

Identifying high-risk areas of schistosomiasis and associated risk factors in the Poyang Lake region, China

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SUMMARY

The epidemiology of schistosomiasis japonicum over small areas remains poorly understood, and this is particularly true in China. We aimed to identify high-risk areas for schistosomiasis and associated risk factors in the Poyang Lake region, China. A cross-sectional study was conducted and 60 of 920 persons (6.5%) were found to be infected with *Schistosoma japonicum*. Locations of households and snail habitats were determined using a hand-held global positioning system. We mapped the data in a geographical information system and used spatial scan statistics to explore clustering of infection, logistic regression and Bayesian geostatistical models to identify risk factors for each individual's infection status and multinomial logistic regression to identify risk factors for living in a cluster area. The risk of schistosomiasis was spatially clustered and higher in fishermen and males, not in persons who lived in close proximity to snail habitats and infected water sources. This study has demonstrated significant spatial variation in the prevalence of schistosomiasis at a small spatial scale. The results suggest that demographic factors (gender, occupation) rather than the distance to infected water are driving human transmission at small-scale spatial levels. Such information can be used to plan locally targeted interventions based on anthelmintic drug administration, snail control and sanitation improvement.

Key words: schistosomiasis, spatial analysis, Bayesian geostatistical modelling, geographical information system, risk factors.

INTRODUCTION

Schistosomiasis is endemic in 76 countries and territories (Engels *et al.* 2002), with an estimated 779 million people at risk of schistosomiasis and 207 million people infected (Steinmann *et al.* 2006). In China, *Schistosoma japonicum* infection remains an important public health problem, with an estimated 726 000 people infected in 2004 (Zhou *et al.* 2007a). At large scales, risk of *Schistosoma* infections is associated with climatic factors and proximity to permanent water bodies (Brooker, 2002; Yang *et al.* 2005; Brooker *et al.* 2006b; Peng *et al.* 2006).

Previous work has shown that schistosomiasis risk is focal at the county level in China. For example, studies have identified high numbers of acute schistosomiasis cases in Guichi, in an area covering

approximately 2500 km² (Zhang *et al.* 2008, 2009a, b). However, there is limited information on the determinants of small-scale spatial variation in schistosomiasis risk, and it is not known whether risk is heterogeneous within such foci. Apart from providing insight into the drivers of transmission, knowledge of small-scale variation is important because debate exists as to whether mass treatment with praziquantel or individual case detection is the optimal approach to schistosomiasis control (Williams *et al.* 2002). If schistosomiasis risk is relatively homogeneous within communities, this would support a mass treatment approach, whereas if substantial heterogeneity was found at this level, support would be added to the individual case detection approach. Identification of high-risk groups, such as occupational groups, could help to prioritize community pre-treatment screening programmes. The purpose of our study was to identify areas of high and low risk of schistosomiasis within a community in a highly endemic area of China, and the factors influencing small-scale spatial variation.

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MATERIALS AND METHODS

Study area and population

This study was conducted in the Ximiao administrative village, Jiangxi province, located adjacent habitats of *Oncomelania hupensis* (the intermediate host snail of *S. japonicum*) in Poyang Lake, the biggest fresh water lake in China. The administrative village comprises 9 smaller 'natural villages' and is known to be a highly endemic area for *S. japonicum*. Residents in the village are infected with *S. japonicum* mainly through contacts with water in the lake or on the beach. The study area covers about 6 km². Study participants included 920 (89.3%) of 1030 people in the resident population aged 5–80 years. The remaining 10.7% refused to participate in the study.

Written informed consent was obtained from all adult participants and from the parents or legal guardians of children. Ethical approval for the study was obtained from village (local government), county (anti-schistosomiasis) and provincial (schistosomiasis headquarters) authorities, and was endorsed by Fudan University.

Demographic and parasitological data

Demographic and parasitological data were obtained via a cross-sectional survey conducted in October 2007. The age, sex, education and occupation of survey participants were obtained from an existing database at the Xingzi Anti-schistosomiasis Station. Occupation was divided into 3 groups: farmers, fishermen and others (comprising students, teachers, businessmen and children in kindergarten, with small numbers in each of these subgroups). Participants were asked to produce a stool specimen and 50 g of each specimen was examined within 24 h of sample collection and 1–12 h after slide preparation (3 slides per sample) by quantitative Kato-Katz (KK) thick smear (Katz *et al.* 1972). *S. japonicum* egg counts were expressed in eggs per gram of stool (EPG), averaged across the 3 slides. Individuals with a positive stool examination result were treated with a single oral dose of praziquantel (40 mg/kg).

Households and snail habitat mapping

Homes of every person enrolled in the study area were visited and the locations of the households were determined using a hand-held global position system (GPS) GPSMAP 76 (Garmin Ltd, Olathe, KS, USA). Snail habitats (i.e. sites where snail colonies were found to be located) near the village were geo-located using the GPS. Distances from each household to the nearest snail habitat were computed using the Distance Matrix extension (www.jennessent.com/arcview/dist_matrix.htm) of the GIS ArcView 3.2 (ESRI, Redlands, CA, USA). In

Poyang Lake area, the distance to the nearest snail habitat is the same as the distance to water contact sites since snail habitats are under water in summer. All infections occur within the lake basin in the bottomlands; there are no snails behind the dikes (Davis *et al.* 2006). The distances were divided into quartiles (≤ 238 m, 238–419 m, 419–681 m and > 681 m).

Spatial cluster detection

We implemented the spatial scan statistic using the software SatTScan (Kulldorff *et al.* 2008). This method is well described in the literature (Kulldorff, 1997) and tests whether events such as disease cases are distributed randomly over space and, if not, identifies the location of significant spatial clusters. The Bernoulli variant of the statistic was used because the outcome was a dichotomous variable (positive, with 1 or more *S. japonicum* eggs detected in the faeces, or negative). The test uses a moving circular window, the maximum size of which we set to include no more than 50% of the total population. The software was set to detect both high- and low-risk clusters. A likelihood ratio test was used to determine if there was a higher, or lower risk of schistosomiasis inside compared to outside each window and to define the 'most likely' cluster (i.e. the cluster that was least likely to have occurred by chance). A *P*-value was obtained by repeating the same analytic exercise on 9999 random replications of the data set, generated under the null hypothesis of no spatial clustering. Only statistically significant clusters ($P \leq 0.05$) were reported. Clusters were mapped using ArcGIS 9.2 (ESRI, Redlands, CA, USA) in order to identify their physical location. Demographic, social and environmental predictor variables were then aggregated to the cluster areas in order to identify their possible relationship with schistosomiasis clustering.

Multivariate analysis

First, binary logistic regression and Bayesian logistic regression model (details are provided in the Appendix) were used to examine the relationship between individual infection status and gender, age, education, occupation and household distance to the nearest snail habitats. Second, multinomial logistic regression analyses were performed to identify risk factors for being located in high-risk cluster, low-risk cluster and non-cluster areas. Large-scale environmental variables such as normalized difference vegetation index (NDVI) and land surface temperature (LST) were not included in our study because they did not vary substantially within the small study area (Brooker, 2007; Raso *et al.* 2005). All variables were selected in above analyses according to their known association with schistosomiasis, and all were entered

Table 1. Characteristics of spatial clusters of *Schistosoma japonicum* infection detected using the spatial scan statistic, Poyang Lake region, China, 2007

Cluster Type*	Number of individuals	Cases (%)	Expected	RR†	LLR§	P
High risk	342	42(12.3)	22.3	3.94	14.25	0.0001
Low risk	229	3(1.3)	14.9	0.16	9.01	0.0261
No cluster	349	15(4.3)	NA	NA	NA	NA

* High risk-cluster with relative risk >1; no cluster-aggregation of non-clustered population. Low risk-cluster with relative risk <1.

† RR-Relative risk.

§ LLR-Log likelihood ratio.

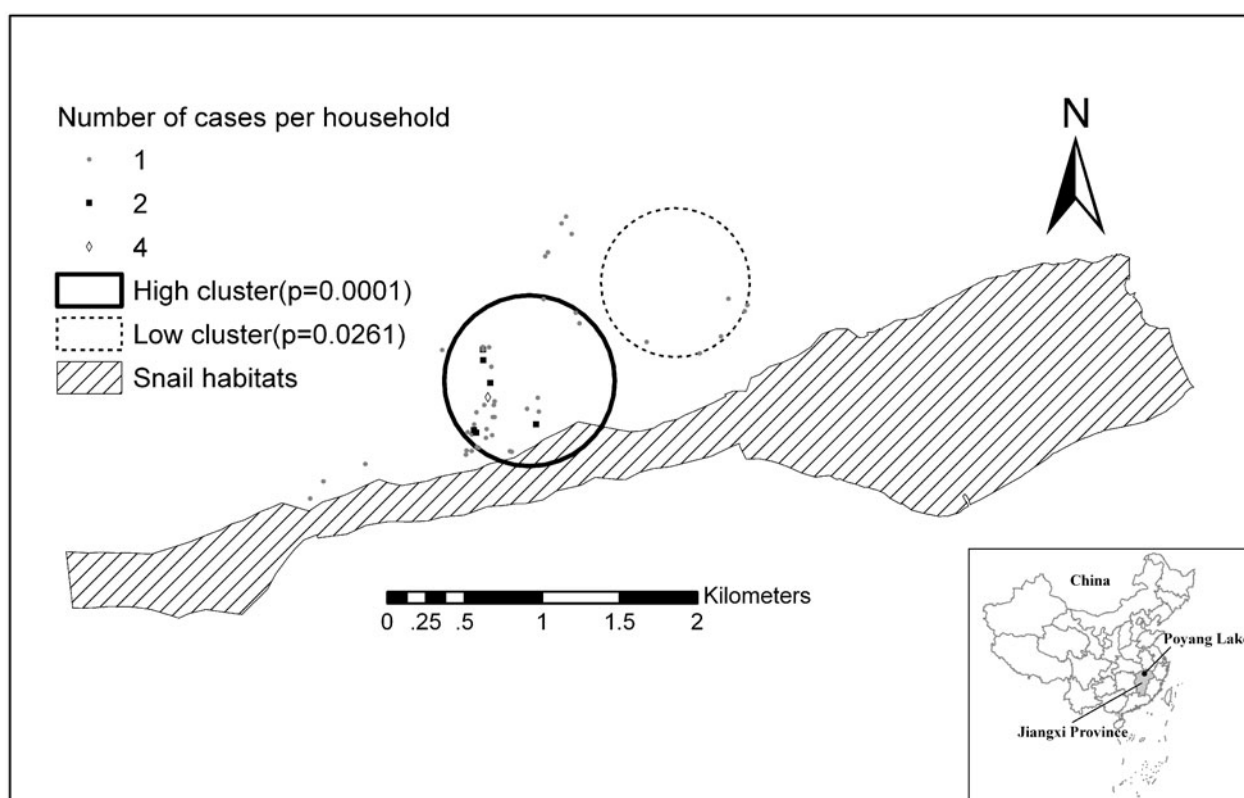


Fig. 1. Map of the household distribution of schistosomiasis cases and the nearby snail habitats at Ximiao village, Poyang Lake region, China and the locations of high and low clusters of cases as identified by the spatial scan statistic.

in the final models. All analyses were carried out using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) and WinBUGS 1.4.3 (MRC Biostatistics Unit, Cambridge and Imperial College, London, UK).

RESULTS

Prevalence of schistosomiasis

Sixty of 920 persons (6.5%) were infected with *S. japonicum*. All cases were chronic. Based on chi-square tests, males had a significantly higher prevalence of schistosomiasis than females ($\chi^2=4.62$,

$P=0.03$). There was no significant difference in risk of infection between age groups ($P=0.44$) and education levels ($P=0.33$). Most cases were fishermen (26/60, 43.3%) and occupation was significantly associated with risk of infection ($\chi^2=21.15$, $P<0.001$). Distance of household to the nearest snail habitat was marginally significant ($\chi^2=7.61$, $P=0.055$).

Spatial clusters of schistosomiasis

The spatial scan statistic detected 1 high-risk and 1 low-risk cluster (Fig. 1, Table 1). There was 1 case at 44 households, 2 cases at 6 households, and 4 cases

Table 2. Prevalence (%) and unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) for schistosomiasis stratified by personal characteristics, Poyang Lake region, China, 2007

Variable*	Number of individuals	Cases (%)	OR(95% CI)	
			Unadjusted*	Adjusted†
Gender§				
Male	460	38(8.3)	1.79(1.04,3.08)	1.75(1.00,3.06)
Female	460	22(4.8)		
Age (years)				
5–	324	22(6.8)	2.11(0.62,7.23)	5.70(0.69,47.25)
20–	155	13(8.4)	2.66(0.74,9.58)	1.46(0.36,5.95)
40–	351	22(6.3)	1.94(0.57,6.63)	1.18(0.32,4.29)
60–80	90	3(3.3)		
Education (years)				
≤6	650	39(6.0)	0.78(0.44,1.31)	1.22(0.65,2.30)
>6	270	21(7.8)		
Occupation§				
Farmers	401	13(3.2)	0.49(0.24,1.00)	2.15(0.36,13.00)
Fishermen	189	26(13.8)	2.35(1.28,4.30)	9.89(1.53,64.13)
Others	330	21(6.4)		
Distance of household to snail habitat (m)				
≤238	232	22(9.5)	1.74(0.86,3.55)	1.03(0.46,2.31)
238–	230	17(7.4)	1.33(0.63,2.80)	1.03(0.47,2.25)
419–	229	8(3.5)	0.60(0.24,1.48)	0.47(0.18,1.18)
>681	229	13(5.7)		

* Derived from the univariate analysis without controlling for potential confounders.

† Adjusted for other variables as potential confounders.

§ Significant variables ($P < 0.05$).

The reference group for sex was female, for age was 60–80 years, for education was >6 years, for occupation was others, and for distance was >681 m.

at 1 household. The prevalence of infection in the high-risk cluster, low-risk cluster and non-cluster areas were 12.3%, 1.3% and 4.3%, respectively. The relative risks of infection in high and low-risk cluster areas were 3.94 and 0.16, respectively. The high-risk cluster had a radius of 550 m, and included 139/364 (38.2%) households and 42/60 (70.0%) cases. The low-risk cluster had a radius of 480 m, and included 93/364 (25.5%) households and 3/60 (5.0%) cases.

Risk factors

In the binary logistic regression analysis (Table 2), males were at greater risk than females (OR 1.75, 95% CI 1.0, 3.1) and fishermen were at greater risk than farmers and other occupational groups (OR 4.6, 95% CI 2.1, 10.1 for fishermen versus farmers and OR 9.9, 95% CI 1.5, 64.1 for fishermen versus other occupational groups). In the Bayesian logistic regression model (Table 3), statistically significant correlations suggested that infection prevalence was higher in males and fishermen, but no association was found between prevalence and age, education and distance to snail habitats. In multinomial logistic regression analyses (Table 4), all variables except for

gender and age were significantly associated with being in a high-risk, low-risk or no cluster area ($P < 0.001$). People who had a higher education level, fishermen and people who lived in closer proximity to snail habitats were more likely to be located in a high-risk cluster.

DISCUSSION

The epidemiology of schistosomiasis *japonicum* over small areas remains poorly understood, and this is particularly true in China, where both the prevalence and mean intensity of *S. japonicum* infection in endemic areas has decreased dramatically in recent decades to historically low levels (Jiang *et al.* 2002; Zhou *et al.* 2005). This study has demonstrated substantial variation in the prevalence of schistosomiasis at a small spatial scale (about 6 km²) in the Poyang lake region from the results of the spatial scan statistic. Education, occupation and distance to snail habitats were significant factors for infection with *S. japonicum* for the probability of living in a high-risk area. However, at individual levels, only demographic factors (gender, occupation) were significant predictors of infection. Occupation, specifically being a fisherman, was strongly associated both with

Table 3. Bayesian logistic regression model of prevalence of infection with *Schistosoma japonicum* among individuals aged 5–80 at 364 households, Poyang Lake region, China, 2007*

Variables†	Posterior distribution		
	Mean(95% CrI)	MC error	S.D.
Age	−0.03(−0.63,0.58)	0.003	0.31
Gender female	−0.59(−1.21,−0.005)	0.002	0.31
Occupation			
Fishermen	1.57(0.77,2.42)	0.003	0.42
Others	0.65(−0.68,2.06)	0.006	0.7
Education (y > 6)	−0.014(−0.68,0.64)	0.003	0.34
Distance of household to snail habitat	−0.098(−0.46,0.24)	0.001	0.18

* CrI: Bayesian credible interval.

MC: Monte Carlo.

S.D.: Standard Deviation.

† The reference group for sex was male, for education was ≤ 6 years, for occupation was farmer.

the individual's risk of schistosomiasis and the probability of living in a high-risk area. The results are consistent with previous findings (Li *et al.* 1997; Huang and Manderson, 2005; Raso *et al.* 2009; Yang *et al.* 2009). In the study area most fishermen are involved daily in activities that put them in contact with infected water, whereas the farmers work mostly in the fields where there are no snail habitats or infected water, and so they come into contact less regularly with the schistosome transmission areas.

Living nearby to snail habitats was significantly associated with the probability of living in a high-risk area. A common assumption is that with increased distance from infected water, water contact becomes less frequent and therefore the infection risk decreases (Raso *et al.* 2009). It is surprising that there was no association between distance to snail habitats or infected water and the individual's risk of schistosomiasis. The results confirmed previous findings (Gazzinelli *et al.* 2006; Raso *et al.* 2009) and suggest that demographic factors (gender, occupation) rather than distance to infected water are driving human transmission at small spatial scales.

The spatial variations in schistosomiasis risk at small and large scales were determined by previous studies (Kloos *et al.* 1997, 1998; Brooker *et al.* 2006a; Clennon *et al.* 2006; Gazzinelli *et al.* 2006; Steinmann *et al.* 2007; Wu *et al.* 2007; Pullan *et al.* 2008; Raso *et al.* 2009). Other Chinese studies (Steinmann *et al.* 2007; Wu *et al.* 2007; Raso *et al.* 2009) investigated schistosomiasis risk at the village level, but ours is the first to investigate risk at the household level.

The results suggest that, due to considerable heterogeneity between occupational and social groups, and between different areas at this small spatial scale, targeted chemotherapy using pre-treatment

screening (particularly in high-risk occupational groups) might be more efficient than mass drug administration. In the study area, we should focus on the high-risk cluster which had a radius of 550 m, and included 139 households and 42 cases. Since the praziquantel-based control of schistosomiasis japonica in China alone is unlikely to eradicate the parasite (Zhou *et al.* 2007c), other control and prevention programmes should be considered. It is necessary to integrate praziquantel-based control of schistosomiasis with health education aimed at altering behaviour among high-risk groups. Targeted chemotherapy using pre-treatment screening, combined with the comprehensive control strategy aimed at reducing the roles of humans and bovines (cattle and buffalo) as sources of infection for snails (Wang *et al.* 2009) may be a good strategy to control transmission of *S. japonicum* in the study area. Further studies are required to determine the relative cost-effectiveness of the different approaches.

One limitation of the present analysis is the method used for diagnosis of schistosomiasis. Some studies have shown that repeated egg counts of one individual by Kato-Katz thick smear can vary considerably, and that many infected individuals remain undetected if only a single examination is performed, particularly in low-transmission areas (Uttinger *et al.* 2001; Berhe *et al.* 2004; Zhou *et al.* 2007b). However, the Kato-Katz technique is a better method for population screening of *S. japonicum* in moderate and high endemic areas than the hatching test and indirect haemagglutination assay (IHA) (Yu *et al.* 2007). Also of concern is the potential bias caused by those who refused to participate. Unfortunately, information on these individuals was not collected so it was not possible to estimate the magnitude or direction of any bias. With

Table 4. Unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (CI) for relative risk (RR) of high cluster (RR = 3.94) and low cluster (RR = 0.16) against non-cluster from a multinomial regression model

Variable¶	Number of individuals			High cluster <i>vs</i> non-cluster		Low cluster <i>vs</i> non-cluster	
	High cluster (%)	Non-cluster (%)	Low cluster (%)	OR (95% CI)		Unadjusted*	Adjusted †
				Unadjusted*	Adjusted †	Unadjusted*	Adjusted †
Gender							
Male	174(37.8)	174(37.8)	112(24.3)	1.04(0.77,1.40)	0.96(0.68,1.36)	0.96(0.69,1.34)	1.15(0.78,1.69)
Female	168(36.5)	175(38.0)	117(25.4)				
Age (years)							
5–	99(30.6)	129(39.8)	96(29.6)	1.98(1.10,3.57)	1.59(0.56,4.49)	1.66(0.94,2.93)	3.00(0.92,9.80)
20–	85(54.8)	50(32.3)	20(12.9)	4.38(2.32,8.27)	1.69(0.78,3.67)	0.89(0.43,1.84)	1.95(0.82,4.64)
40–	139(39.6)	121(34.5)	91(25.9)	2.96(1.65,5.31)	1.85(0.93,3.67)	1.68(0.95,2.97)	2.66(1.36,5.23)
60–80	19(21.1)	49(54.4)	22(24.4)				
Education§ (years)							
≤6	196(30.2)	259(39.8)	195(30.0)	0.47(0.34,0.64)	0.58(0.39,0.86)	1.99(1.29,3.08)	1.19(0.71,2.00)
>6	146(54.1)	90(33.3)	34(12.6)				
Occupation§							
Farmers	76(19.0)	191(47.6)	134(33.4)	0.48(0.34,0.70)	0.55(0.24,1.27)	0.95(0.68,1.35)	1.66(0.60,4.59)
Fishermen	160(84.7)	29(15.3)	0	6.71(4.19,10.76)	3.63(1.51,8.74)	0.02(0.00,0.39)	0.62(0.19,1.99)
Others	106(32.1)	129(39.1)	95(28.8)				
Distance of household to snail habitat§ (m)							
≤238	131(56.5)	101(43.5)	0	7.78(4.86,12.47)	3.72(2.26,6.13)	0.03(0.00,0.55)	0.79(0.39,1.58)
238–	109(47.4)	59(25.7)	62(27.0)	11.09(6.69,18.37)	6.74(4.04,11.24)	7.03(4.08,12.13)	5.90(3.53,9.85)
419–	73(31.9)	15(6.6)	141(61.6)	29.20(14.78,57.67)	14.68(7.79,27.67)	62.91(32.09,123.33)	41.79(22.94,76.12)
>681	29(12.7)	174(76.0)	26(11.4)				

* Derived from the univariate analysis without controlling for potential confounders.

† Adjusted for other variables as potential confounders.

§ Significant variables ($P < 0.05$).

¶ The reference group for sex was female, for age was 60–80 years, for education was > 6 years, for occupation was others, and for distance was > 681 m.

regard to the spatial scan statistic, a disadvantage is the subjective nature of the selection of the maximum cluster size (Lawson, 2006). However, the spatial scan statistic is statistically robust (using Monte Carlo simulation for significance testing) and has wide application in infectious disease and parasitic infection studies (Cousens *et al.* 2001; Chaput *et al.* 2002; Enemark *et al.* 2002; Mostashari *et al.* 2003; Brooker *et al.* 2004; Jennings *et al.* 2005; Langkjer *et al.* 2007).

In summary, this study identified high-risk areas of schistosomiasis and associated factors that partly explain the observed spatial heterogeneity. The results support a targeted approach to schistosomiasis control based on pre-treatment screening. The spatial scan statistic and geographical information systems (GIS) combined with Bayesian geostatistical models and multinomial logistic regression analyses can provide powerful tools for understanding the epidemiology of diseases and for improving disease prevention and control, especially in vector-borne or environment-related diseases. Future studies should be aimed at better understanding the dynamics and spatial heterogeneity of schistosomiasis at local scales and we propose to extend our study to other ecological settings, such as mountainous regions.

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APPENDIX

Model building and assessment

The model was of the form

$$Y_i \sim \text{bernoulli}(p_i)$$

where Y_i was the positive infection status of individuals, p_i was the risk for positive infection status in individuals.

$$\begin{aligned} \text{logit}(p_i) = & \alpha + \beta \times \text{age}_i + \delta 1 \times \text{female}_i \\ & + \delta 2 \times \text{fishermen}_i + \delta 3 \times \text{others}_i \\ & + \delta 4 \times \text{education}_i + \lambda_i \end{aligned}$$

where α was the intercept, β was the coefficient for age, $\delta 1$ was the coefficient for female gender, $\delta 2$ was

the coefficient for occupation as fishermen, $\delta 3$ was the coefficient for occupation as others, $\delta 4$ was the coefficient for education (year > 6).

$$\lambda_i = \varepsilon \times \text{dist}_i + \theta_i$$

where ε was the coefficient for distances of households to the nearest snail habitat, θ_i was defined by the isotropic, exponentially decaying correlation function

$$f(d_{ij}; \phi) = \exp[-(\phi d_{ij})]$$

where d_{ij} are the distances between pairs of points i and j , and ϕ is the rate of decline of spatial correlation per unit of distance. Non-informative priors were specified for the intercept (uniform prior with bounds $-\infty$ and $+\infty$) and the coefficients (normal prior with mean = 0 and precision, the inverse of variance = 1×10^{-4}). The prior distribution of ϕ was also uniform with upper and lower bounds set at 0.5 and 200. The precision of θ_i was given a non-informative prior gamma.

Model fitting used Markov Chain Monte Carlo simulation techniques. A burn-in of 1000 iterations was allowed, followed by 10 000 iterations where values for the intercept and coefficients were stored. Diagnostic tests for convergence of the stored variables were undertaken, including visual examination of history and density plots of the model parameters, and by computing Monte Carlo errors (MCE; if MCE was less than 0.05, it was decided that sufficient iterations had been conducted): convergence was successfully achieved after 10 000 iterations. The chains were also examined for autocorrelation by visual examination of the inbuilt autocorrelation function of WinBUGS.

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