

A GROWING DEGREE-DAYS BASED TIME-SERIES ANALYSIS FOR PREDICTION OF *SCHISTOSOMA JAPONICUM* TRANSMISSION IN JIANGSU PROVINCE, CHINA

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Abstract. It has been suggested that global warming may alter the frequency and transmission dynamics of vector-borne diseases. To test this claim for schistosomiasis, we conducted a time-series analysis from 1972–2002 for 39 of the 70 counties of Jiangsu province, eastern China, where *Schistosoma japonicum* is partially endemic. We used a modeling approach to estimate the annual growing degree-days (AGDD), employing a lower temperature threshold of 15.3°C. Our final model included both temporal and spatial components, the former consisting of second order polynomials in time plus a seasonality component, whereas the spatial trend was formed by second order polynomials of the coordinates plus the thin-plate smoothing splines. We found that temperature increased over the past 30 years in all observing stations. There were distinct temporal trends with seasonality and periodicities of 12, 6, and 3 months, whereas only marginal spatial variation was observed. The predicted AGDDs for 2006 and 2003 showed increases for the entire Jiangsu province, with the AGDDs difference between these two time points exhibiting an increase from north to south. Our data suggest that changes in temperature will alter the extent and level of schistosomiasis transmission, which is relevant for the control of *S. japonicum* in a future warmer China.

INTRODUCTION

Temperature is a key feature for the timing of biologic processes, and hence the growth and development of living biota. The amount of heat energy an organism accumulates is often expressed as a unit termed “growing degree-day” (GDD).^{1–4} GDD can be articulated as $T_{avg} - T_{base}$, where T_{avg} is the average daily temperature, and T_{base} is the base temperature or developing threshold of an organism.^{5,6} This threshold is often considered as the lowest temperature below which growth and development does not occur. Two different interpretations have been reported with regard to how T_{base} is incorporated into the above GDD equation.⁵ The most widely used application, particularly in simulation models, is as follows: if T_{avg} is less than T_{base} , then T_{avg} is set equal to T_{base} , and hence GDD becomes 0.^{5–8} Some applications also used an upper threshold, since temperatures exceeding a critical value result in slower development of an organism or its development is ceased altogether.⁹

Growing degree-day can be summed over an entire year. It is then termed annual GDD, AGDD in short, which is an important aggregate measure that has been found to correlate with the spatial distribution of living organisms.^{10–12} The heat units an organism requires to complete its development are fairly constant, given by the temperature above a critical threshold summed over the time period this lower temperature threshold is exceeded. It follows that organisms with high heat unit requirements are more likely to develop into mature stages in areas where AGDD is high.¹³

There is mounting evidence of climate change due to anthropogenic activities, namely increased release of greenhouse gases into the atmosphere.^{14–18} The predicted warming will result in increased AGDD, and hence alter biologic processes and physical systems, including human health.¹⁷ Al-

though the relation between climate change and human health is a complex one, it has been estimated that > 150,000 deaths per year are attributable to global warming and changes in precipitation that occurred over the past 30 years.^{19,20} Several studies have been carried out to predict phenological changes under the scenario of warmer ambient temperatures, including the use of GDD.¹⁰ For example, Malone and colleagues²¹ used a modified forecast system based on GDD and the local Thornthwaite water budget to predict the risk of fascioliasis transmission in East Africa. The T_{base} used in the forecast system was 10°C for *Fasciola hepatica* and 16°C for *F. gigantica*. In another application, a GDD-water budget analysis was combined with satellite climatology to assess the thermal-hydrological preferences and limits of tolerance of different parasite-vector communities, and hence to delineate the environmental foci of disease agents.^{22,23}

With regard to schistosomiasis, only few attempts have been made thus far to predict changes in the frequency and transmission dynamics due to global warming.^{24–27} The two studies by Martens and colleagues^{25,26} came to different conclusions regarding the extent of schistosomiasis transmission under the scenario of a warmer climate. Among other reasons the lack of long-term, high-quality datasets may explain the reported discrepancy.

Focusing on distinct eco-epidemiologic settings in eastern China, with a sound knowledge-base on intermediate host snail biology, and an existing temperature dataset, we performed a time-series analysis spanning a 31-year period commencing in 1972, to develop a regional climate model. The established model was then used to predict the monthly temperatures between 2003 and 2006 at a spatial resolution of 0.01 degrees longitude and latitude. Employing a previously determined lower temperature threshold for *Schistosoma japonicum* larvae development in the intermediate host snail, the predicted temperatures were then transformed to a measure of AGDD, to forecast the transmission of schistosomiasis japonica. This study forms part of a comprehensive investigation of the effects of climate change on the frequency and transmission dynamics of schistosomiasis in China.²⁸

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MATERIALS AND METHODS

Study area. We focus on Jiangsu province, located in eastern China. This is one of the 7 provinces in China where *S. japonicum* remains endemic.^{29,30} Transmission of the disease is restricted to the southern parts of the province, which has been explained by temperature suitability for the intermediate host snail (i.e., *Oncomelania hupensis*).^{31,32}

Temperature data. Temperature data, covering the period from 1972–2002, were purchased from Wuxi Meteorological Center (Wuxi, China) for 39 of the 70 counties (56%) of Jiangsu province. Monthly mean temperatures were derived by averaging the continuous temperature data. Since the exact positions of the observing stations were not available, we assumed that the data were obtained at the centroids of the respective counties. The coordinates (latitude and longitude) of the counties' centroids were extracted in ArcGIS 8.2 software (ESRI; Redlands, CA, USA). As shown in Figure 1, the selected counties are evenly distributed across Jiangsu province.

Statistical analysis. Data management and statistical analysis were carried out in SAS software (SAS Institute Inc.; Cary, NC, USA). Spatio-temporal models were fitted to the monthly mean temperature data assuming a normal error distribution. Different models were fitted describing the spatial and temporal effects by temporal harmonic curves, month effects, temporal and spatial polynomial trends, north-south differentials, county effects, spatial thin-plate smoothing splines, and interactions thereof. Models with spatial and temporal random effects were also fitted. The Akaike's information corrected criterion (AICC)³³ was used to identify the best fitting model, as determined by the smallest AICC.

The final model with the best fit captured the temporal trend via second order polynomials and seasonality through harmonic curves. This model also included a spatial trend term, consisting of second order polynomials of the coordinates plus thin-plate smoothing splines.³⁴ A detailed mathematical description of the model is presented in the Appendix.

For future predictions, the previously mentioned spatio-temporal model was projected on a regular grid of 0.01 degrees resolution between 116 and 122 degrees longitude and between 31 and 35 degrees latitude for the period 1972–2006. This spatial resolution corresponds to approximately 1×1 km.

The AGDDs of *S. japonicum* for the years 2003 and 2006 were estimated on the basis of a lower temperature threshold of 15.3°C . This value was established in our preceding laboratory investigations; it represents the lowest temperature at which *S. japonicum* larvae develop in *O. hupensis*. Let $AGDD_{it}$ be the value at location i in the year t as follows:

$$AGDD_{it} = 30 \sum_{j=1}^{12} (C_{ijt} - 15.3) \times 1(C_{ijt} > 15.3) \quad (1)$$

where $1(\cdot)$ is the indicator function, giving the value 1 if the condition in the parenthesis is true and 0 otherwise. C_{ijt} is the temperature in $^{\circ}\text{C}$ at location i in month j and year t . The $AGDD_{diff}$ was derived by subtracting the predicted AGDD for the year 2006 with that of 2003.

RESULTS

Temperature trend analysis for 1972–2002. Figure 2 shows the time-series of monthly mean temperatures between 1972

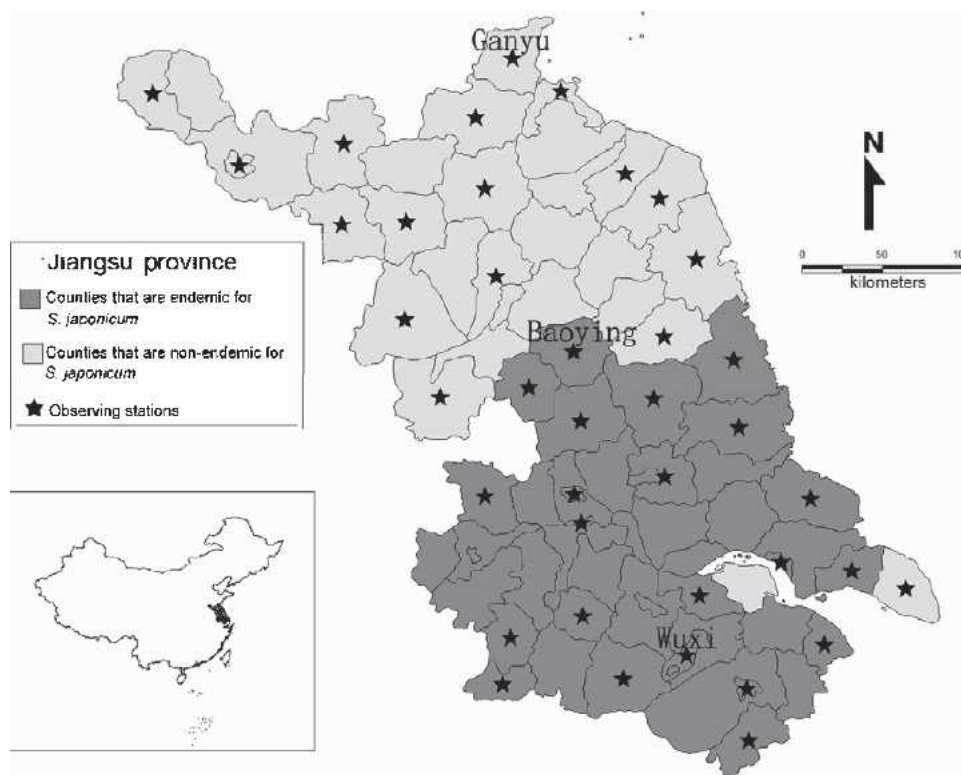


FIGURE 1. Map of Jiangsu province located in eastern China along the Pacific coast. Counties shaded in dark represent *Schistosoma japonicum*-endemic areas. The centroids of the 39 counties from which temperature data were available are indicated with asterisks.

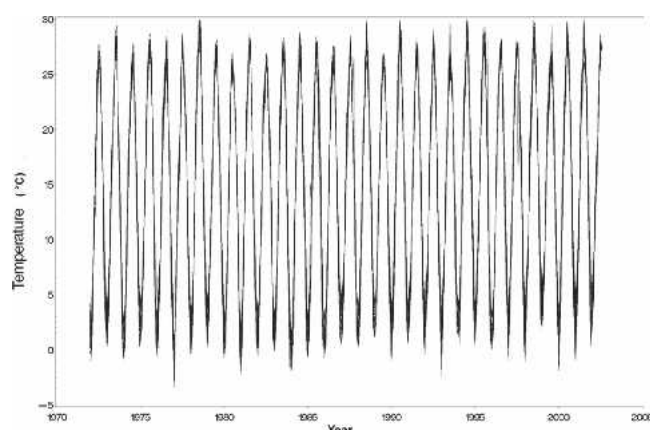


FIGURE 2. Monthly mean temperatures for the period 1972–2002 for the 39 selected counties in Jiangsu province, China.

and 2002 for the 39 counties of Jiangsu province where temperature data were available. The plot depicts a strong temporal pattern, as expected by seasonality. We observed only very small spatial variation using the county as the unit of analysis.

The estimated periodogram for all 39 locations is shown in Figure 3. It confirms the seasonality with periodicities of 12 months (largest peak with frequency $1/12 = 0.08$), 6 months (second largest peak with frequency $1/6 = 0.17$), and 3 months (local mode in the right part with frequency $1/3 = 0.33$).

The best fitting spatio-temporal model according to the AICC consisted of a polynomial spatio-temporal trend, and temporal harmonics of periodicities 3, 4, 6, and 12 months. Parameter estimates of the regression model are shown in Table 1. The time-variable counts the number of months, commencing in January 1972. It shows a small downward trend in its linear component, but is dominated by the strong positive increase in the quadratic part. The sines and cosines fitted are numbered following the frequency orders (i.e., $1/12$, $1/6$, $1/4$, and $1/3$). The harmonic curves with higher frequencies were not found statistically significant.

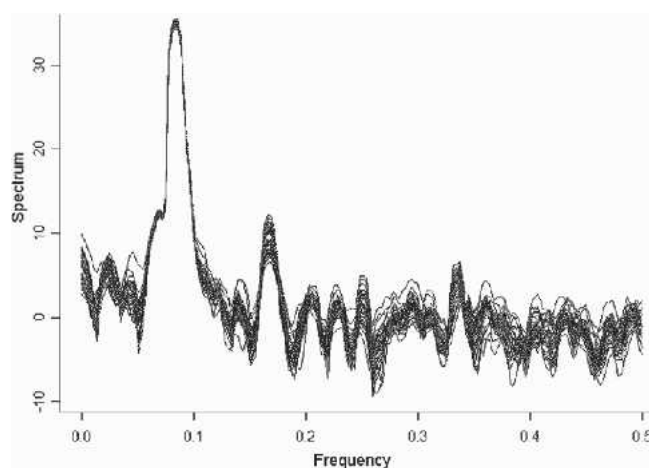


FIGURE 3. Estimated periodogram (Daniell smoother) of the detrended time-series of monthly averaged temperatures for the 39 selected counties of Jiangsu province, China.

A decrease in the absolute value of parameter estimates for the harmonic curves was found with decreasing periodicity. The least significant curve had a periodicity of 3 months. The parameter estimates for the coordinates indicated a spatial trend in temperatures ranging from southeast to northwest with highest predictions of temperature increases in the southeastern part of Jiangsu province.

Temperature forecasts and risk prediction of schistosomiasis transmission. The time-series of predicted mean temperatures for 1972–2006 is depicted in Figure 4A. It revealed an increase in the temporal trend, particularly since the early 1990s. The AICC indicated that the variation in mean temperature is largely explained by seasonality, rather than spatial differentials. In the absence of a spatio-temporal interaction, we pooled the data and only present the overall temporal trend, which included the seasonality, as well as a second order polynomial trend.

The standard error of predicted temperatures for three selected cities—Ganyu in north, Baoying in central, and Wuxi in south of Jiangsu province—is depicted in Figure 4B.

The $AGDD_{2003}$, $AGDD_{2006}$, and $AGDD_{diff}$ were calculated based on the predicted temperature from the fitted regression model, and are presented in Figure 5. The predicted AGDD increased gradually from north to south in both 2003 and 2006. The regions with different AGDD levels in 2006 (Figure 5B) showed a northward shift, which occurred after 2003 (Figure 5A). Figure 5C predicts an increase in the estimated difference in AGDD between 2006 and 2003 for the entire Jiangsu province. The predicted increase in AGDD was particularly pronounced in the southern part of the study area.

DISCUSSION

It has been estimated that the increase in temperature and changes in precipitation that occurred at an unprecedented pace over the past 30 years were responsible for the losses of as many as 150,000 lives and 5 million disability-adjusted life years per annum worldwide.¹⁹ Currently available climate models consistently predict that the global mean temperature

TABLE 1

Parameter estimates for the monthly averaged temperature data from 1972–2002 for the 39 selected counties in Jiangsu province, China, using a regression model

Parameter	Estimate	95% Confidence interval
Intercept	−691.46	−1137.98, −248.30
Longitude	10.62	4.21, 17.10
Latitude	5.46	1.49, 9.47
Longitude * Latitude	−0.051	−0.085, −0.018
(Longitude) ²	−0.038	−0.061, −0.015
Time	−0.0026	−0.0033, −0.0019
(Time) ²	0.000018	0.000016, 0.000019
Cosine 1	−12.42	−12.44, −12.39
Sine 1	−1.38	−1.40, −1.35
Cosine 2	−0.51	−0.53, −0.48
Sine 2	0.41	0.39, 0.44
Cosine 3	−0.24	−0.26, −0.21
Sine 3	−0.12	−0.14, −0.09
Cosine 4	0.17	0.15, 0.20
Sine 4	0.26	0.23, 0.28
σ^2	1.41	1.38, 1.45

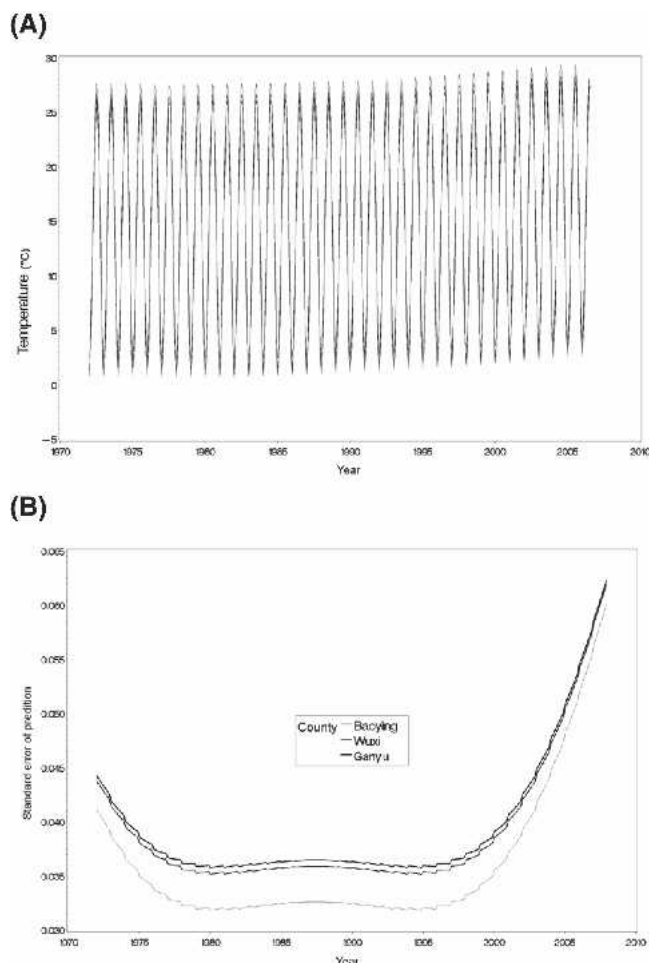


FIGURE 4. Predicted mean average temperature for the three cities Ganyu (north), Baoying (central) and Wuxi (south) for the years 1972–2006, based on data for the years 1972–2002. (A), Predicted monthly temperature. (B), Standard error of prediction.

will continue to rise—according to different assumptions—by a range of 1.4°C–5.8°C until 2100 when considering 1990 as the reference benchmark.¹⁶ An important feature of global warming is the strong heterogeneity both in space and time. For example, the temperature increases in continental and high latitude regions are higher than those in coastal and tropical regions. Meanwhile, worldwide winter temperature is predicted to increase more pronouncedly than during the summer.^{35,36}

In China, the current trend of warming will also continue in the 21st century, based on plausible extrapolations using different models.³⁷ We have recently documented that the mean January temperature in China has increased by almost 1°C over the past 30 years.²⁴ In some parts of northern China increases exceeding 3°C were noted over this period for the month of January. The present study not only confirmed that China's temperature is warming, but further predicted a growing trend in the years to come. Our predictions are based on a time-series analysis utilizing monthly mean temperatures over a 31-year period, collected in an ensemble of 39 observing stations across Jiangsu province. One must bear in mind that variability of the prediction becomes larger when extrapolated values are further away from the present time. There-

fore, the current study only predicted temperatures until the year 2006, since higher standard error for future prediction renders the prediction less reliable (see Fig. 4B). In any event, the mean temperature in January 2006 in Baoying county (3.2°C) was predicted to be 0.4°C higher than that in January 2003 (2.8°C).

Our current working hypothesis is that an increase in AGDD will alter the extent and level of schistosomiasis transmission in China. The underlying principle is that the number of parasite generations will increase by speeding up their development in longer growing seasons and extending the current area where parasite larvae and intermediate host snail can proliferate.^{38,39} As expected, our prediction maps revealed that AGDD in the southern part of Jiangsu province is higher than in the northern part. Thus transmission intensity of *S. japonicum* in south Jiangsu is expected to be higher than in the north of the province. Previous research established a minimum GDD of 842.9 for development of *S. japonicum* larvae in the intermediate host snail.⁴⁰ It follows that *S. japonicum* can only thrive in areas where AGDD exceeds this threshold, which is at the root of Figures 5A and 5B. From the maps depicted on these two figures we can speculate that *S. japonicum* transmission could occur in the whole Jiangsu province. However, this will require availability of suitable snail habitats and means to spread the snails there (e.g., networks of natural and artificial water courses). Another crucial feature is the mean January temperature, as previous research has shown that *O. hupensis* can only survive in areas with mean January temperatures exceeding 0°C. This in turn delineates the potential transmission zones of the disease. Our recent work suggests that the distribution limits of *O. hupensis*, driven by the January 0–1°C isotherm, has shifted from 33°15' N latitude to 33°41' N latitude between the 1960s and the 1990s, which can be explained by global warming.²⁴ We have speculated that *S. japonicum* thus can be transmitted in these new areas, given that there are suitable breeding sites for *O. hupensis*. Indeed, previous experiments with *O. hupensis* kept in cages showed that the snails can survive and reproduce further north of the current endemic areas.⁴¹

Our time-series analysis found that the temperature increase in the southern part of Jiangsu province is considerably higher than in the northern part, which seems to contradict the global picture^{35,36} and our previous results from China.²⁴ One possible reason for this discrepancy is that previous reports were based on studies conducted at large scales (i.e., global or continental regions), whereas the current study focused on a relatively small scale (i.e., a single province within China). Fundamental challenges arise for pattern recognition and the interfacing of phenomena that occur at different scales of space, time, and organizational complexity.^{42–44} Another reason might be the differences in topography; whereas the southern part of Jiangsu province is hilly, the northern part is flat. Previous studies suggested that the impact of climate change is more sensitive in mountainous areas than in lowland regions. Taken together, scaling, spatio-temporal pattern recognition, and topography are important issues to be considered for risk prediction of schistosomiasis under the scenario of a warmer future world.

The data used in the current study were average monthly temperatures. Whereas T_{avg} has been widely used for estimating GDD, particularly for modeling,⁵ other applications

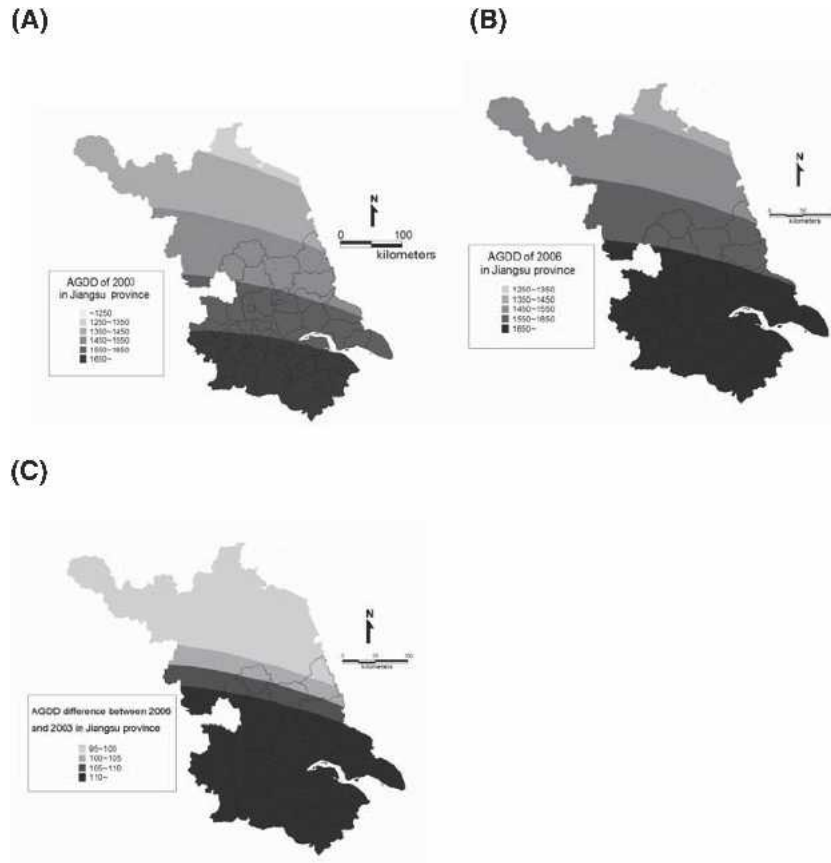


FIGURE 5. Annual growing degree-days (AGDD) for 2003 (A) and 2006 (B), and the AGDD difference (AGDD_{diff}) between 2006 and 2003 (C) in Jiangsu province, China.

used minimum (T_{min}) and maximum temperatures (T_{max}). Depending on whether T_{avg} or half the sum of T_{max} plus T_{min} are used, the T_{base} , and hence estimation of GDD, can vary.⁵ In the current study, daily night-time minimum or daily day-time maximum temperatures were not available. This in turn could add a bias to the study results, since the development of parasite larvae in the intermediate host snail could cease when the night-time minimum temperature drops below a critical threshold or the day-time maximum temperature exceeds an upper threshold. It has been reported that natural temperature fluctuations aid the development of parasite larvae in the intermediate host snail,²⁸ which had not been taken into account when estimating the parasite temperature threshold (i.e., 15.3°C), as it was done under stable laboratory conditions. Other sources of potential biases in predicting temperature changes are that night-time minimum temperatures are expected to increase more than daytime maximum temperatures and, as articulated before, winter temperatures are predicted to increase more pronouncedly than summer temperatures.^{35,36} Furthermore, in the absence of exact geographical coordinates of the observing stations, we assumed that temperatures were obtained from the centroids of the respective counties. Since counties in Jiangsu are small, numerous, and similarly shaped, it is unlikely that the placement of location at the county centroids introduced a severe bias, and our analysis is not sensitive to the approach chosen for selection of the location.

It is important to note that the key feature of using heat unit accumulation as expressed in GDD is that it focuses entirely on temperature, and that this measure has been widely and effectively used to describe timing of biologic processes. Various modifications have been suggested to enhance the biologic meaning of the GDD equation.⁵ In future applications, it will be interesting to incorporate other factors, such as human activities, including changes in agro-ecosystems, water-resource development, and management and rapid urbanization, since they can alter climate change at regional levels.^{45,46} The previously mentioned points illustrate that the prediction of global warming at different scales is a very complex manner. Further studies are warranted to improve upon the present time-series analysis model by considering other factors than temperature.

We conclude that climate change has occurred in China over the past 30 years.^{24,28} It is predicted that temperature will continue to increase in the years to come, which is likely to bring along a myriad of implications, including altered frequency and transmission dynamics of schistosomiasis japonica. This in turn might jeopardize progress made for transmission control or even interruption since the launch of China's national schistosomiasis control program in the mid-1950s.^{29,30} Rigorous surveillance⁴⁷ will be mandatory also in previously schistosome-free areas, so that further progress can be made with the ultimate goal of eliminating schistosomiasis from the mainland of China.

APPENDIX

Let C_{ijt} be the monthly average temperature in °C at location $i = 1, \dots, 39$ in month j and year t . We fit a linear regression model on C_{ijt} of the form:

$$C_{ijt} = \mu(jt)_{\text{temporal}} + \mu(i)_{\text{spatial}} + \varepsilon_{ijt}, \quad \varepsilon_{ijt} \sim N(0, \sigma^2)$$

The term $\mu(jt)_{\text{temporal}}$ captures the temporal trend and consists of a second order polynomial in time and an additive component h_t to describe seasonality as follows:

$$h_t = \sum_{i=1}^4 [\alpha_i \cos(t \times i \times \pi/6) + \beta_i \sin(t \times i \times \pi/6)]$$

The term $\mu(i)_{\text{spatial}}$ defines the spatial trend term consisting of second order polynomials of the coordinates plus thin-plate smoothing splines. For a location s these are defined as $\sum_{i=1}^m \beta_i \eta(\|s - \tilde{s}_i\|)$, where \tilde{s}_i are fixed knots, $\|s - \tilde{s}_i\|$ is the Euclidean distance between s and \tilde{s}_i , and $\eta(z)$ is equal to $z^2 \log(z)$.⁴⁸ We have chosen 5 knots at locations determined by the centers of clusters found by the CLARA software.⁴⁹

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