

Potential Impact of Climate Change on Schistosomiasis Transmission in China

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Abstract. Appraisal of the present and future impact of climate change and climate variability on the transmission of infectious diseases is a complex but pressing public health issue. We developed a biology-driven model to assess the potential impact of rising temperature on the transmission of schistosomiasis in China. We found a temperature threshold of 15.4°C for development of *Schistosoma japonicum* within the intermediate host snail (i.e., *Oncomelania hupensis*), and a temperature of 5.8°C at which half the snail sample investigated was in hibernation. Historical data suggest that the occurrence of *O. hupensis* is restricted to areas where the mean January temperature is above 0°C. The combination of these temperature thresholds, together with our own predicted temperature increases in China of 0.9°C in 2030 and 1.6°C in 2050 facilitated predictive risk mapping. We forecast an expansion of schistosomiasis transmission into currently non-endemic areas in the north, with an additional risk area of 783,883 km² by 2050, translating to 8.1% of the surface area of China. Our results call for rigorous monitoring and surveillance of schistosomiasis in a future warmer China.

INTRODUCTION

Growing evidence points to emissions of greenhouse gases related to human activities as a key factor of climate change, which in turn affects human health and well-being.^{1–5} On average, the Earth's climate has warmed by about 0.6°C over the past 100 years with temperature increases especially pronounced since the mid-1970s, particularly over land in the northern hemisphere at high altitudes and during the winter months.⁶ Based on the outcome for the average climate for the period 1961–1990, the World Health Organization (WHO) currently estimates that > 150,000 deaths and a burden of 5.5 million disability-adjusted life years (DALYs) can be attributed to climate change and climate variability each year.⁴ An ensemble of recent climate simulations predicts an increase in the mean global temperature from 1990–2100 of 2.4–5.4°C.⁷ Climate warming will be accompanied by perturbations in the global hydrologic cycle,⁸ precipitation, and pronounced changes in water availability.⁹ Collectively, predicted risk profiles of climate-sensitive diseases tend to worsen for most parts of the world, and hence require adaptation and mitigation strategies.^{3,4}

Reviews are available about how climate change and climate variability are likely to affect health, drawing on empirical studies that document past and present risks, and predictive models that conjecture future risks.^{1–5} However, most of the published work focuses on directly acting temperature effects (e.g., excess mortality and morbidity due to heat waves, floods, and droughts), effects on the risk of disasters and malnutrition, and changes in the transmission of infectious diseases.^{1–5} With regard to a changing climate and infectious diseases, most studies have centered on malaria.^{10–15} Time-series analysis and predictions suggest that the population at risk of malaria in Africa will slightly increase due to

rising temperatures, primarily through expansion of the disease into higher altitudes, and lengthened malaria transmission seasons.⁴ The potential impact of climate change on the global distribution of dengue has also been modeled. Under the scenario of contributing factors other than temperature remaining unchanged, the models predict that a large proportion of the human population would be at risk.¹⁶

Only a few attempts have been made to predict changes in the spatial distribution of schistosomiasis transmission due to global warming; results have been conflicting.^{17,18} Although an early model of global warming predicted that the area conducive for schistosomiasis transmission would expand,¹⁷ later models forecasted a decrease in the epidemic potential of schistosomiasis.¹⁸ Although the nature and extent of climate change on the transmission of schistosomiasis remain poorly understood,¹⁹ there is consensus that the most sensitive areas are around the borders of the current transmission.² Clearly, new research is warranted to develop regional climate change models and to assess the biologic significance of model outcomes.^{4,15}

Despite huge efforts in implementing and sustaining the national schistosomiasis control program in China, recent data suggest that the disease is re-emerging.^{20–22} Regional climate change in the face of profound demographic, ecologic, and socioeconomic transformations has been advanced as a contributing factor.^{20,21,23} Here, we present the results from a biology-based model developed with an emphasis on the effects of rising temperature on the future transmission of schistosomiasis in China.

MATERIALS AND METHODS

Digital map and temperature data. A digital map of China (scale: 1:1,000,000) was obtained from the Chinese State Bureau of Surveying and Mapping (Beijing, China). Average daily temperatures from 1951–2000 at 193 observing stations across China were made available from the Chinese National Satellite Meteorological Center (Beijing, China).

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Biologic model and experiments. With the aim of assessing the effect of temperature on different critical stages of the life cycle of *Schistosoma japonicum*, we have developed a biologic model of the parasite and its intermediate host. Some of the data needed to generate this model were available in the literature, while additional laboratory and field experiments had to be carried out to fill some of the current data gaps.

Adult *Oncomelania hupensis*, the intermediate host snail of *S. japonicum* in China,²⁴ were collected in November 2001 from the marshlands in Xinba, Jiangsu province (geographical coordinates: 119.53° E longitude, 32.28° N latitude). Snails were transferred to the laboratory, kept at 25°C and tested for *S. japonicum*-cercarial shedding after 2 and 4 weeks. All snails were non-infected, and hence they were used for assessing the effect of temperature on hibernation of *O. hupensis* as described elsewhere.²⁴ In brief, groups of 30 snails were placed in Petri dishes and transferred to a colder environment (temperature: 13°C). After acclimatization for 2 days, these snails were subjected to constant temperature reductions at a rate of either 0.5 or 1°C per day. Each day, snails with a closed operculum and/or lack of movement were tested by pinching the operculum and the foot-head portion. Snails that showed no reaction were transferred to de-chlorinated water at a temperature of 13°C and kept for 2 hours. When activity resumed, snails were considered in hibernation state before observation by pinching. The remaining snails were subjected to further temperature decreases until hibernation took place. The temperature when this occurred was recorded for each snail.

The duration of a single *O. hupensis* generation was investigated under quasi-natural conditions. In April 2001, 200 adult *O. hupensis* were placed in a container containing mud and covered with a fine-meshed net in open breeding sites in Wuxi, China. As soon as eggs were discovered on the mud, the adult snails were removed and the development of eggs into young adult snails (F_1) followed. Shortly before reaching maturity, the snails were removed, sexed, and couples transferred into separate containers kept in the same open breeding sites. Containers were checked daily for the presence of eggs. The duration from the first discovery of eggs from mother snails until eggs were laid by the F_1 generation was considered a full development period. The ambient temperature was measured hourly throughout the study 1.5 m above ground level by a thermometer (Model ZJ1-2B, Shanghai).

In the third experiment, 750 infection-free *O. hupensis* were collectively exposed to ~ 15,000 *S. japonicum* miracidia (Wuxi isolate) for 4 hours at a temperature of 25°C. These snails were divided into five equally sized groups, placed in culture boxes, and raised at temperatures of 18, 21, 24, 27, or 30°C, respectively. An additional group of 150 snails was left uninfected and kept at a temperature of 24°C. The culture boxes were checked daily and dead snails were removed and counted. The initial cercarial shedding test was done after 30 days (snails kept at 30°C) or 70 days (18°C). Snails that shed cercariae were removed and counted. The remaining snails were tested again 5 days later. This procedure was repeated until no cercariae were released from snails after three consecutive tests. Snails that failed to shed cercariae were dissected to assess their infection status.

Statistical analysis and predictive modeling. For statistical analysis and predictive modeling we used SAS version 8.0 (SAS Institute Inc., NC). A probit analysis was used to es-

tablish the relationship between temperature (T) and the hibernation rate of *O. hupensis* (h), as expressed by Equation 1.

$$\text{probit}(h) = a + b * \log T, \quad (1)$$

where probit (h) is the probability of h , $\log T$ is the natural logarithm of T , a is the intercept, and b the regression coefficient.

The temperature at which 50% of snails were in hibernation (ET_{50}) was considered as the lowest temperature (T_h) for snail development, as shown in Equation 2.

$$T_h = ET_{50} = \log^{-1}(-a/b) \quad (2)$$

We assumed that the temperature at which the development of *S. japonicum* within *O. hupensis* is arrested (T_0) can be estimated from a regression model established between the development rate (d) and the temperature during the prepatent period, which was obtained from the exposure experiment. According to Equation 3, d was estimated as 1 divided by the average prepatent period (N), which is the time from snail exposure to *S. japonicum* cercariae until parasites are shed by the snail, as follows:

$$d = 1/N \quad (3)$$

The accumulated degree-days (ADD) was calculated as the difference between the mean daily temperature (T_{mean}) and T_0 summed over the prepatent period of *S. japonicum* within *O. hupensis* ($ADD_{S.j.}$), and the development period for *O. hupensis* ($ADD_{O.h.}$). Mean values of ADD were calculated according to Equations 4 and 5, based on the experiments carried out under quasi-natural conditions, with units expressed as degree-days.

$$ADD_{S.j.} = \sum (T_{mean} - T_0); T_{mean} > T_0 \quad (4)$$

$$ADD_{O.h.} = \sum (T_{mean} - T_h); T_{mean} > T_h \quad (5)$$

For each observing station i , the $ADD_{S.j.}$ and $ADD_{O.h.}$ were calculated using the respective temperature data and the predicted temperature increases (T_p) for China by 2030 (+1.7°C) and 2050 (+2.2°C)²⁵ according to Equations 6 and 7:

$$ADD_{S.j.(i)} = \sum_{j=1}^{365} (T_{mean(i)} + T_p - T_0); (T_{mean(i)} + T_p) > T_0 \quad (6)$$

$$ADD_{O.h.(i)} = \sum_{j=1}^{365} (T_{mean(i)} + T_p - T_h); (T_{mean(i)} + T_p) > T_h \quad (7)$$

The potential transmission index (PTI) was calculated for each of the 193 observing stations i in 2030 and 2050, according to Equation 8. Only those PTI_i values above 1 were considered to be of relevance (i.e., where *S. japonicum* transmission potentially can occur).

$$PTI_i = PTI_{S.j.(i)} * PTI_{O.h.(i)}; PTI_{S.j.(i)} \text{ and } PTI_{O.h.(i)} > 1, \text{ or } PTI_i = 0 \text{ otherwise} \quad (8)$$

The PTI for *S. japonicum* and *O. hupensis* was calculated from Equations 9 and 10, respectively.

$$PTI_{S.j.(i)} = ADD_{S.j.(i)} / ADD_{S.j.} \quad (9)$$

$$PTI_{O.h.(i)} = ADD_{O.h.(i)} / ADD_{O.h.} \quad (10)$$

Historical data suggest that the distribution of *O. hupensis* in China is restricted by the mean January temperature because snails have not been recorded in areas where the temperature falls below 0°C, the threshold termed the “freezing line.”^{23,26} Using a time-series analytical approach for the period 1951–2000 and the predicted temperature increases for the years 2030 and 2050, we mapped the geographic distribution of the freezing line for these two time points. We used an autoregressive integrated moving average (ARIMA) model^{27,28} for each observing station. Because our recent time-series analysis of the monthly mean temperature in Jiangsu province showed strong seasonality with periodicity of 12 months,²⁹ we developed a seasonal ARIMA(p,d,q)(P,D,Q)₁₂ model. The model with the lowest Akaike’s information criterion (AIC)³⁰ was used for prediction at each station.

Risk mapping. For mapping purposes, we used a kriging approach of the spatial analyst model, employing ArcGIS software version 8.3 (ESRI, Redlands, CA). The ordinary kriging model used is as follows: $Z(s) = \mu + \varepsilon(s)$, where (s) is the vector of locations and $Z(s)$ is the vector of values at the respective locations. This model is based on a constant mean, μ , for the data (no trend), and random errors, $\varepsilon(s)$ assuming spatial dependence.³¹

We adhered to the following six-step procedure. First, we selected the most suitable order to carry out the ordinary

kriging analysis and developed the prediction map based on PTI_i for each observing station. Second, we generated the current distribution of PTI_i , by taking into account the distribution of *O. hupensis* and *S. japonicum* based on the temperature requirements of the intermediate host snail and the parasite to develop within the snail, and the freezing line for the year 2000. Third, these data were fed into a geographic information system (GIS) and used to delineate the potential schistosomiasis transmission area. Fourth, we produced a map with the prediction error (i.e., uncertainty of the prediction). Fifth, a validation of the predicted schistosomiasis transmission risk in 2000 was performed. We used an agreement test estimated by the Kappa coefficient, employing 239 village-level data extracted from the national sampling data in 2004 and 500 points sampled at random from non-endemic areas.^{32,33} Sixth, we produced predictive maps for the transmission of *S. japonicum* in the years 2030 and 2050, which combines the predicted PTI_i and the predicted freezing lines for the respective years.

RESULTS

Biologic model and effect of temperature. Figure 1 depicts schematically a biologic model emphasizing components of

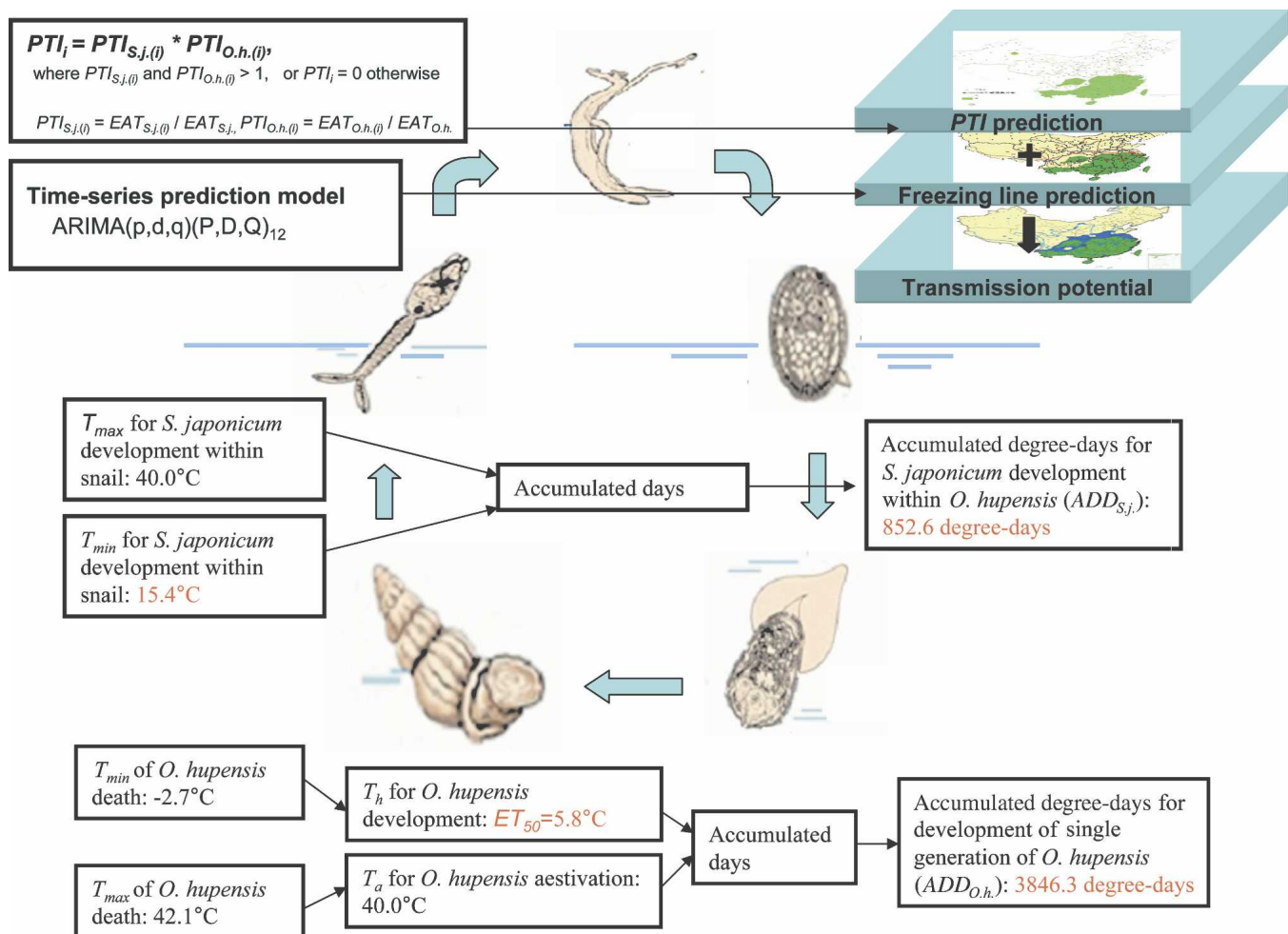


FIGURE 1. Biology-driven model to assess the effect of temperature on individual components of the transmission cycle of *Schistosoma japonicum*. This figure appears in color at www.ajtmh.org.

the *S. japonicum* life cycle that are influenced by temperature. Based on hypothesized future temperatures the aggregation of specific effects on the intermediate host snail, as well as the parasite itself, was then used for predictive modeling (i.e., mapping of the spatial distribution of the potential schistosomiasis transmission areas) in China in the years 2030 and 2050.

At temperatures below 13°C the relationship between temperature (T) and the hibernation rate of *O. hupensis* (h) could be expressed by probit (h) = $3.79 - 4.95 * \log T$ (Pearson goodness-of-fit test: $\chi^2 = 11.6$, $P = 0.394$). The temperature at which half of the snails tested were found in a state of hibernation (ET_{50}) was 5.8°C (95% confidence interval [CI]: 5.5–6.2°C). Subsequently, this value was used for estimating $ADD_{O,h}$, a measure of the thermal energy needed for the development of *O. hupensis*.

Our laboratory investigations revealed a strong association between temperature and the prepatent period of *S. japonicum* within *O. hupensis* (Table 1). At the lowest temperature investigated (21°C), the prepatent period was 128.9 ± 16.1 days, whereas it was halved (62.7 ± 14.2 days) at a temperature of 30°C.

The development rate (d) of *S. japonicum* within *O. hupensis* showed a positive correlation with T , as expressed by the following regression model: $d = 0.025 * \ln T - 0.068$ ($R^2 = 0.53$, $P < 0.001$). The lowest temperature threshold, at which the development of *S. japonicum* within *O. hupensis* ceased (T_0), was 15.4°C (95% CI: 14.2–16.7°C). Taking into account this estimated T_0 , the ADD could be calculated for parasite development in the intermediate host snail; it ranged between 728.2 degree-days (snails kept at a temperature of 21°C) and 919.2 degree-days (30°C). We found a mean $ADD_{S,j}$ of 852.6 degree-days.

Table 2 summarizes the results from the *O. hupensis* development experiments carried out under quasi-natural conditions. Overall, 63 snail pairs were monitored and the minimum and maximum duration to complete a full generation was 200 and 385 days, respectively. The observed mean of the $ADD_{O,h}$ to complete a single generation was 3846.3 degree-days.

Predictive risk modeling. For predictive modeling using the ARIMA model, the time-series of the mean monthly temperatures at each observing station was first converted into a stationary one by means of a single seasonal differencing operation, using 0 for parameter d and 1 for parameter D in ARIMA(p,d,q)(P,D,Q)₁₂. Next, an autocorrelation function

TABLE 2

Development duration, accumulated temperature, and accumulated degree-days ($ADD_{O,h}$) of *O. hupensis* ($n = 63$ snail pairs), kept under quasi-natural conditions

Feature	Minimum	Maximum	Mean \pm SD
Development duration for one generation of <i>O. hupensis</i> (days)	200	385	334.2 ± 7.5
Accumulated temperature (degree-days)	4683.1	6558.9	5821.4 ± 70.1
$ADD_{O,h}$ (degree-days)	3509.1	4402.1	3846.3 ± 32.6

(ACF) and a partial autocorrelation function (PACF) was used for each series and we found that the autocorrelation coefficients were significant at non-seasonal lag 1 and/or the first seasonal lag 12. Thereafter, we compared the AIC values of all possible ARIMA(p,q)($P,1,Q$)₁₂ models for each series, respectively, with parameters p , q , P and Q set either 0 or 1. Approximately half of the best fitting models with lowest AIC values were ARIMA(1,0,1)(0,1,1)₁₂. Another 24.5% of the models were ARIMA(1,0,0)(0,1,1)₁₂. Finally, based on the best fitting models, the mean monthly temperatures at each observing station were predicted for the next 50 years.

Table 3 summarizes the historical mean January temperatures derived from 193 stations across China from 1960 to 2000. These data suggest that the median of the average January temperature over the mainland of China has significantly increased by 0.9°C over the past 40 years (Friedman test, $\chi^2 = 478.0$, $P < 0.001$). The median of the predicted average January temperatures for 2030 and 2050 are -3.8°C and -3.1°C , respectively. Compared with 2000, these medians translate to increases of 0.9 and 1.6°C ($P < 0.001$).

Figure 2 depicts the risk map for schistosomiasis transmission and the respective prediction error distribution map in China as of 2000, taking into account the various critical temperatures that govern the transmission cycle of the disease. We found a good agreement between the predicted risk map for schistosomiasis transmission and the parasitological data from the national sampling survey in 2004; the validation agreement test showed a Kappa coefficient of 0.70 ($P < 0.001$). It should be noted, however that the current distribution map of schistosomiasis in China²⁰ is influenced by past and ongoing control efforts, as shown in a recent time-series analysis of the spatio-temporal distribution of *S. japonicum* in Jiangsu province.³⁴

TABLE 1

Relationship between temperature (T) and the prepatent period (N), and estimates of the accumulated degree-days ($ADD_{S,j}$) of *S. japonicum* for development within *O. hupensis*

T (°C)	N^* (days)	NT^* (degree-days)	$T_{mean} - T_0^*$ (°C)	$N * (T_{mean} - T_0)^{\dagger}$ [= $ADD_{S,j}$] (degree-days)
18	—	—	—	—
21	128.9 ± 16.1	2706.7 ± 337.0	5.65	728.2 ± 90.7
24	95.0 ± 21.0	2280.0 ± 504.8	8.65	821.8 ± 181.9
27	71.9 ± 12.7	1942.1 ± 344.0	11.65	828.0 ± 148.4
30	62.7 ± 14.2	1882.2 ± 425.7	14.65	919.2 ± 207.9
Mean $ADD_{S,j}$				852.6 ± 183.1

* Values are expressed as means \pm standard deviation (SD).

$\dagger T_0 = 15.4^\circ\text{C}$.

Modified from ref. 24.

TABLE 3

Median, lower, and upper quartile of mean January temperatures across China in 1960, 1970, 1980, 1990, and 2000, and predicted mean January temperatures for 2030 and 2050

Year	Temperature (°C)		
	Median	Lower quartile (Q_1)	Upper quartile (Q_3)
1960*	-5.6	-14.9	4.9
1970*	-5.6	-14.4	3.5
1980*	-5.0	-13.9	5.0
1990*	-4.3	-12.3	5.3
2000*	-4.7	-15.1	4.5
2030†	-3.8	-11.6	5.3
2050†	-3.1	-10.8	5.7

* Measured and averaged temperature values.

† Predicted temperature values.

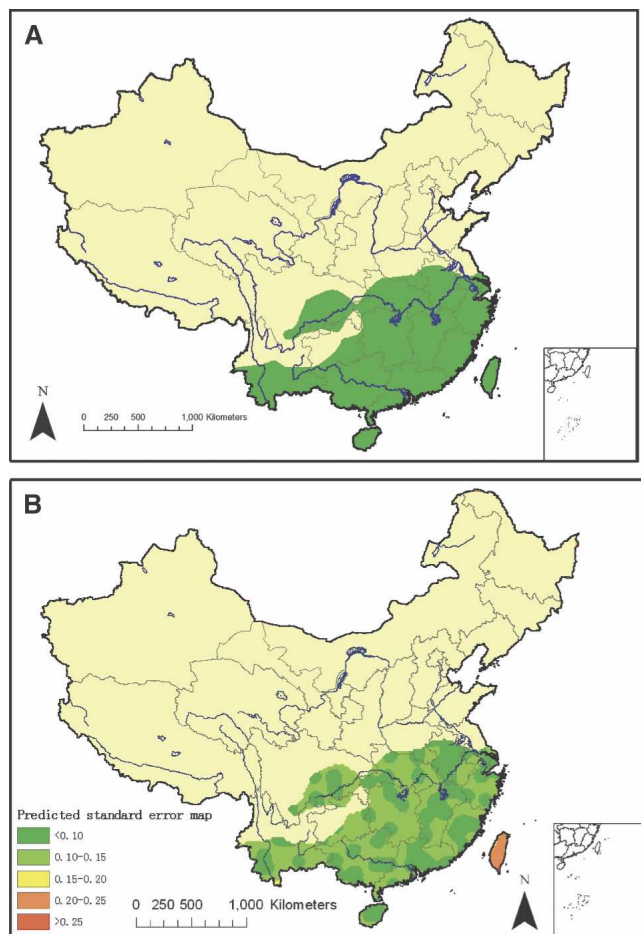


FIGURE 2. Risk map of schistosomiasis transmission in China in 2000 (A) (green color denotes potential risk areas for schistosomiasis transmission), and corresponding prediction error distribution map (B).

Predictive risk maps for transmission of schistosomiasis in China in the years 2030 and 2050 are depicted in Figure 3. Comparison with the situation in 2000 reveals that the potential transmission areas of the disease will significantly expand; we estimate that by 2030 an additional 662,373 km², and by 2050 an estimated 783,883 km², might become potential risk areas for schistosomiasis transmission. Disease transmission is thus likely to occur in previously non-endemic areas, such as the southern parts of Shandong and Henan provinces. Interestingly, there is another part in north-western China where disease transmission is predicted on the basis of the *PTI*. However, taking into account the predicted spatial distribution of the freezing line, it is unlikely that disease transmission can occur north of this freezing line, and hence the north-western part of China is likely to remain schistosome-free.

DISCUSSION

The national schistosomiasis control program in China, launched in the mid-1950s and sustained over the past 50 years, is widely acknowledged as one of the most successful disease control programs since implemented.^{20,21,35} The number of human infections has been reduced by over 90% reaching a historic low level of just below 700,000 infections in the

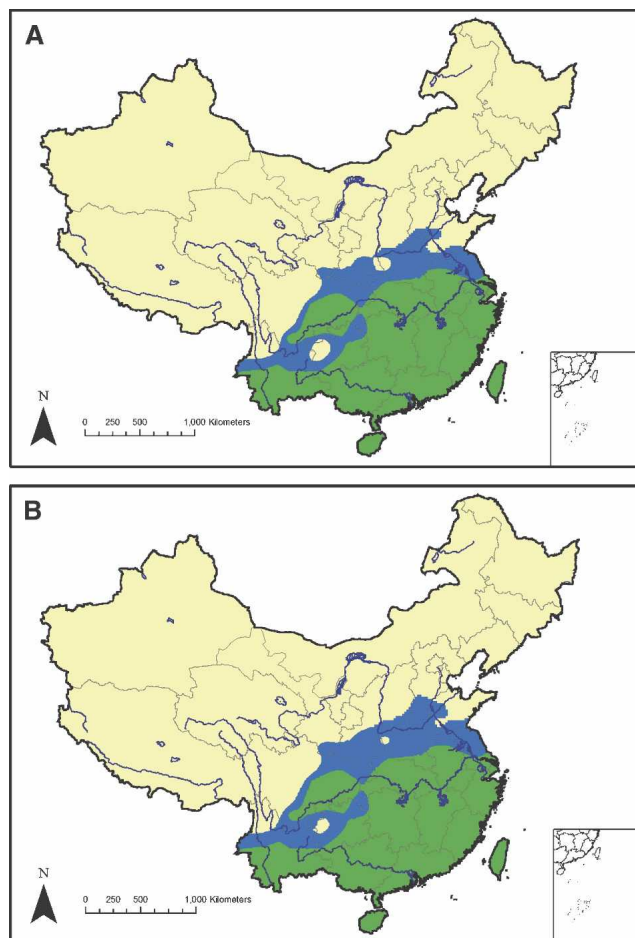


FIGURE 3. Predicted risk map of schistosomiasis transmission in China in 2030 (A) and 2050 (B) (green color denotes potential risk areas for schistosomiasis transmission in 2000, and blue color denotes predicted additional risk areas).

year 2000.^{20,21} However, recent data suggest that schistosomiasis is re-emerging in some settings that had previously reached the criteria of either transmission control or transmission interruption.²² Along with other reasons, climate change and ecologic transformations have been suggested as the underlying causes.^{20,21,23,36,37}

Our attempt to assess the potential impact of climate change on the transmission of schistosomiasis in China was facilitated by the development of a biologic model, which was conceived by readily available data from the literature and supplemented by new data obtained from laboratory and field investigations. Emphasis was placed on the effect of temperature on individual components of the disease transmission cycle. Three findings warrant special mention. First, historical data suggest that the distribution of *O. hupensis* in China is restricted to areas where the mean January temperature is above 0°C, which roughly corresponds to 33.25° N latitude.^{23,26} Consequently, the mean January temperature can be used to delineate a “freezing line” north of which *O. hupensis* cannot survive, and hence transmission of *S. japonicum* would not be possible. Second, our laboratory experiments found a temperature of 5.8°C as the physiologic tolerance of *O. hupensis*. With regard to the development of *S. japonicum* within *O. hupensis*, a temperature of 15.4°C was found as the

lowest threshold. Below this temperature, parasite development within the snail is arrested. Third, taking into account the previously mentioned temperature thresholds, we estimated the mean *ADD* for the development of *S. japonicum* in its intermediate host snail as 852.6 degree-days, and the mean *ADD* for the development of a generation of *O. hupensis* as 3846.3 degree-days. The aggregation of these findings, coupled with predicted temperature increases in China by 2030 and 2050, allowed us to draw up future risk maps for schistosomiasis transmission.

According to available temperature data for 1960 and 2000, the median January temperature, averaged across the 193 observing stations in China, increased by 0.9°C. This finding corroborates another recent time-series analysis, based on the average January temperatures from an ensemble of 652 observing stations in China, which found a temperature increase of 0.96°C between the 1960s and the 1990s.²³ It has been predicted, on the basis of recent meteorological models using mean annual temperatures for the whole of China, that the mean temperature will continue to rise; indeed at an accelerated pace with predicted increases by 2030 and 2050 of 1.7 and 2.2°C, respectively.²⁵ Our own model predictions are somewhat lower but they point in the same direction. We predict that the mean January temperature in China will increase by 0.9 in 2030 and by 1.6°C in 2050. Based on our biologic model, these temperature increases will result in an altered disease transmission, which will extend northward into currently non-endemic areas. For 2050 we predict that a surface area of 783,883 km² might become at risk of schistosomiasis transmission, which translates to 8.1% of the total surface area of China. It is also conceivable that the transmission intensity will increase in areas already endemic for schistosomiasis. Our predictions are of considerable concern because they might explain, at least partially, the recent observations of re-emergence of schistosomiasis in areas where the criteria for transmission control, or even interruption, had been achieved.^{20–22}

A limitation of our current modeling approach is that it emphasizes the role of temperature, but does not take into account the role of rainfall and the potential interaction between temperature and rainfall. It is difficult to say whether our model is conservative or whether these additional effects might further amplify the extent of changes predicted on the basis of temperature alone. Thus, recent improvements in modeling global trends in streamflow, precipitation, and water availability⁹ should become an integral part of present and future predictions of climate change and variability on infectious disease dynamics, including schistosomiasis. Flooding of the Yangtze River is implicated in snail dispersal and epidemic outbreak of schistosomiasis.³⁷ However, floods usually originate far away, in the Tanggula mountains and only partially from local heavy rains.

Finally, our predictions of the potential impact of regional climate change on the transmission of schistosomiasis in China must be juxtaposed to profound demographic, ecological, and socioeconomic changes that are taking place in this part of the world.³⁸ Recently, it has been emphasized that the interplay of climate change and health should not be viewed in isolation, but rather be taken into account alongside other ecological changes and socioeconomic development.⁴ This claim is particularly pertinent in the case of China where huge ecological transformations are underway, most notably

the implementation of water-resource development projects, such as the Three Gorges dam³⁶ and the South-to-North water transfer project.^{23,39,40} The implementation and maintenance of water-resource development projects have a history of facilitating the transmission of schistosomiasis,⁴¹ and hence it is likely that such projects in China, in the face of a warming climate, will have a huge impact on schistosomiasis. Rigorous monitoring and surveillance thus is of pivotal importance if the goal of schistosomiasis elimination from China should not be compromised.

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