	Yes	No	Yes	No	Yes
Observations	1,951	1,951	1,951	1,951	1,951	1,951
R-squared	0.026	0.251	0.033	0.258	0.042	0.259

Standard errors in parentheses, clustered by country

*** p<0.01, ** p<0.05, * p<0.1

Table 4: Estimated School-Aged Children Infected with Hookworm (in millions)

Region	CCSM4		CESM1-CAM5		HadGEM2-AO		Averages		Total Child Population
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural	
East Asia & Pacific	27.37 - 29.82	51.77 - 54.09	27.54 - 31.23	51.67 - 57.08	30.76 - 41.27	51.05 - 55.37	30.6 - 32.06	51.5 - 55.51	129.57
Europe & Central Asia	12.33 - 7.77	4.49 - 7.73	8.29 - 11.35	4.59 - 6.93	7.56 - 10.98	4.29 - 6.77	7.88 - 11.55	4.46 - 7.14	19.12
Latin America & Caribbean	16.74 - 19.04	13.04 - 15.21	16.84 - 19.44	13.22 - 15.58	17.3 - 20.03	13.61 - 16.08	16.96 - 19.5	13.29 - 15.62	25.77
Middle East & North Africa	1.82 - 6.12	1.77 - 5.41	2.07 - 5.26	1.92 - 4.64	2.07 - 5.24	1.98 - 4.66	1.99 - 5.54	1.89 - 4.9	10.51
North America	11.17 - 9.9	2.16 - 2.47	9.82 - 11.18	2.16 - 2.49	9.61 - 10.65	2.09 - 2.34	9.78 - 11	2.14 - 2.43	26.2
South Asia	14.08 - 16.5	47.72 - 53.23	14.29 - 15.62	48.58 - 50.93	14.29 - 15.7	48.83 - 51.35	14.22 - 15.94	48.37 - 51.83	263.13
Sub-Saharan Africa	14.78 - 16.45	48.63 - 49.95	14.57 - 16.2	48.59 - 49.86	14.63 - 122.28	49.94 - 50.8	14.66 - 51.64	49.05 - 50.2	12.1
Total	98.29 - 105.6	169.58 - 188.09	93.42 - 110.28	170.73 - 187.51	96.22 - 226.15	171.79 - 187.37	96.09 - 147.23	170.7 - 187.63	486.4

Table 5: Additional children at risk of hookworm infection under 2100 scenario (in millions), by climate model and RCP

RCP 4.5 (using 1996-2005 and 2100 HEI average)								
Region	CCCSM4		CESM1-CAM5		HadGEM2-AO		Average	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	-0.28 - -0.81	-0.25 - -0.74	0.93 - 1.97	1.87 - 3.98	0.92 - 1.95	1.79 - 3.77	0.52 - 1.04	1.13 - 2.34
Latin America & Caribbean	0.15 - 0.44	0.22 - 0.66	0.72 - 1.53	0.45 - 0.97	0.71 - 1.5	0.24 - 0.51	0.53 - 1.16	0.31 - 0.71
Middle East & North Africa	0.36 - 1.06	0.42 - 1.23	0.3 - 0.64	0.3 - 0.64	-0.1 - -0.21	-0.11 - -0.24	0.19 - 0.49	0.2 - 0.55
South Asia	-0.27 - -0.79	-0.8 - -2.34	-0.44 - -0.94	-1.48 - -3.15	-0.59 - -1.25	-1.65 - -3.48	-0.43 - -0.99	-1.31 - -2.99
Sub-Saharan Africa	0 - -0.01	1.47 - 4.31	0.05 - 0.1	-0.63 - -1.33	-0.18 - -0.37	-0.55 - -1.16	-0.04 - -0.1	0.1 - 0.61
Total	-0.04 - -0.11	1.06 - 3.12	1.56 - 3.3	0.51 - 1.11	0.76 - 1.62	-0.28 - -0.6	0.77 - 1.6	0.43 - 1.22
RCP 8.5 (using 1996-2005 and 2100 HEI average)								
Region	CCCSM4		CESM1-CAM5		HadGEM2-AO		Average	
	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	0.48 - 1.41	0.66 - 1.94	0.24 - 0.51	0.53 - 1.12	0.11 - 0.22	0.86 - 1.81	0.28 - 0.72	0.68 - 1.62
Latin America & Caribbean	-0.21 - -0.61	-0.26 - -0.75	0.04 - 0.09	0.11 - 0.24	0.11 - 0.23	-0.4 - -0.85	-0.02 - -0.1	-0.18 - -0.46
Middle East & North Africa	0.13 - 0.38	0.11 - 0.32	0.04 - 0.09	0.08 - 0.17	0.6 - 1.26	0.76 - 1.6	0.26 - 0.58	0.32 - 0.7
South Asia	-1.1 - -3.24	-3.16 - -9.29	-0.11 - -0.24	-0.1 - -0.21	-0.97 - -2.06	-2.73 - -5.77	-0.73 - -1.84	-2 - -5.09
Sub-Saharan Africa	-0.43 - -1.26	-0.64 - -1.89	-0.58 - -1.24	-0.53 - -1.13	-0.78 - -1.65	-3.36 - -7.1	-0.6 - -1.38	-1.51 - -3.37
Total	-1.13 - -3.32	-3.29 - -9.67	-0.37 - -0.79	0.09 - 0.19	-0.93 - -2	-4.87 - -10.31	-0.81 - -2.02	-2.69 - -6.6

Table 6: Public Health Costs associated with changes in hookworm infections under 2100 scenario (in millions of US\$)

	Drug treatment costs (assuming 10 school years of mass drug treatment)		Cost to avert total DALY (assuming low levels of infection)		Cost to avert total DALY (assuming high levels of infection)	
RCP 4.5						
Region	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	2.41 - 9.32	5.22 - 21.05	1.57 - 17.09	3.4 - 38.59	17.36 - 251.77	37.62 - 568.51
Latin America & Caribbean	2.42 - 10.41	1.41 - 6.41	1.58 - 19.09	0.92 - 11.75	17.44 - 281.22	10.17 - 173.18
Middle East & North Africa	0.86 - 4.45	0.93 - 4.91	0.56 - 8.15	0.61 - 9	6.18 - 120.1	6.72 - 132.53
South Asia	-2 - -8.95	-6.02 - -26.91	-1.3 - -16.41	-3.92 - -49.33	-14.41 - -241.84	-43.36 - -726.76
Sub-Saharan Africa	-0.21 - -0.86	0.45 - 5.47	-0.13 - -1.58	0.3 - 10.03	-1.49 - -23.27	3.26 - 147.83
Total	3.48 - 14.37	1.99 - 10.93	2.28 - 26.34	1.31 - 20.04	25.08 - 387.98	14.41 - 295.29
RCP 8.5						
Region	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	1.27 - 6.44	3.13 - 14.6	0.83 - 11.8	2.04 - 26.77	9.13 - 173.91	22.57 - 394.38
Latin America & Caribbean	-0.09 - -0.87	-0.84 - -4.1	-0.06 - -1.59	-0.55 - -7.51	-0.62 - -23.48	-6.05 - -110.7
Middle East & North Africa	1.18 - 5.19	1.45 - 6.27	0.77 - 9.51	0.95 - 11.5	8.48 - 140.08	10.45 - 169.46
South Asia	-3.36 - -16.6	-9.19 - -45.82	-2.19 - -30.44	-6 - -84.01	-24.18 - -448.48	-66.25 - -1237.71
Sub-Saharan Africa	-2.75 - -12.45	-6.95 - -30.35	-1.79 - -22.83	-4.53 - -55.63	-19.8 - -336.3	-50.09 - -819.69
Total	-3.75 - -18.29	-12.4 - -59.4	-2.44 - -33.55	-8.09 - -108.88	-26.99 - -494.27	-89.37 - -1604.26

Table 7: Human capital loss associated with changes in hookworm infections under 2100 scenario

	Loss/Gain in enrollment (in thousands)		Loss/Gain in full-time school attendance (in thousands)		Loss/Gain in literacy (in thousands)		Loss/Gain in income (in million US\$)	
RCP 4·5								
Region	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	31·85 - 98·8	69·01 - 223·1	65·32 - 164·77	141·53 - 372·07	30·75 - 60·79	66·62 - 137·28	20·95 - 41·43	45·4 - 93·54
Latin America & Caribbean	31·99 - 110·36	18·66 - 67·96	65·62 - 184·05	38·27 - 113·34	30·89 - 67·9	18·01 - 41·82	21·05 - 46·27	12·28 - 28·49
Middle East & North Africa	11·33 - 47·13	12·32 - 52·01	23·24 - 78·6	25·28 - 86·74	10·94 - 29	11·9 - 32	7·45 - 19·76	8·11 - 21·81
South Asia	-26·43 - -94·91	-79·52 - -285·2	-54·2 - -158·28	-163·1 - -475·64	-25·51 - -58·4	-76·78 - -175·49	-17·39 - -39·79	-52·32 - -119·58
Sub-Saharan Africa	-2·73 - -9·13	5·98 - 58·01	-5·6 - -15·23	12·26 - 96·75	-2·64 - -5·62	5·77 - 35·7	-1·8 - -3·83	3·93 - 24·32
Total	46·01 - 152·25	26·45 - 115·88	94·38 - 253·91	54·24 - 193·26	44·43 - 93·67	25·52 - 71·31	30·26 - 63·84	17·4 - 48·58
RCP 8·5								
Region	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural
East Asia & Pacific	16·74 - 68·25	41·39 - 154·77	34·34 - 113·82	84·89 - 258·11	16·16 - 41·99	39·96 - 95·23	11·01 - 28·61	27·23 - 64·89
Latin America & Caribbean	-1·13 - -9·21	-11·09 - -43·44	-2·32 - -15·36	-22·75 - -72·45	-1·09 - -5·67	-10·71 - -26·73	-0·74 - -3·86	-7·3 - -18·21
Middle East & North Africa	15·55 - 54·97	19·17 - 66·5	31·89 - 91·68	39·33 - 110·91	15·01 - 33·82	18·51 - 40·92	10·23 - 23·05	12·61 - 27·88
South Asia	-44·35 - -176	-121·51 - -485·72	-90·97 - -293·52	-249·21 - -810·04	-42·82 - -108·29	-117·31 - -298·86	-29·18 - -73·79	-79·94 - -203·65
Sub-Saharan Africa	-36·32 - -131·98	-91·88 - -321·67	-74·5 - -220·1	-188·44 - -536·46	-35·07 - -81·21	-88·7 - -197·93	-23·9 - -55·34	-60·45 - -134·87
Total	-49·51 - -193·97	-163·92 - -629·56	-101·56 - -323·48	-336·18 - -1049·93	-47·81 - -119·36	-158·25 - -387·37	-32·58 - -81·33	-107·85 - -263·96

Declarations

Authors' contributions: GCM conceived the study and guided analysis, KR collected data and conducted analysis. Both authors wrote the manuscript.

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Figures

Figure 1

Data from Nwosu (1978) on the proportion of *Ancylostoma tubaeforme* eggs developing to infective stage as a function of temperature.

Figure 2

Hookworm Ecology Index average from 1998-2005 calculated using the Hadley model. Map created in ArcGIS 10.3. Country boundaries are from gadm.org. Data displayed are authors' calculations. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

Figure 3

Within-country relationship between Hookworm Ecology Index and Hookworm Prevalence Rate. Graph shows local polynomial plot with 95% confidence intervals and density of within-country deviation of HEI data values.

Figure 4

Percent change in Hookworm Ecology Index from the 1998-2005 average to the 2099 HEI calculated from the Hadley model. Map created in ArcGIS 10.3. Country boundaries are from gadm.org. Data displayed are authors' calculations. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.