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Strategy formulation for schistosomiasis japonica control in different environmental settings supported by spatial analysis: a case study from China

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Abstract. With the aim of exploring the usefulness of spatial analysis in the formulation of a strategy for schistosomiasis japonica control in different environmental settings, a population-based database was established in Dangtu county, China. This database, containing the human prevalence of schistosomiasis at the village level from 2001 to 2004, was analyzed by directional trend analysis supported with ArcGIS 9.0 to select the optimum predictive approach. Based on the approach selected, different strata of prevalence were classified and the spatial distribution of human infection with *Schistosoma japonicum* was estimated. The second-order ordinary kriging approach of spatial analysis was found to be optimal for prediction of human prevalence of *S. japonicum* infection. The mean prediction error was close to 0 and the root-mean-square standardised error was close to 1. Starting with the different environmental settings for each stratum of transmission, four areas were classified according to human prevalence, and different strategies to control transmission of schistosomiasis were put forward. We conclude that the approach to use spatial analysis as a tool to predict the spatial distribution of human prevalence of *S. japonicum* infection improves the formulation of strategies for schistosomiasis control in different environmental settings at the county level.

Keywords: schistosomiasis, spatial analysis, kriging, prediction, geographical information systems, control strategy.

Introduction

Schistosomiasis japonica is one of many zoonotic parasitic diseases along the Yangtze River and in the south of China. The central Government has, however, noted the serious situation and the national disease control programme has recently instituted a high-priority approach with regard to the major, communicable diseases in the area, in particular schistosomiasis, HIV/AIDS, tuberculosis, and hepatitis B (Utzinger et al., 2005). Due to its great impact on the populations in endemic areas, schistosomiasis restrains social and economic development (Zhou et al., 2005b).

In spite of great efforts and the remarkable progress made over the past 50 years since the inception of the national programme on schistosomiasis control, hyper-endemic areas still remain in lake and marshland regions, as well as in some of the mountainous regions in seven provinces of southern China. While, especially in the lake and marshland regions, the control strategy on schisto-

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somiasis is far from ideal due to large variations in environmental settings and social-economic status (Yuan et al., 2002; Utzinger et al., 2005; Zhou et al., 2005c). Therefore, it is necessary to study the control strategy for different ecosystems in hyper-endemic areas for sustained control of schistosomiasis, under the current situation.

The advent of geographical information systems (GIS) and remote sensing (RS) techniques provides important advances to our understanding of key environmental factors for the transmission of infectious diseases. Incorporation of these new technologies, often in conjunction with innovative spatial statistical approaches, are increasingly used for the prediction of the prevalence of *Schistosoma japonicum* infection (Zhou et al., 2001; Guo et al., 2005; Yang et al., 2005). Kriging is a widely used geostatistical technique for the analysis of spatial correlations and for constructing prediction maps in the field of public health (Waller and Gotway, 2004; Jerrett et al., 2005; Goovaerts, 2006).

The purpose of this study is to present kriging based on data from a few sites as a solution to the problem of predicting the spatial distribution of *S. japonicum* infection over a whole region. A further aim is to attempt formulating a schistosomiasis control strategy based on predictions for different environmental settings also at small scales, i.e. at the county level.

Materials and methods

Study area

For the study, we selected a highly endemic area, i.e. the Dangtu county, Anhui province, located in the lower researches of the Yangtze River. Most of this area belongs to the plain regions with waterway networks. However, some marshes and lakes also exist, as well as a few hilly and mountainous regions (Yuan, 1993). Schistosomiasis has been relatively well controlled in Dangtu but has recently re-emerged due to environmental and social factors. For example, snail infested-areas, both in terms of snail density and the number of positive snails in the county, were all found to be increasing (Shen, 2005). The Dangtu county carries a total population of 220,000 and there are 13 *S. japonicum*-endemic townships. In 2003 the average *S. japonicum* infection rate of humans and cattle was 1.2% and 1.3%, respectively (Chen et al., 2005).

Epidemiological data

The historical data about human infection from 2001 to 2004 were collected and used to establish an epidemiological database using FoxPro 6.0 software (Microsoft Corporation, USA). There are 282 villages in Dangtu, 114 of which identified as endemic villages (Chen et al., 2005; Yao, 2006).

Each year about one-third to half of the endemic villages were surveyed and residents were screened for *S. japonicum* infection by the indirect hemagglutination test (IHA) (Wang et al., 2000) and then confirmed by the Kato-Katz thick smear method (Katz et al., 1972). Those with the highest rates of human infection for each of the 114 historically identified endemic villages were extracted for further analysis.

Spatial data

The geographical coordinates (latitude/longitude) of the centre of each endemic village were recorded using GPS Map76 (Garmin Corp., Kansas, USA). The GIS database was established using ArcGIS 9.0 (ESRI Corp., USA) to record the coordinates and the highest infection rates for each village that had been deemed endemic in the 2001-2004 period.

Spatial correlation analysis

Spatial correlation analysis (Paul and Michael, 1996; Elliott et al., 2000; Eileen et al., 2004) was performed by the semivariogram model, which provides a measure of variance as a function of distance between data points. The semivariance is calculated as half of the mean-squared difference between two values separated by the distance h, i.e.

$$\hat{\gamma}(h) = \frac{1}{2N(h)} \sum_{i=1}^{N(h)} [Z(x_i) - Z(x_i+h)]^2$$

where Z is a value at a particular location, $N(h)$ the number of paired data at the distance h, and $\gamma(h)$ the semivariance. Denoting the spatial correlation parts of Z, it equals the expected squared difference value of observed points based on the fixed distance h.

Semivariogram, a graph of semivariance plotted against separation distance h, conveys information about the continuity and spatial variability of the process. If observations close together are more alike than those farther apart, the semivariance increases as the separation distance increases, reflecting the decline of spatial autocorrelation with distance. Often, the semivariance will level off to nearly a constant value (called the sill) at a large separation distance (called the range). Beyond this distance, observations are spatially uncorrelated, reflected by a (near) constant variance in paired differences. We used the spatial analyst module of ArcGIS 9.0 and selected the exponential model instead of the spherical model to fit the spatial correlation of infection rate with *S. japonicum*. Since the semivariance in our study did not really level off to a constant value, but increased very slowly beyond the range of distance, the formula is as follows:

$$\gamma(h) = \begin{cases} C_0 + C_e\,[1-\exp(-h/a_e)] & h > 0 \\ 0 & h = 0 \end{cases}$$

where C_0 is the nugget effect and C_e is the partial sill (so C_0+C_e is the sill). Although a_e is called the range, the "effective range" is $3a_e$ since the semivariance $\gamma(h)$ approaches the sill (C_0+C_e) asymptotically, i.e. the minimum distance at which spatial autocorrelation becomes less than 0.05 is $3a_e$.

Directional trend analysis

Using the explore data tools of the spatial analyst module of ArcGIS 9.0, we investigated the directional trend of the infection data identifying the presence/absence of trends at a certain direction in the input dataset, and selected the suitable order for the ordinary kriging analysis for the next step.

Ordinary kriging analysis

The ordinary kriging model is $Z(s) = \mu+\varepsilon(s)$ where s is a point location and $Z(s)$ the value at that location. The model is based on a constant mean μ for the data (no directional trend) and random errors $\varepsilon(s)$ with spatial dependence. The predictor forms as the weighted sum of the data, i.e.

$$\hat{Z}(s_0) = \sum_{i=1}^{N} \lambda_i\, Z(s_i),$$

where $Z(s_i)$ is the measured value at the ith point, $i = 1, \ldots, N$, λ_i an unknown weight for the measured value at the ith point, s_0 the prediction location, and N the number of observed points. The weight, λ_i, where

$$\sum_{i=1}^{N} \lambda_i = 1$$

depends on the semivariogram, the distance to the prediction location, and the spatial relationships among the measured values around the prediction point. By using the geostatistical module of ArcGIS 9.0, in accordance with the result of directional trend analysis, we selected the suitable order to carry out the ordinary kriging analysis and developed the prediction map based on the human infection rate for each endemic village. We then categorized the predicted infection rate to create the schistosomiasis endemic map with classified strata, based on the "Chinese Operational Scheme of Schistosomiasis Control" enacted by the Ministry of Health (MoH) in 2004 (Zhou et al., 2005c). The five epidemic strata were classified according to directives issued by the MoH (2000) and depicted in Table 1.

Table 1. Definition of the five strata of schistosomiasis prevalence.

S. japonicum infection rate	Stratum
Human prevalence above 10%	1
Human prevalence between 5 and 10%	2
Human prevalence between 1 and 5%	3
Human prevalence below 1%	4
No infection found in humans, cattle or snails for 5 years	5

At the same time, the map of the standard error of the prediction, i.e. the uncertainty of the prediction, was produced to qualify the prediction result enabling us to put forward a particular control strategy for each endemic stratum according to their specific environmental characteristics.

Results

Spatial correlation of infection rates

Fig. 1 depicts the semivariogram demonstrating spatial correlation of the infection rates. The x-axis refers to the distance between any two observed points and the y-axis refers to the corresponding semivariance. Each dot in the semivariogram represents a pair of locations, not the individual location of the endemic village itself.

The fitted semivariogram model was:

$$\gamma(h) = \begin{cases} 0.62804 + 1.449\,[1\text{-}\exp(-h/a_e)] & h > 0 \\ 0 & h = 0 \end{cases}$$

In this exponential model, the range was 30.115 km, the "effective range" about 90 km, the nugget value 0.628, and the sill value 1.449. The ratio of nugget to sill was 0.433, and the spatial correlation of the infection rate was moderate within the effective range (90 km). More than half (56.7%) of the total spatial variability came from spatial autocorrelation and 95% of the observed points became uncorrelated beyond this distance.

Directional trend analysis

The result of the directional trend analysis is shown in Fig. 2. Each vertical stick in the directional trend analysis plot represents the location and infection rate value of each village. All the points were projected onto the perpendicular planes of east-west and north-south. Two best-fit lines, calculated using polynomial models, were drawn through the projected points modeling trends in specific directions. The light green line in Fig. 2 presents as a U-structure, which indicates that the infection rate exhibits a strong trend in the east–west direction, while it is weaker from north to south. Thus, we

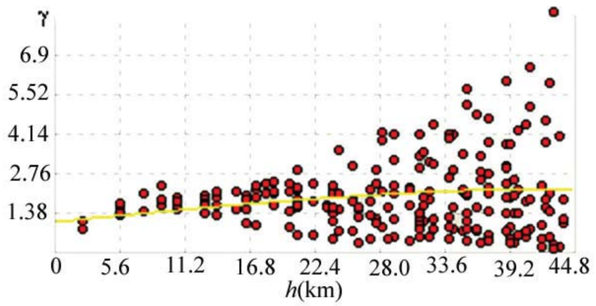

Fig. 1. Graph of semivariogram in the spatial correlation analysis based on the population-based prevalence of schistosomiasis in Dangtu county.

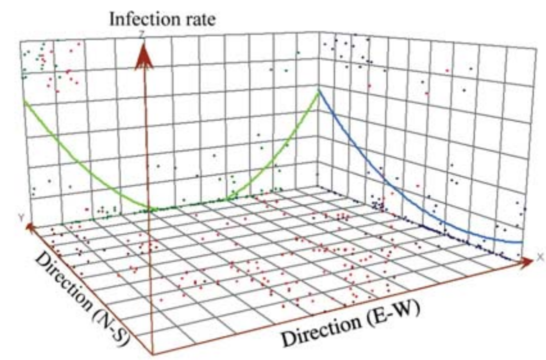

Fig. 2. Result of trend analysis of *S. japonicum* infection rate in Dangtu county.

could use second-order ordinary kriging to remove the impact of this prediction trend.

Prediction by ordinary kriging

Based on the result of directional trend analysis, we developed a prediction map by using second-order ordinary kriging, which is shown in Fig. 3. The darker the colour, the higher the predicted *S. japonicum* infection rate. The apparent spatial pattern of *S. japonicum* infection in Dangtu county presented an infection situation which was the most serious in the north-west and south-east, while the south-western, north-eastern and central areas were much less affected with medium infection rates in the transition areas. From the category map, developed as part of the study, we found that most endemic villages in Dangtu county fell in the 4th and 5th epidemic strata accounting for 72.7% of all the endemic villages in the north-west and south-east part of the county. This was followed by the 3rd stratum, accounting for 14.1% of all the endemic villages, and the 2nd stratum, accounting for 13.2% of the endemic villages which were found in the centre of the county (Fig. 4).

Prediction error analysis

Cross-validation was used to evaluate the prediction error which could be expressed by several statistics including mean prediction error (mean), root-mean-square prediction error (root-mean-square), average kriging standard error (average standard error), mean standardised prediction errors (mean standardised), and root-mean-square standardised prediction errors (root-mean-square standardised). The former four statistics should be as small as possible, and the root-mean-square standardised should be close to 1. The analysis results, shown in Table 2, suggest that the second-order ordinary kriging model is good enough for the prediction.

Fig. 5 depicts the standard error of the prediction based on second-order ordinary kriging, in which the darker colour indicates the higher prediction

Table 2. Prediction errors based on the second-order ordinary kriging model.

Variables	Value
Mean	0.007
Root-mean-square	1.124
Average standard error	1.022
Mean standardised	0.005
Root-mean-square standardised	1.068

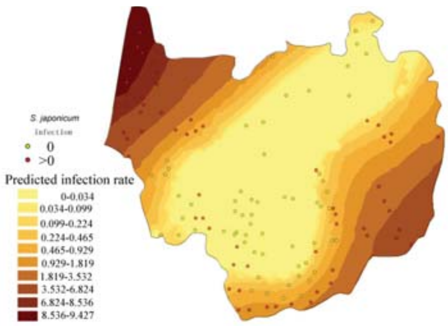

Fig. 3. Prediction map of *S. japonicum* infection in Dangtu county.

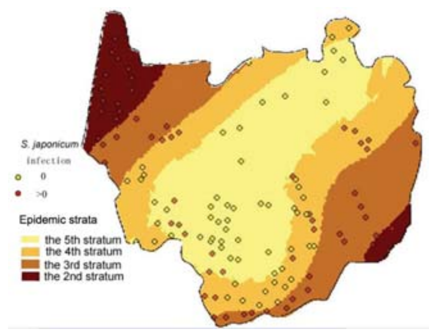

Fig. 4. Category map of epidemic strata of *S. japonicum* infection in Dangtu county.

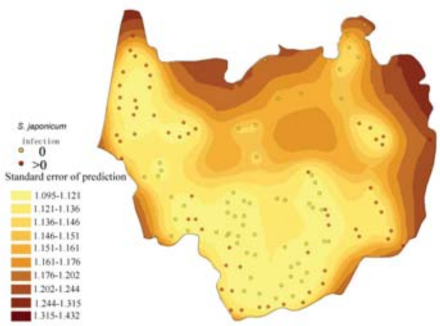

Fig. 5. Map of the standard error of the prediction based on the second-order ordinary kriging model.

error indicating that the prediction errors are larger in marginal areas due to the lower number of observed points in these areas.

Discussion

The last half-century of schistosomiasis control in China has reduced the overall prevalence of human *S. japonicum* infection by more than 90%, an achievement which is basically the result of a sustained, multifaceted national strategy adapted to different eco-epidemiological settings. This approach continues to be successful but with a steadily falling prevalence, the input from local resources and environmental factors will become increasingly important (Utzinger et al., 2005; Zhou et al., 2005a,c). At present, health resources are still scarce in China, forcing schistosomiasis surveillance to rely on small regions or sampled villages. For this reason it is very important to reliably predict the overall status of schistosomiasis from sampled points and to formulate an improved strategy for the national schistosomiasis control programme (Zhou et al., 2005b). The aim of the present study has been to show the ability to predict the spatial distribution of infection rates by using ordinary kriging at the county level. Moreover, we have shown that the approach on spatially mapping epidemic strata could provide a basis for the formulation of an improved strategy for the control of schistosomiasis.

Geostatistics theoretically combines geology and statistics to produce a novel methodology linking a geological analysis with various statistical approaches to highlight spatial correlated variability. Kriging, one of spatial analytical approaches in geostatistics for optimal spatial prediction, can be used to comprehensively consider structural changes and randomness of the variables. In this way, breaking the restriction of classic statistics, by setting semivariogram function as the main tool, a practical approach is provided for the study of the spatial phenomena and their regulation. There are now many different types of kriging software which differ in underlying assumptions and analytical goals (Curran and Atkinson, 1998). Ordinary kriging is a common way of interpolation used in, for example, mining for block modeling to find the best unbiased linear interpolated estimate. Recently, this method has been used to analyze the spatial correlation and for the construction of spatial prediction maps in the field of public health to estimate the strength and scale of disease patterns, which can be used to produce a continuous surface map of infection (Solymosi et al., 2004; Waller and Gotway, 2004; Jerrett et al., 2005; Allen and Wong, 2006; Goovaerts, 2006). For instance, Sakai et al. (2004) analysed more than 2.5 million cases of influenza-like illnesses (ILI), which occurred between 1992 and 1999, based on kriging analysis and showed the starting areas of peak ILI activity were mostly found in western Japan. Applying the kriging method allowed better visualization and understanding of spatio-temporal trends in seasonal ILI activity and this approach is likely to be an important tool for future influenza surveillance. The kriging approach has also been used in the field of schistosomiasis by exploring the spatial distribution of *Oncomelenia* snails in marshland of Jiangning county in 2000 (Zhang et al., 2005). Prediction maps, based on temperature, vegetation and wetness only, resulting from this study show that the variation of snail distribution, and the spatial autocorrelation, are related to the distance when the distance is less than 30 m (Zhang et al., 2005). Law et al. (2004) analyzed and mapped the distribution of four reportable sexually-transmitted diseases and suggested that geostatistical techniques could be used to visualize disease patterns and to identify emerging outbreaks.

It is suitable to predict the spatial distribution of the prevalence of *S. japonicum* infection with population-based prevalence data for each endemic village. Because the annually sampled villages in Dangtu county during 2001 to 2004 overlapped in some areas, we conducted the spatial analysis by selecting the highest infection rate during four years as study variable.

To reflect the infection status the following four steps were instituted. Firstly, we conducted spatial autocorrelation analysis by using semivariogram function analysis to decide whether there were spatial correlations within these observed points or villages. In the parameter of the semivariogram function, the sill value usually means total variability inside the system and there are no spatial correlations outside this range since the semivariance does not change with distance. The range is the most important part in the semivariogram function and it describes some characteristics of spatial variety with distance difference. Within the range, the nearer two points are, the more similarities they have. If the distance between the observed point and the unobserved point exceeds the above-mentioned range, the known point has no effect on the interpolation of the unknown point (Paul and Michael, 1996; Elliott et al., 2000). The ratio of the nugget value to the sill value indicates the degree of spatial correlation.

In case the ratio is less than 25%, a strong spatial correlation exists; if it is between 25% and 75%, the spatial correlation is medium; and when it exceeds 75%, the spatial correlation is very weak. If the pairs of points in the semivariogram produce a horizontal straight line, there may be no spatial correlation in the data, thus it would be meaningless to create a surface (Elliott et al., 2000). In this study, the ratio of nugget value to sill value was 0.433, illuminating the spatial correlation of the infection rate is medium. Other variations may result from random variation or other reasons such as social factors which need to be further studied.

The directional trend analysis was performed as a second step. Principally, if a trend exists in the prevalence data, it should be identified first and followed up in a further analysis. According to Paul and Michael (1996), the removal of the directional trend allows the analysis to be followed-up without being influenced by that trend and, once it is added back, a more accurate surface can be produced. In this study, the directional trend analysis revealed that our prevalence data presented a U-type trend, thus a second-order curve was the best method for removing the influence of the predictive trend.

Thirdly, we created a prediction map to illustrate the spatial pattern of infection rate. The relationship between schistosomiasis or the intermediate host snail and environmental factors, such as vegetation and temperature, as well as socio-economic factors, such as income and water contact, has been widely explored (Raso et al., 2005; Yang et al., 2005; Zhang et al., 2005, Clements et al., 2006). In consideration of the environmental factors and social background in the Dangtu county, the directional trend and moderate spatial correlation resulting from the study is partially due to the spatially correlated distribution of vegetation and temperature as well as the water-contact behaviour related to the Yangtze River and its branches. Even when some of the aforementioned factors were taken into account, spatial correlation still occurred in schistosomiasis transmission or the distribution of the intermediate host snail (Raso et al., 2005; Zhang et al., 2005; Clements et al., 2006). It is necessary to pay attention to, and make use of, spatial correlation when making predictions since it is unlikely that all the factors explaining the spatial correlation in infection can be included in one study.

Finally, in our analysis the prediction errors were estimated spatially. The analysis revealed that the prediction errors were larger at margin areas and areas with few observed points. A likely explanation of this observation is that kriging is a spatial interpolation method and that the prediction ability outside the distribution of sampled points is less reliable. Furthermore, the sampled endemic villages were asymmetrically distributed and the prediction ability is less good for areas with a low number of observed points. This reminded us to pay attention to the randomicity of the spatial distribution of the samples when carrying out spatial correlation analysis and interpreting the results.

The second purpose of the study was to formulate the schistosomiasis control strategy for each stratum based on the results of the spatial analysis. From the prediction map, we found that the majority of the endemic villages in Dangtu county belong to one of four strata (2nd to 5th), while no village of the 1st stratum was found. Villages sorted into the 2nd stratum were mainly found in the lake and marshland region in the north-west near the Yangtze River, and along the west bank of Sejiu Lake in the south-east. Those belonging to the 3rd stratum were distributed in the marshlands along the three main rivers of the Dangtu county, i.e. Guxi River, Qinghe River and Yunliang Rivers, all of which are directly linked to the Yangtze River and therefore show similar water levels. Villages belonging to the 4th stratum were in general not in the vicinity of rivers or lakes, while 5th stratum villages were located in the central part of Dangtu county far away from water bodies. Since different control strategies can be defined according to the principle of the national schistosomiasis control strategy, we recommend that the control strategy be defined based on the local environmental settings as well as epidemic strata at base level or village level, at least in the Dangtu county. Consequently, for villages in the 2nd stratum, the strategy should be to reduce the human infection rate and lighten the morbidity by chemotherapy. In addition, snails should be prevented from spreading into the embankments made to keep the water out of the villages and their immediate vicinity.

Detection and elimination of the snail should be strengthened in parallel with diagnosis and treatment of patients. If necessary, mass chemotherapy should be performed. In 3rd stratum villages, the priority should be to prevent snails from spreading, reducing sources of infection for the livestock. In 4th stratum villages, an integrated strategy should be instituted with a focus on environmental management with the aim of changing snail habitats and thus reduce the infection sources. In villages of the 5th stratum, the priority should be to prevent schistosomiasis from re-emerging by improved surveillance systems monitoring not only the human population but also snails and livestock.

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