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Infection and biogeographical characteristics of *Paragonimus westermani* and *P. skrjabini* in humans and animal hosts in China: a systematic review and meta-analysis --Manuscript Draft--

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Abstract:	<p>Abstract</p> <p>Background Paragonimiasis, primarily caused by <i>Paragonimus westermani</i> and <i>P. skrjabini</i> in China, is a common food-borne parasitic zoonosis. Despite numerous epidemiological surveys conducted over the past decades, the national distribution of <i>Paragonimus</i> infection and its associated environmental determinants remain poorly understood. In this paper, we summarize the infection of <i>P. westermani</i> and <i>P. skrjabini</i> and describe key biogeographical characteristics of the endemic areas in China.</p> <p>Methods Data on <i>Paragonimus</i> infection in humans, snails, second intermediate hosts, and animal reservoirs were extracted from eight electronic databases. A random-effects meta-analysis model was used to estimate the pooled prevalence. All survey locations were georeferenced and plotted on China map, and scatter plots were used to illustrate the biogeographical characteristics of regions reporting <i>Paragonimus</i> infection.</p> <p>Results A total of 28,948 cases of human paragonimiasis have been documented, with 2,401 cases reported after 2010. Among the 11,443 cases with reported ages, 88.05% were children or adolescents. The pooled prevalence of <i>P. skrjabini</i> is 0.45% (95% CI: 0.27 – 0.66%) in snails, 31.10% (95% CI: 24.77 – 37.80%) in the second intermediate host, and 20.31% (95% CI: 9.69 – 33.38%) in animal reservoirs. For <i>P. westermani</i>, the pooled prevalence is 0.06% (95% CI: 0.01 – 0.13%) in snails, 52.07% (95% CI: 43.56 – 60.52%) in the second intermediate host, and 21.40% (95% CI: 7.82 – 38.99%) in animal reservoirs. <i>P. westermani</i> and <i>P. skrjabini</i> are primarily distributed in regions with low altitude, high temperature, and high precipitation. In northeastern China, only <i>P. westermani</i> infections have been documented, with no presence of <i>P. skrjabini</i>, while in more southern areas, infections of both <i>P. westermani</i> and <i>P. skrjabini</i> have been reported.</p> <p>Conclusions Paragonimiasis remains prevalent in China, particularly among children and adolescents. Variations exist in the intermediate hosts and geographical distribution of <i>P. westermani</i> and <i>P. skrjabini</i>. Additionally, temperature and precipitation may influence the distribution of <i>Paragonimus</i>.</p>
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1 **Infection and biogeographical characteristics of *Paragonimus westermani* and *P.***
2 ***skrjabini* in humans and animal hosts in China: a systematic review and meta-**
3 **analysis**

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20 All authors read and approved the final manuscript.

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25

26 **Abstract**

27 **Background**

28 Paragonimiasis, primarily caused by *Paragonimus westermani* and *P. skrjabini* in
29 China, is a common food-borne parasitic zoonosis. Despite numerous epidemiological
30 surveys conducted over the past decades, the national distribution of *Paragonimus*
31 infection and its associated environmental determinants remain poorly understood. In
32 this paper, we summarize the infection of *P. westermani* and *P. skrjabini* and describe
33 key biogeographical characteristics of the endemic areas in China.

34 **Methods**


35 Data on *Paragonimus* infection in humans, snails, second intermediate hosts, and
36 animal reservoirs were extracted from eight electronic database  random-effects
37 meta-analysis model was used to estimate the pooled prevalence. All survey
38 locations were georeferenced and plotted on China map, and scatter plots were used to
39 illustrate the biogeographical characteristics of regions reporting *Paragonimus*
40 infection.

41 **Results**

42 A total of 28,948 cases of human paragonimiasis have been documented, with 2,401
43 cases reported after 2010. Among the 11,443 cases with reported ages, 88.05% were
44 children or adolescents. The pooled prevalence of *P. skrjabini* is 0.45% (95% CI: 0.27
45 – 0.66%) in snails, 31.10% (95% CI: 24.77 – 37.80%) in the second intermediate host,
46 and 20.31% (95% CI: 9.69 – 33.38%) in animal reservoirs. For *P. westermani*, the
47 pooled prevalence is 0.06% (95% CI: 0.01 – 0.13%) in snails, 52.07% (95% CI: 43.56
48 – 60.52%) in the second intermediate host, and 21.40% (95% CI: 7.82 – 38.99%) in

49 animal reservoirs. *P. westermani* and *P. skrjabini* are primarily distributed in regions
50 with low altitude, high temperature, and high precipitation. In northeastern China,
51 only *P. westermani* infections have been documented, with no presence of *P.*
52 *skrjabini*, while in more southern areas, infections of both *P. westermani* and *P.*
53 *skrjabini* have been reported.

54 **Conclusions**

55 Paragonimiasis remains prevalent in China, particularly among children and
56 adolescents. Variations exist in the intermediate hosts and geographical distribution of
57 *P. westermani* and *P. skrjabini*. Additionally,  temperature and precipitation may
58 influence the distribution of *Paragonimus*.

59 

60 **Author summary**


61 Paragonimiasis, a foodborne zoonotic parasitic disease caused by lung flukes
62 (*Paragonimus*), remains a significant neglected public health threat in many Asian
63 countries, including China. Human infection occurs through the ingestion of raw or
64 undercooked freshwater crab or crayfish containing the metacercariae stage. Given
65 the popularity of consuming raw or undercooked freshwater products in many areas of
66 China, understanding the infection status and spatial distribution of *Paragonimus* in
67 humans and animal hosts is crucial for controlling paragonimiasis. Our study provides
68 a comprehensive summary of the infection levels of the two most important zoonotic
69 *Paragonimus* species, *P. westermani* and *P. skrjabini*, in humans and animal hosts in
70 China, along with a description of the spatial distribution and environmental
71 characteristics of their endemic areas. We observe a wide distribution of *Paragonimus*
72 infection in China, with a significant infection rate found in freshwater crabs and

73 crayfish. Our findings underscore the importance of avoiding the consumption of raw
74 or undercooked freshwater products to prevent foodborne diseases, including
75 paragonimiasis.

76

77 **Introduction**

78 Paragonimiasis is a food-borne zoonotic disease caused by several species of lung
79 flukes belonging to genus *Paragonimus* [1]. It typically causes subacute to chronic
80 pneumonia. The symptoms, including chronic cough, chest pain, dyspnea, and
81 hemoptysis, mimic those of tuberculosis and lung cancer [2]. Human
82 paragonimiasis is widely distributed in Asia, Americas, and Africa, and is
83 still a significant neglected public health threat in China. An estimated 293.8 million
84 individuals are at risk of *Paragonimus* infection, with 195 million of them residing in
85 China [3, 4].

86 More than 30 *Paragonimus* species have been documented in China, among
87 which *P. westermani* and *P. skrjabini* are the most important zoonotic species [2, 5]. *P.*
88 *westermani* (Japanese lung fluke or oriental lung fluke) is most commonly distributed
89 in eastern Asia and in South America, and is the most common cause of human
90 paragonimiasis. *P. skrjabini* is especially prevalent in China, with cases appearing
91 more recently in India and Vietnam as well. *P. westermani* followed by *P. skrjabini*
92 are the major pathogens for human paragonimiasis in China 

93 Parasites of *Paragonimus* spp. have a three-host life cycle, with aquatic snails
94 serving as the first intermediate host, freshwater decapod crustaceans as the second
95 intermediate host, while human and other mammals as the definitive host. Human
96 infection is acquired by eating inadequately cooked or pickled freshwater crabs or

97 cray fishes containing the infective forms called metacercariae [6, 7]. Drinking
98 untreated stream or river water is also considered to be a possible route of infection
99 [8].

100 Given the three host nature of the parasite and the fact that consuming raw or
101 undercooked freshwater products is still popular in many areas of China, the infection
102 status of *Paragonimus* in animal hosts is closely related to the epidemic of human
103 paragonimiasis [9]. Therefore, comprehending the level of infection in animals will
104 provide valuable insights for controlling human paragonimiasis. However,
105 prevalence estimates of *Paragonimus* infection in the literature vary greatly
106 across different studies. To date, there has been no comprehensive estimation of
107 *Paragonimus* infection in humans and animal hosts. In addition, very few attempts
108 at the spatial and environmental characteristics of *Paragonimus* infection in
109 China have been made. Consequently, the aims of the current study are to
110 summarize the infection level of two most important zoonotic *Paragonimus* species, *P.*
111 *westermani* and *P. skrjabini*, in humans and animal hosts in China, and to describe the
112 spatial distribution and environmental characteristics of their endemic areas.

113

114 **Method**

115 **Literature retrieval and selection**

116 This systematic review followed the Preferred Reporting Items for Systematic
117 Reviews and Meta-analyses (PRISMA) reporting guidelines [10].

118 A systematic literature search was conducted to identify all studies reporting
119 *Paragonimus* infection in humans and animals from inception to January 1, 2024,
120 using the following electronic databases: China National Knowledge Infrastructure

121 (CNKI), Chinese Wanfang database (CWFD), Chongqing VIP, SinoMed, Medline,
122 Embase, PubMed, and Web of Science. Full-text search was performed using the
123 terms ‘paragonimiasis’, ‘*Paragonimus*’, ‘lung fluke’, ‘lung trematode’, in conjunction
124 with ‘China’. The search was limited to English and Chinese languages.

125 After removing duplicates, two reviewers (KL and YC-S) independently
126 reviewed all the titles and abstracts, with assistance of a third reviewer (RT-
127 P) to reach a consensus in case of disagreement. Subsequently, the full texts
128 were assessed for inclusion by the same reviewers. All studies included in
129 the meta-analysis were published in English or Chinese, and were primary
130 research articles, and epidemiological studies reporting infection rate of
131 *Paragonimus* in humans and animal hosts. Studies were further excluded from
132 meta-analysis if they were letters to the editor, non-epidemiological studies, or had a
133 sample size of fewer than 20 [11]. Additionally, we collected case reports and case
134 series of human infections to summarize the characteristics of cases of human
135 paragonimiasis.

136 **Data extraction and quality assessment**

137 The following information was extracted from the included articles: title, first author,
138 language, year of publication, year of investigation, study location, *Paragonimus*
139 species, diagnostic techniques used in the study, sample size, number of positive cases,
140 **infection rate**, and taxonomic category of animal host for infection in animals. In
141 population-based surveys, the participants first underwent immunological testing
142 (usually skin testing), and those who tested positive further underwent etiological
143 testing. In this case, the infection rate was calculated using the total number of

144 participants as the denominator, with etiologically confirmed positives as the
145 numerator.

146 Two reviewers (KL and YC-S) independently evaluated the quality of each
147 included study using a standardized assessment tool developed by Hoy [12]. This tool
148 provides ten items to assess the risk of bias, with each item given a score of 0 or 1 for
149 the absence or presence of bias. A summary score of 0–3 indicates a low risk of bias,
150 4–6 indicates a moderate risk of bias, and 7–10 indicates a high risk of bias.

151 **Statistical analysis**

152 Freeman-Tukey double arcsine transformation was used to normalize the infection
153 rate and ensure the validity of subsequent analyses [13]. Heterogeneity across studies
154 was assessed using Cochran's Q test and I^2 statistics, where I^2 statistics quantified the
155 percentage of variation across studies (with I^2 values indicating low, moderate, and
156 high heterogeneity at 25%, 50%, and 75%, respectively). If the heterogeneity is
157 statistically significant, a random-effects model was used for meta-analysis;
158 otherwise, a fixed-effects model was used [14, 15]. The random-effects model was
159 ultimately used to estimate the pooled prevalence in this study, following the results
160 of the heterogeneity test. Additionally, subgroup and meta-regression analyses were
161 employed to explore the potential source of heterogeneity across studies and assess
162 the effects of moderators on the infection rates.

163 R^2 , QM and QE statistics were utilized to interpret the results of subgroup and
164 meta-regression analyses [11]. R^2 represents the proportion of true heterogeneity that
165 can be explained by the moderator; QM and its P -value determine the significance of
166 the moderators in explaining heterogeneity; and QE and its P -value evaluate the
167 significance of unexplained residual heterogeneity [16, 17].

168 Funnel plots and Egger's test were employed to assess potential publication bias.
169 Sensitivity analyses were conducted to evaluate the robustness of the pooled estimate
170 [18, 19]. Initially, outlier analyses were performed using Baujat plots. Studies located
171 in the top right quadrant of the Baujat plot, or with studentized residuals exceeding 2
172 in absolute value, were considered potential outliers. After removing identified
173 outliers, the overall pooled prevalence estimates were recalculated and compared with
174 the main findings. Furthermore, we examined whether excluding smaller-sample data
175 points (i.e., data points with the lowest quintile of sample sizes) yielded findings
176 similar to the main results.

177 All statistical analyses were performed using R4.2.1 software (Lucent
178 Technologies, Jasmine Mountain, USA). For all tests, p values less than 0.05 were
179 considered statistically significant.

180 **Data collection on environmental factors and visualization of** 181 **the spatial distribution and biogeographical characteristics**

182 Baidu Map was used to determine the latitude and longitude coordinates of each study
183 location. For human infection, all etiological confirmed paragonimiasis cases
184 documented in population surveys, case reports, and case series were included in the
185 spatial analyses. Environmental factors for each location, including annual mean
186 temperature, annual precipitation, mean temperature of warmest quarter, precipitation
187 of warmest quarter, mean temperature of coldest quarter, precipitation of coldest
188 quarter were obtained from the WorldClim database (<https://www.worldclim.org/>)
189 [20]. Altitude data was obtained from the Space Shuttle Radar Topography Mission
190 (SRTM, <http://www.gscloud.cn/>) [21].

191 To visualize the spatial distribution of *P. westermani* and *P. skrjabini* infection,
192 we georeferenced the etiologically definite human paragonimiasis cases and the
193 infection rates of various animal hosts, and plotted them on a map of China using
194 software ArcGIS10.7 (Environmental System Research Institute, Redlands, USA).
195 Additionally, scatter plots were used to illustrate the biogeographical characteristics
196 of regions reporting *P. westermani* and *P. skrjabini* infection. T-tests were further
197 conducted to explore the potential differences in biogeographical characteristics
198 between the two *Paragonimus* species.

199

200 **Results**

201 **Literature selection and quality assessment**

202 Initially, 876 publications were identified through literature search. After removing
203 duplicates, 10,642 articles were screened based on titles and abstracts, resulting in
204 1,880 articles for full-text assessment. Following full-text assessments, 38 studies
205 were ultimately included in the meta-analysis for human infections, 107 for snail
206 infections, 172 for infections in the second intermediate host, and 22 for infections in
207 animal reservoirs (Fig 1).

208

209 **Fig 1. Flow diagram of study selection for the systematic review and meta-analysis**

210

211 In the risk of bias assessment, all the studies were rated as having low to
212 moderate bias (S1-S4 Tables). Specifically, 6 out of 38 publications for human
213 infections, 81 out of 107 publications for snail infections, 143 out of 172 for the

214 second intermediate hosts, and 20 out of 22 for animal reservoirs were rated as having
215 low bias. The most common risk identified was the lack of random selection of the
216 sample.

217 **Infection of *P. westermani* and *P. skrjabini* in humans**

218 A total of 28,948 cases of human paragonimiasis have been reported in the
219 literature, of which 2,401 cases occurred after 2010, 14,654 cases were male, and
220 6,089 cases were from rural areas (see Table 1). Notably, A total of 10,076 cases of
221 infection in children or adolescents have been reported, with 8,695 cases reported
222 before 2010 and 1,381 reported after 2010. As shown in Fig 2, human infections of
223 *Paragonimus* have been documented in all provinces except for Tibet, Qinghai,
224 Gansu, and Ningxia. The cases of human infection are mainly documented in
225 provinces or municipalities in the Yangtze River Basin, including Chongqing (6,035),
226 Zhejiang (5,324), Hubei (4,945), Sichuan (2,896), and Hunan (1,414), which together
227 account for 71.12% of the total national cases (see Table 1). It is worth noting that
228 after 2010, there are still a considerable number of reported cases in areas such as
229 Chongqing (1,073) and Sichuan (595), and many other provinces and municipalities
230 also continue to report cases.

231 Only a few cases differentiated whether the infection was caused by *P.*
232 *westermani* and *P. skrjabini*. Cases of *P. westermani* infection are widely distributed,
233 while *P. skrjabini* infections are primarily concentrated in more southern regions (Fig
234 2).

235

236 **Table 1. Characteristics of human paragonimiasis cases documented in China**

	Before 1990	1990-1999	2000-2009	After 2010	Total
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Province					
Chongqing	779	984	3199	1073	6035
Zhejiang	1879	1649	1595	201	5324
Hubei	2466	989	1440	50	4945
Sichuan	640	537	1124	595	2896
Guizhou	1202	295	197	149	1843
Hunan	755	546	106	7	1414
Shaanxi	489	311	161	14	975
Liaoning	261	604	33	3	901
Fujian	490	33	341	4	868
Anhui	636	95	2	0	733
Shanghai	182	193	215	26	616
Heilongjiang	542	13	3	0	558
Jiangsu	82	369	38	40	529
Henan	176	104	44	64	388
Beijing	99	24	12	67	202
Shandong	0	176	5	0	181
Jiangxi	157	9	6	0	172
Yunnan	17	1	31	89	138
Jilin	92	3	0	2	97
Guangdong	4	23	19	15	61
Shanxi	0	14	14	0	28
Guangxi	1	23	1	0	25
Hebei	9	1	1	1	12
Hainan	0	0	3	0	3
Inner Mongolia	0	0	1	0	1
Taiwan	0	0	0	1	1
Tianjing	1	0	0	0	1
Xinjiang	0	1	0	0	1
Macao	0	0	0	0	0
Gansu	0	0	0	0	0
Ningxia	0	0	0	0	0
Qinghai	0	0	0	0	0
Tibet	0	0	0	0	0

Hong Kong	0	0	0	0	0
Age					
< 18	2613	2660	3422	1381	10076
≥ 18	386	454	298	229	1367
Not specified	7960	3883	4871	791	17505
Gender					
Male	4201	4227	4587	1639	14654
Female	1677	1932	2220	677	6506
Not specified	5081	838	1784	85	7788
Source					
Urban	540	263	327	52	1182
Rural	1462	1270	2992	365	6089
Not specified	8957	5464	5272	1984	21677
Total	10959	6997	8591	2401	28948

237

238 **Fig 2. Spatial distribution of human paragonimiasis cases documented in China.**

239

240 A total of 38 studies, containing 662,003 participants, reported screening for
 241 *Paragonimus* infection in human populations (see S1 Table), with 253 confirmed
 242 cases being reported and pooled prevalence of 0.05% (95% **CI: 0.00 - 0.12%**). The
 243 heterogeneity across the studies was high ($I^2 = 93.3\%$, Table 2; forest plot shown in
 244 S1a Fig). Subgroup analysis and the **meta-regression model** indicated that none of the
 245 moderators could significantly explain the heterogeneity (see S5 Table).

246

247 **Table 2. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* infection in**

248 **humans** 

	No. of data points	Sample size	No. of positive	Pooled prevalence, % (95% CI)	I^2 , %	R^2 , % (QM P value)	QE P value
Pathogen	54	662003	253	0.05 (0.00; 0.12)	93.3	0.00 (0.575)	< 0.0001
<i>P. westermani</i>	30	58811	127	0.07 (0.00; 0.19)	90.1		

<i>P. skrjabini</i>	9	10636	22	0.04 (0.00; 0.22)	87.1		
Not specified	15	592556	104	0.03 (0.00; 0.16)	95.2		
Year of investigation						4.36 (0.290)	< 0.0001
Before 1990	36	57540	184	0.08 (0.01; 0.20)	88.4		
1990–1999	7	32729	35	0.08 (0.00; 0.33)	91.6		
2000–2010	5	81900	25	0.02 (0.00; 0.21)	66.7		
After 2010	6	489834	9	0.00 (0.00; 0.06)	33.0		
Gender						4.17 (0.156)	< 0.0001
Man	8	16340	1	0.00 (0.00; 0.11)	0		
Woman	7	5174	0	0.00 (0.00; 0.13)	0		
Not specified	39	640489	252	0.09 (0.02; 0.19)	95.2		
Specimen						0.00 (0.357)	< 0.0001
Sputum	38	100117	187	0.04 (0.00; 0.12)	90.3		
Stool	14	492277	22	0.03 (0.00; 0.18)	79.2		
Stool or sputum	2	69609	44	0.45 (0.04; 1.27)	98.5		

249 R^2 represents the proportion of true heterogeneity that can be explained by the moderator, the **QE**

250 P value shows the significance of residual heterogeneity that is unaccounted for by the moderator,

251 and the **QM** P value shows whether the moderator is statistically significant in explaining

252 heterogeneity.

253

254 **Infection of *P. westermani* and *P. skrjabini* in the first**

255 **intermediate hosts**

256 A total of 57 studies reported the presence of *P. westermani* infection in the first

257 intermediate host (snails), with prevalence ranging from 0.00% to 6.72% (see S2

258 Table). The pooled prevalence of *P. westermani* in the first intermediate host was 0.11%

259 (95% CI : 0.02–0.25%), and there was high heterogeneity across the studies ($I^2=$

260 93.6%, Table 3; forest plot is presented in S1b Fig). *Semisulcospira* spp. was

261 identified as the most common vector of *P. westermani*, with a pooled prevalence of

262 0.12% (95% CI : 0.02–0.28%). Additionally, *Tricula* spp., *Erhaiini* spp., and

263 *Bythinella* spp. were identified as potential vectors of *P. westermani*.

264 Fifty studies reported *P. skrjabini* infection in the first intermediate host, with
 265 prevalence varied from 0.00% to 14.80% (see S2 Table). The pooled prevalence of *P.*
 266 *skrjabini* in the first intermediate host was 0.46% (95% CI: 0.27–0.70%), and the
 267 heterogeneity across studies was high ($I^2=93.4\%$, Table 3; forest plot was shown in
 268 S1c Fig). The majority of infections in snails were reported in *Tricola* spp., with a
 269 pooled prevalence of 0.58% (95% CI: 0.28–0.96%). Additionally, *Pseudobythinella*
 270 spp., *Bythinella* spp., *Semisulcospira* spp., *Oncomelania* spp., *Erhaiina* spp., and
 271 *Akiyoshia* spp. were also potential vectors of *P. skrjabini*.

272 Spatial distribution of *P. westermani* and *P. skrjabini* infection in the first
 273 intermediate hosts is depicted in Fig 3. In the northeast area of China, *Semisulcospira*
 274 spp. serve as the primary transmission vectors of *Paragonimus*, and only *P.*
 275 *westermani* infection has been reported in this region. In more southern areas,
 276 *Semisulcospira* spp. are identified as the primary transmission vectors of *P.*
 277 *westermani*, while *Tricola* spp. are identified as the primary transmission vectors of *P.*
 278 *skrjabini* (Figs 3a and 3b).

279 Subgroup analysis and the meta-regression model indicated that the infection rate
 280 of *P. westermani* and *P. skrjabini* in the first intermediate host did not exhibit
 281 significant differences across different snail genera and time periods (see Table 3, S6
 282 Table).

283

284 **Table 3. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* infection**
 285 **in the first intermediate hosts**

	No. of data points	Sample size	No. of positive	Pooled prevalence, % (95% CI)	I^2 , %	R^2 , % (QM P value)	QE P value
<i>P. westermani</i>	61	263423	639	0.11 (0.02; 0.25)	93.6		

Year of investigation						3.35 (0.149)	< 0.0001
Before 1990	32	120342	425	0.14 (0.01; 0.36)	91.7		
1990–1999	12	69290	52	0.04 (0.00; 0.27)	89.4		
2000–2009	11	58357	81	0.00 (0.00; 0.24)	85.6		
After 2010	6	15434	81	0.62 (0.14; 1.39)	97.3		
Genus of snail						0.00 (0.637)	< 0.0001
<i>Semisulcospira</i>	54	240158	599	0.12 (0.02; 0.28)	94.1		
<i>Tricola</i>	5	15918	11	0.04 (0.00; 0.41)	62.5		
<i>Erhaiini</i>	1	6227	26	0.42 (0.00; 2.49)	NE		
<i>Bythinella</i>	1	1120	3	0.27 (0.00; 2.27)	NE		
<i>P. skrjabini</i>	75	411797	1343	0.46 (0.27; 0.70)	93.4		
Year of investigation						0.00 (0.678)	< 0.0001
Before 1990	22	112904	428	0.52 (0.18; 1.01)	92.6		
1990–1999	14	75143	247	0.34 (0.02; 0.90)	93.9		
2000–2009	24	193038	502	0.34 (0.07; 0.75)	91.9		
After 2010	15	30712	166	0.74 (0.26; 1.43)	95.5		
Genus of snail						0.00 (0.830)	< 0.0001
<i>Tricola</i>	36	253031	643	0.58 (0.28; 0.96)	94.6		
<i>Pseudobythinella</i>	11	64914	340	0.57 (0.11; 1.32)	90.5		
<i>Bythinella</i>	10	9481	79	0.41 (0.01; 1.19)	84.7		
<i>Semisulcospira</i>	9	63806	178	0.06 (0.00; 0.60)	79.6		
<i>Erhaiini</i>	3	5789	26	0.80 (0.00; 2.66)	92.4		
<i>Akiyoshia</i>	3	2575	20	0.71 (0.00; 2.48)	89.5		
<i>Oncomelania</i>	2	10925	57	0.20 (0.00; 2.28)	0.0		
<i>Assiminea</i>	1	1276	0	0.00 (0.00; 1.83)	NE		

286 NE: not estimated; R^2 represents the proportion of true heterogeneity that can be explained by the
287 moderator, the QE P value shows the significance of residual heterogeneity that is unaccounted
288 for by the moderator, and the QM P value shows whether the moderator is statistically significant
289 in explaining heterogeneity.

290

291 **Fig 3. Spatial distribution of *P. westermani* and *P. skrjabini* infection in the first**
292 **intermediate hosts in China. (a) *P. westermani* infection in the first intermediate hosts; (b)**
293 ***P. skrjabini* infection in the first intermediate hosts**

294

295 **Infection of *P. westermani* and *P. skrjabini* in the second**
296 **intermediate hosts**


297 In total, 94 studies reported *P. westermani* infection in the second intermediate host
298 (see S3 Table), with a pooled prevalence of 52.02% (95% CI: 44.35–59.64%) and
299 high heterogeneity across studies ($I^2 = 99.6\%$, Table 4; forest plot presented in S1d
300 Fig). Genus *Cambaroides* was identified as the primary second intermediate host for
301 *P. westermani* in the northeastern areas of China (Fig 4a), with a pooled prevalence of
302 59.79% (95% CI: 42.65 - 75.79%; Table 4). In other areas of China, *Sinopotamon* spp.
303 were the primary second intermediate host, with a pooled prevalence of 52.86% (95%
304 CI: 43.68 – 61.94%); other freshwater crabs such as *Nanhaipotamon* spp. and
305 *Huananpotamon* spp. could also serve as the second intermediate host (see Table 4,
306 S3 Table).

307 Eighty-one studies reported *P. skrjabini* infection in the second intermediate host
308 (see S3 Table), with a pooled prevalence of 30.37% (95% CI: 24.72–36.34%) and
309 high heterogeneity across studies ($I^2 = 99.8\%$, Table 4; forest plot presented in S1e
310 Fig). In the northeastern region of China, only *P. westermani* has been reported in the
311 second intermediate host, with no reports of the existence of *P. skrjabini* (see Fig 4b).
312 The second intermediate hosts of *P. skrjabini* included crabs of the Potamidae,
313 Lithodidae, and Parathelphusidae families. Crabs of the Potamidae family were the
314 most common second intermediate host, with *Sinopotamon* spp. being the most
315 significant, exhibiting a pooled prevalence of 31.53% (95% CI: 24.92% - 38.53%).
316 Additionally, other freshwater crabs such as *Nanhaipotamon* spp., *Potamon* spp., and
317 *Tenuilapotamon* spp. of the Potamidae family, *Somanniathelphusa* spp. of the

318 Parathelphusidae family, and *Malayopotamon* spp. of the Lithodidae family can also
 319 serve as the second intermediate hosts for *P. skrjabini* (see Table 4).

320 Subgroup analysis and the meta-regression model indicated that the infection
 321 rates of *P. westermanni* and *P. skrjabini* in the second intermediate host did not exhibit
 322 significant differences among different crustacean genera, across different time
 323 periods, and with different detection methods (see Table 4, S7 Table).

324

325 **Table 4. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* infection in**
 326 **the second intermediate host** 

	No. of data points	Sample size	No. of positive	Pooled prevalence, % (95% CI)	I^2 , %	R^2 , % (QM P value)	QE P value
<i>P. westermanni</i>	100	165276	40049	52.02 (44.35; 59.64)	99.6		
Year of investigation						3.27 (0.097)	< 0.0001
Before 1990	44	86716	24212	62.67 (51.44; 73.25)	99.5		
1990–1999	15	66150	10488	43.24 (24.96; 62.51)	99.8		
2000–2009	22	6490	2762	41.69 (26.41; 57.82)	98.8		
After 2010	19	5920	2587	45.80 (29.06; 63.03)	99.5		
Genus of hosts						0.00 (0.492)	< 0.0001
<i>Sinopotamon</i>	70	157429	35929	52.86 (43.68; 61.94)	99.7		
<i>Nanhaipotamon</i>	3	175	53	26.02 (0.26; 69.67)	95.0		
<i>Huananpotamon</i>	2	1349	697	27.65 (0.00; 79.19)	98.8		
<i>Malayopotamon</i>	1	21	3	14.29 (0.00; 88.26)	NE		
<i>Lithodes</i>	1	72	61	84.72 (14.42; 100.00)	NE		
<i>Eriocheir</i>	1	85	16	18.82 (0.00; 88.53)	NE		
<i>Cambaroides</i>	20	5515	3110	59.79 (42.65; 75.79)	99.4		
<i>Macrobrachium</i>	2	630	180	28.57 (0.00; 79.70)	0.00		
Detection method						0.00 (0.501)	< 0.0001
Artificial digestion	55	94460	26665	50.15 (39.81; 60.49)	99.4		
Direct compression	25	8923	4135	59.75 (44.42; 74.17)	99.5		
Not specified	20	61893	9249	47.42 (30.79; 64.34)	99.7		
<i>P. skrjabini</i>	109	198209	41426	30.37 (24.72; 36.34)	99.8		

Year of investigation						1.90 (0.184)	< 0.0001
Before 1990	24	21578	4833	32.76 (19.69; 47.33)	99.1		
1990–1999	22	84633	6773	21.85 (11.35; 34.57)	99.8		
2000–2009	23	66211	23849	40.59 (27.31; 54.59)	99.9		
After 2010	40	25787	5971	30.13 (18.95; 42.62)	99.2		
Genus of hosts						7.59 (0.065)	< 0.0001
<i>Sinopotamon</i>	74	167883	37566	31.53 (24.92; 38.53)	99.8		
<i>Nanhaipotamon</i>	7	1318	480	34.30 (13.74; 58.42)	80.5		
<i>Potamon</i>	5	1911	458	26.03 (6.31; 53.05)	99.1		
<i>Tenuilapotamon</i>	3	3195	2182	27.96 (3.52; 63.48)	99.6		
<i>Aparapotamon</i>	3	1880	307	15.66 (0.00; 48.85)	78.0		
<i>Bottapotamon</i>	3	189	127	75.72 (39.60; 98.48)	96.1		
<i>Malayopotamon</i>	2	104	62	42.94 (5.44; 85.95)	95.8		
<i>Huananpotamon</i>	2	82	27	33.89 (1.83; 78.46)	0.0		
<i>Sinolapotamon</i>	1	3596	6	0.17 (0.00; 38.11)	NE		
<i>Tiwaripotamon</i>	1	3898	2	0.05 (0.00; 36.44)	NE		
<i>Neilupotamon</i>	1	116	6	5.17 (0.00; 58.20)	NE		
<i>Parvuspotamon</i>	1	223	73	32.74 (0.00; 89.38)	NE		
<i>Potamiscus</i>	1	24	23	95.83 (38.43; 100.00)	NE		
<i>Tenuipotamon</i>	1	141	38	26.95 (0.00; 85.44)	NE		
<i>Lithodes</i>	3	13627	69	9.41 (0.00; 39.93)	97.0		
<i>Somanniathelphusa</i>	1	22	0	0.00 (0.00; 47.47)	NE		
Detection method						1.75 (0.135)	< 0.0001
Artificial digestion	68	172632	35089	26.01 (19.38; 33.23)	99.9		
Direct compression	28	17125	4220	36.91 (25.41; 49.19)	98.3		
Not specified	13	8452	2117	40.59 (23.73; 58.66)	99.2		

327 NE: not estimated; R^2 represents the proportion of true heterogeneity that can be explained by the
328 moderator, the QE P value shows the significance of residual heterogeneity that is unaccounted
329 for by the moderator, and the QM P value shows whether the moderator is statistically significant
330 in explaining heterogeneity.

331

332 **Fig 4. Spatial distribution of *P. westermani* and *P. skrjabini* infection in the second**
333 **intermediate hosts in China. (a) *P. westermani* infection in the second intermediate hosts;**
334 **(b) *P. skrjabini* infection in the second intermediate hosts.**

335


336 **Infection of *P. westermani* and *P. skrjabini* in animal**
337 **reservoirs**

338 Overall, 10 studies reported *P. westermani* infection in animal reservoirs (see S4
339 Table), with a pooled prevalence of 21.40% (95% CI: 7.82–38.99%) and high
340 heterogeneity across studies ($I^2 = 94.9\%$, Table 5; forest plot presented in S1g Fig).
341 Cats (37.15% (95% CI: 9.61 - 69.92%)) and dogs (11.68% (95% CI: 0.00 - 36.56%))
342 were identified as the most common animal reservoirs for *P. westermani*.

343 Twelve studies reported *P. skrjabini* infection in animal reservoirs (see S4 Table),
344 with a pooled prevalence of 20.31% (95% CI: 9.69–33.38%) and high heterogeneity
345 across studies ($I^2 = 95.2\%$, Table 5; forest plot presented in S1f Fig). Similar to *P.*
346 *westermani*, cats (36.35% (95% CI: 20.74–53.51 %)) and dogs (5.79% (95% CI:
347 0.00–23.03 %)) were identified the most common animal reservoirs for *P. skrjabini*.

348 Subgroup analysis and meta-regression models indicated that animal categories,
349 lifestyle (wild or domestic), or detection methods could significantly explain the
350 observed heterogeneity (see Table 5, S8 Table).

351

352 **Table 5. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* infection**
353 **in animal reservoir** 

	No. of data points	Sample size	No. of positive	Pooled prevalence, % (95% CI)	I^2 , %	R^2 , % (QM P value)	QE P value
<i>P. westermani</i>	13	1353	307	21.40 (7.82; 38.99)	94.9		
Year of investigation						5.40 (0.266)	< 0.0001
Before 1990	7	999	275	34.00 (12.82; 59.07)	94.0		
1990–1999	3	269	25	12.25 (0.00; 46.27)	95.2		
After 2010	3	85	7	6.37 (0.00; 37.97)	75.4		

Family of hosts						0.00 (0.609)	< 0.0001
Canidae	6	936	210	11.68 (0.00; 36.56)	96.2		
Felidae	5	299	74	37.15 (9.61; 69.92)	96.1		
Viverridae	1	66	13	19.70 (0.00; 85.85)	NE		
Mustelidae	1	52	10	19.23 (0.00; 85.87)	NE		
Life style						0.00 (0.702)	< 0.0001
Domestic	10	1214	274	24.70 (4.93; 40.41)	96.1		
Wild	3	139	33	22.57 (1.18; 68.23)	69.3		
Detection method						0.00 (0.545)	< 0.0001
Sedimentation	2	55	7	12.44 (0.00; 60.11)	42.5		
Direct compression	2	54	22	41.81 (2.41; 89.04)	0.00		
Kato-Katz	1	30	0	0.00 (0.00; 51.65)	NE		
Not specified	8	1214	278	23.59 (6.13; 47.41)	96.6		
<i>P. skrjabini</i>	20	1067	180	20.31 (9.69; 33.38)	95.2		
Year of investigation						10.34 (0.168)	<0.0001
Before 1990	5	199	53	30.53 (8.60; 58.19)	94.5		
1990–1999	5	408	17	3.52 (0.00; 21.03)	91.3		
2000–2009	5	167	56	30.31 (8.36; 58.09)	83.4		
After 2010	5	293	54	23.88 (4.94; 50.39)	96.3		
Family of hosts						26.53 (0.046)	< 0.0001
Felidae	11	433	146	36.35 (20.74; 53.51)	93.7		
Canidae	5	319	20	5.79 (0.00; 23.03)	79.5		
Muridae	1	223	0	0.00 (0.00; 29.15)	NE		
Viverridae	1	43	8	18.60 (0.00; 72.12)	NE		
Suidae	1	21	0	0.00 (0.00; 39.21)	NE		
Mustelidae	1	28	6	21.43 (0.00; 76.78)	NE		
Life style						20.34 (0.018)	< 0.0001
Domestic	11	480	130	33.12 (17.50; 50.78)	95.3		
Wild	9	587	50	8.09 (0.40; 22.06)	92.3		
Detection method						25.37 (0.029)	< 0.0001
Direct compression	6	231	90	45.69 (23.38; 68.90)	92.7		
Sedimentation	9	542	65	13.88 (3.16; 29.65)	94.9		
Kato-Katz	2	194	5	1.28 (0.00; 24.62)	70.6		
Not specified	3	100	20	15.93 (0.05; 46.32)	89.7		

354 NE: not estimated; R^2 represents the proportion of true heterogeneity that can be explained by the

355 moderator, the QE P value shows the significance of residual heterogeneity that is unaccounted

356 for by the moderator, and the **QM** *P* value shows whether the moderator is statistically significant
357 in explaining heterogeneity.

358

359 **Publish bias and sensitivity analysis**

360 Asymmetry in the funnel plots and the results of Egger's test indicated the presence of
361 publication bias (see S2 Fig). The sensitivity analysis results demonstrated that the
362 pooled prevalence estimate did not change significantly after the removal of outlier
363 data points or data points with small sample sizes (95% *CI* overlapped; see S9 Table).

364

365 **Biogeographical characteristics of *P. westermani* and *P.*** 366 ***skrjabini* infections**

367 To investigate the biogeographical characteristics of *Paragonimus* occurrences, we
368 created scatter plots using the climate features of *P. westermani* and *P. skrjabini*
369 endemic sites and 1000 random points. The results indicate that, compared to random
370 points, endemic sites of *P. westermani* and *P. skrjabini* are mainly distributed in
371 regions with lower altitude and higher temperature and precipitation (see S10 Table
372 and Fig 5). Specifically, endemic sites of *P. westermani* are predominantly distributed
373 in areas with an altitude below 1166.0m, annual temperature above 1.0°C, annual
374 precipitation above 541.0mm, mean temperature of the warmest quarter above 18.3°C,
375 and precipitation of the warmest quarter above 304.0mm. On the other hand, endemic
376 sites of *P. skrjabini* are distributed in areas with altitude below 2188.0m, annual
377 temperature above 10.9°C, annual precipitation above 578.0mm, mean temperature of
378 the warmest quarter above 19.5°C, and precipitation of the warmest quarter above
379 257.0mm. When comparing the two *Paragonimus* species, the endemic points of *P.*

380 *westermani* have lower altitudes (below 1166.0m for *P. westermani*; 2188.0m for *P.*
381 *skrjabini*) and lower mean temperature of the coldest quarter (above -20.1°C for *P.*
382 *westermani*; -0.8°C for *P. skrjabini*).

383

384 **Fig 5. Environmental characteristics of areas with reported *Paragonimus* infections in**
385 **China.**

386

387 **Discussion**

388 In this study, we summarized the infection status and geographical distribution of *P.*
389 *westermani* and *P. skrjabini* in humans and animal hosts in China. Our findings
390 indicate that *Paragonimus* infection is widely distributed and remains prevalent in
391 China, with variations in the transmission vectors, second intermediate hosts, and
392 geographical distribution between *P. westermani* and *P. skrjabini*. Furthermore,
393 environmental factors such as temperature and precipitation may influence the
394 distribution of *Paragonimus*.

395 After years of educational efforts, the reported number of human paragonimiasis
396 cases has significantly decreased in most areas of China (see Table 1). However, it is
397 noteworthy that after 2010, a considerable number of reported cases persist in areas
398 such as Chongqing (1073) and Sichuan (595), with many other provinces and
399 municipalities also continuing to report cases, highlighting the need for ongoing
400 control efforts against paragonimiasis. Another notable issue is the significant
401 involvement of children and adolescents in paragonimiasis cases, both before and
402 after 2010 [22-24]. In certain endemic areas, particularly in rural or mountainous
403 regions, practices such as local children drinking untreated water and consuming

404 undercooked shrimp and crab are more common among children compared to adults
405 [25, 26], underscoring the necessity for enhanced health education on paragonimiasis
406 in schools in key areas. Additionally, human infection may be more widespread and
407 underestimated due to a lack of training of health workers to identify paragonimiasis
408 and a deficient case-reporting system [27].

409 The distribution regions of *P. westermani* and *P. skrjabini* in China exhibit both
410 differences and overlaps. In the northeastern areas of China, only *P. westermani* has
411 been documented, while in the southern part of China, both species coexist. The
412 difference in the distribution of the two *Paragonimus* species is likely due to
413 variations in their second intermediate hosts. Specifically, *Sinopotamon*, primarily
414 distributed in the southern part of China, serves as the main second intermediate host
415 for both *P. westermani* and *P. skrjabini* [28, 29]. On the other hand, *Cambaroides*,
416 which inhabits the northeastern region of China, can only serve as the second
417 intermediate host for *P. westermani* [30]. On the other hand, *Cambaroides*, which
418 inhabits the northeastern region of China, can only serve as the second intermediate
419 host for *P. westermani* [30]. It has been reported that *P. westermani* and *P. skrjabini*
420 share some common intermediate hosts, such as *Semisulcospira*, *Tricola*, *Erhaiini*,
421 and *Bythinella* in the first intermediate host, and *Huananpotamon* in the second
422 intermediate host [31, 32]. Additionally, the cercariae and metacercariae of *P.*
423 *westermani* and *P. skrjabini* are morphologically similar[33]. Therefore, in areas
424 where the two *Paragonimus* species overlap, there may be misclassification when
425 detecting the infection in intermediate hosts. To accurately differentiate between the
426 different *Paragonimus* species, nucleic acid detection is recommended to be
427 conducted simultaneously in epidemiological surveys.

428 The infection rates of *Paragonimus* in intermediate hosts exhibit significant

429 variation. In the first intermediate host, the infection rate of *P. westermani* ranged
430 from 0.00% to 6.72%, while the infection rate of *P. skrjabini* ranged from 0.00% to
431 14.80% (see S2 Table). In the second intermediate host, the infection rate ranged from
432 0% to 100% (see S3 Table). None of the known moderators, including the taxonomic
433 category of the intermediate host, year of survey, and detection methods, can
434 significantly explain the heterogeneity across studies (see S6 and S7 Tables).
435 Therefore, it is necessary to conduct random sampling surveys in different regions to
436 further understand the factors that influence the infection rates of *Paragonimus* in
437 intermediate hosts.

438 In many regions of China, it is common for residents to consume marinated or
439 drunken crabs in their raw state [4, 34]. However, the methods of salting and soaking
440 in alcohol are not completely effective in killing the metacercariae [35, 36]. Another
441 prevalent practice is the consumption of freshwater crabs and crayfish through stir-
442 frying, but inadequate heating may not fully eliminate the parasites [37, 38]. Human
443 infection occurs through the consumption of inadequately cooked freshwater
444 crustaceans containing the infective metacercariae. Given the persistently high
445 infection rates of *Paragonimus* in the second intermediate host (with a pooled
446 prevalence of 52.02% (95% CI: 42.65 - 75.79%) for *P. westermani* and 30.37% (95%
447 CI: 24.72 - 36.34%) for *P. skrjabini*; see Table 4), and the continued popularity of
448 consuming raw or undercooked freshwater crustaceans in many areas of China,
449 paragonimiasis remains a significant public health threat to the Chinese population.

450 The analysis of biogeographical characteristics revealed that temperature and
451 precipitation might influence the distribution of *Paragonimus* (see Fig. 4).
452 Temperature may affect the distribution of *Paragonimus* by influencing the survival
453 of the intermediate host (snails and crustaceans) or by affecting the development of

454 *Paragonimus*. For example, research by Hu et al. indicates that the development of
455 the eggs of *P. heterotremus* is closely related to the external temperature [39].
456 Development is slow or even halted at temperatures below 12°C, and does not occur
457 at temperatures above 37°C. Chiu has found that the optimum temperature for the
458 development of *P. iloktsuensis* in *T. chiui* is 22 to 30°C [40]. Our study results
459 indicate that, compared to *P. skrjabini*, *P. westermani* can survive in regions with
460 lower temperatures, such as northeastern China (see Fig. 5), suggesting that *P.*
461 *westermani* exhibits great tolerance to low temperatures. Similarly, Fan and
462 colleagues have found that metacercariae of *P. westermani* can still develop into
463 mature worms in rats after storage at 4°C for up to 234 days [41].


464 *Paragonimus* infections have been predominantly documented in eastern China.
465 This geographical distribution is closely associated with water supply, with
466 precipitation playing a crucial role in the distribution of aquatic snails and crustaceans
467 [42], both of which are integral to the *Paragonimus* life cycle. The higher levels of
468 precipitation in eastern China create environments that are more conducive to the
469 survival and proliferation of intermediate hosts, thereby increasing the risk of
470 *Paragonimus* infections in these areas [43].

471 In this study, we pooled studies from numerous sites to achieve a relatively large
472 sample size to summarize the infection rate of *P. westermani* and *P. skrjabini* in
473 humans, intermediate hosts, and animal reservoirs. However, several limitations of
474 our study should be considered. Firstly, the absence of literature reporting
475 *Paragonimus* infections in certain areas does not necessarily indicate that
476 *Paragonimus* infections do not exist there; it may be due to a lack of research in those
477 areas or unpublished research findings. Secondly, significant heterogeneity was
478 detected across studies, and most of the heterogeneity could not be explained by

479 known moderators. Lastly, publication bias exists in this study, which may cause bias
480 in the estimates of pooled prevalence. Therefore, the results of our study should be
481 interpreted with caution. Despite these limitations, our study systematically
482 summarizes the infection status of *P. westermani* and *P. skrjabini* in humans,
483 intermediate hosts, and animal reservoirs in China, and elucidates their spatial
484 distribution. The findings may provide valuable insights for the control of
485 paragonimiasis in China.

486

487 **Conclusions**

488 *Paragonimus* infection remains widely distributed and prevalent in China, with
489 children and adolescents at high risk in endemic areas. Variations exist in the
490 intermediate hosts and geographical distribution of *P. westermani* and *P. skrjabini*
491 infections in China. *P. skrjabini* infections are predominantly concentrated in more
492 southern regions compared to *P. westermani*. Additionally,  temperature and
493 precipitation may influence the distribution of *P. westermani* and *P. skrjabini*.

494

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518

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641

642 **Supporting information**

643 **S1Table. Publications reporting *Paragonimus* infection in humans.**

644 **S2Table. Publications reporting *Paragonimus* infection in the first intermediate**
645 **hosts.**

646 **S3Table. Publications reporting *Paragonimus* infection in the second**
647 **intermediate hosts.**

648 **S4Table. Publications reporting *Paragonimus* infection in animal reservoirs.**

649 **S5Table. Multivariable meta-regression analyses for *Paragonimus* infection in**
650 **humans.**

651 **S6Table. Multivariable meta-regression analyses for *Paragonimus* infection in the**
652 **first intermediate hosts.**

653 **S7Table. Multivariable meta-regression analyses for *Paragonimus* infection in the**
654 **second intermediate hosts.**

655 **S8Table. Multivariable meta-regression analyses for *Paragonimus* infection in**
656 **animal reservoirs.**

657 **S9Table. Sensitivity analysis of the pooled prevalence of *Paragonimus* in humans,**
658 **the first intermediate hosts, the second intermediate hosts, and animal reservoirs.**

659 **S10Table. Environmental characteristics of areas with reported *P. westermani***
660 **and *P. skrjabini* infections in China.**

661 **S1Fig. Forest plots of prevalence of *Paragonimus* species in humans, the first**
662 **intermediate host, the second intermediate host, and animal reservoirs. (a)**
663 ***Paragonimus* in humans; (b) *P. westermani* in the first intermediate host; (c) *P.***
664 ***skrjabini* in the first intermediate host; (d) *P. westermani* in the second**
665 **intermediate host; (e) *P. skrjabini* in the second intermediate host; (f) *P. skrjabini***
666 **in animal reservoir; (g) *P. westermani* in animal reservoir.**

667 **S2Fig. Funnel plot for assessing publication bias in studies reporting prevalence**
668 **of *Paragonimu***
669 **s species in humans, the first intermediate host, the second intermediate host,**
670 **and animal reservoirs (a) *Paragonimus* in humans; (b) *P. skrjabini* in the first**
671 **intermediate host; (c) *P. westermani* in the first intermediate host; (d) *P. skrjabini***

672 in the second intermediate host; (e) *P. westermani* in the second intermediate host;
673 (f) *P. skrjabini* in animal reservoir; (g) *P. westermani* in animal reservoir.

674

675 **Figures and Tables**

676 **Fig 1. Flow diagram of study selection for the systematic review and meta analysis.**

677 **Fig 2. Spatial distribution of human paragonimiasis cases documented in China.**

678 **Fig 3. Spatial distribution of *P. westermani* and *P. skrjabini* infection in the first**
679 **intermediate hosts in China. (a) *P. westermani* infection in the first intermediate hosts; (b)**
680 ***P. skrjabini* infection in the first intermediate hosts;**

681 **Fig 4. Spatial distribution of *P. westermani* and *P. skrjabini* infection in the second**
682 **intermediate hosts in China. (a) *P. westermani* infection in the second intermediate hosts;**
683 **(b) *P. skrjabini* infection in the second intermediate hosts.**

684 **Fig 5. Environmental characteristics of areas with reported *Paragonimus* infections in**
685 **China.**

686 **Table 1. Characteristics of human paragonimiasis cases documented in China.**

687 **Table 2. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* in**
688 **humans.**

689 **Table 3. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* in the**
690 **first intermediate host.**

691 **Table 4. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* in the**
692 **second intermediate host.**

693 **Table 5. Estimates of pooled prevalence and subgroup analysis of *Paragonimus* in**
694 **animal reservoirs.**

695

696 **Data reporting**

697 The data that supports the findings of this study are available in the supplementary
698 material of this article.

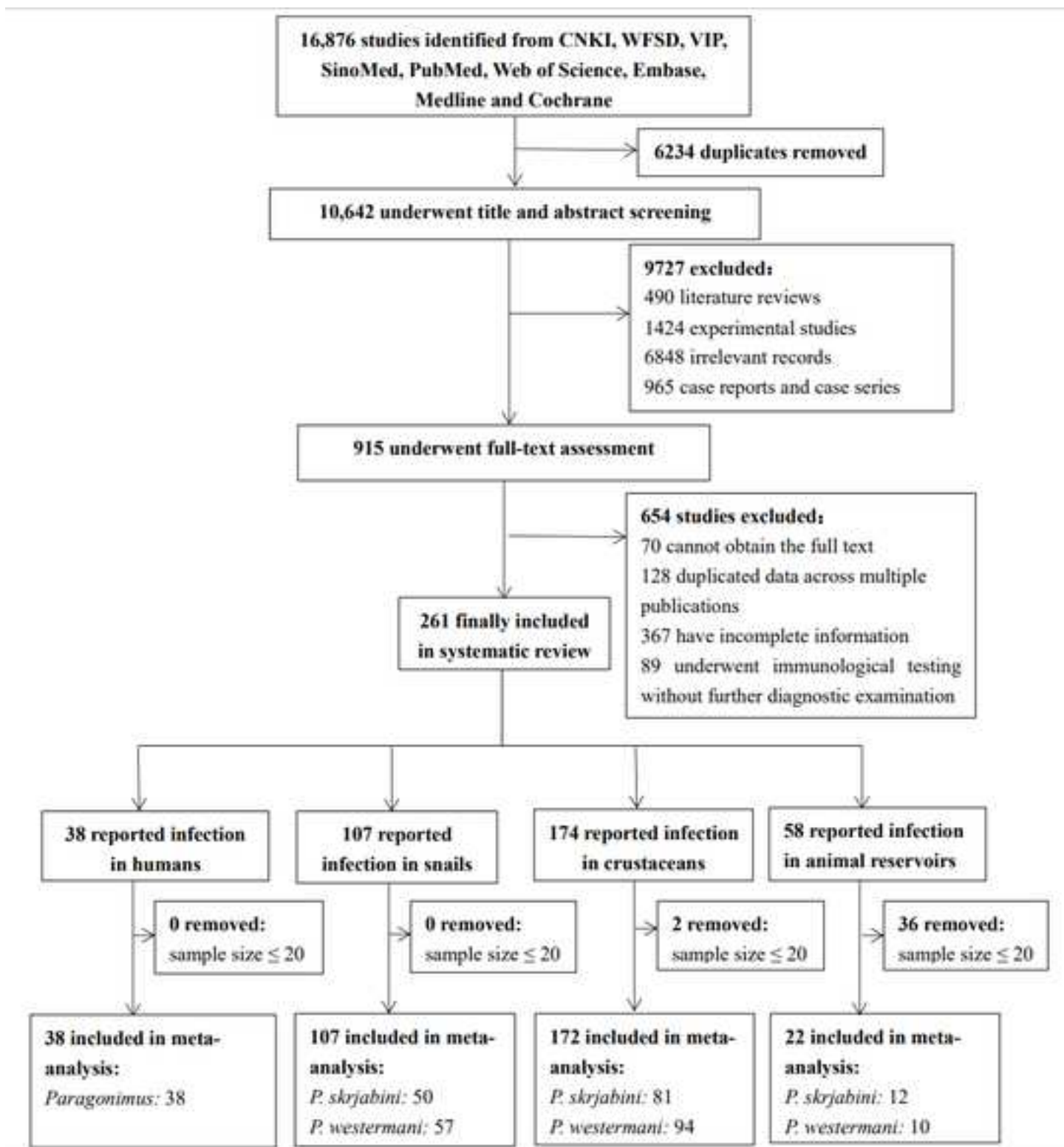


Fig 2. Spatial distribution of human paragonimiasis cases documented in China.

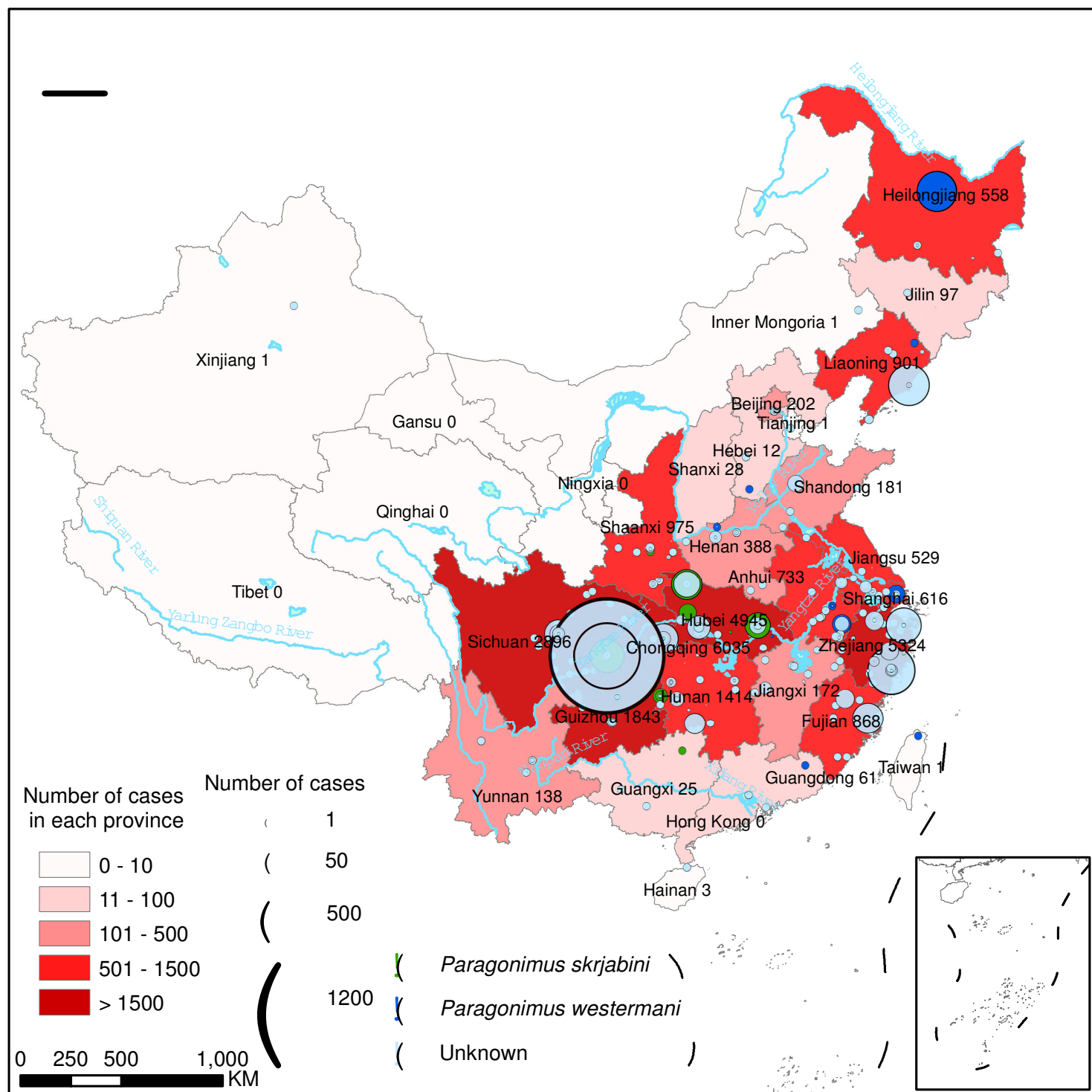


Fig 3a. Spatial distribution of *P. westermani* infection in the first intermediate hosts.

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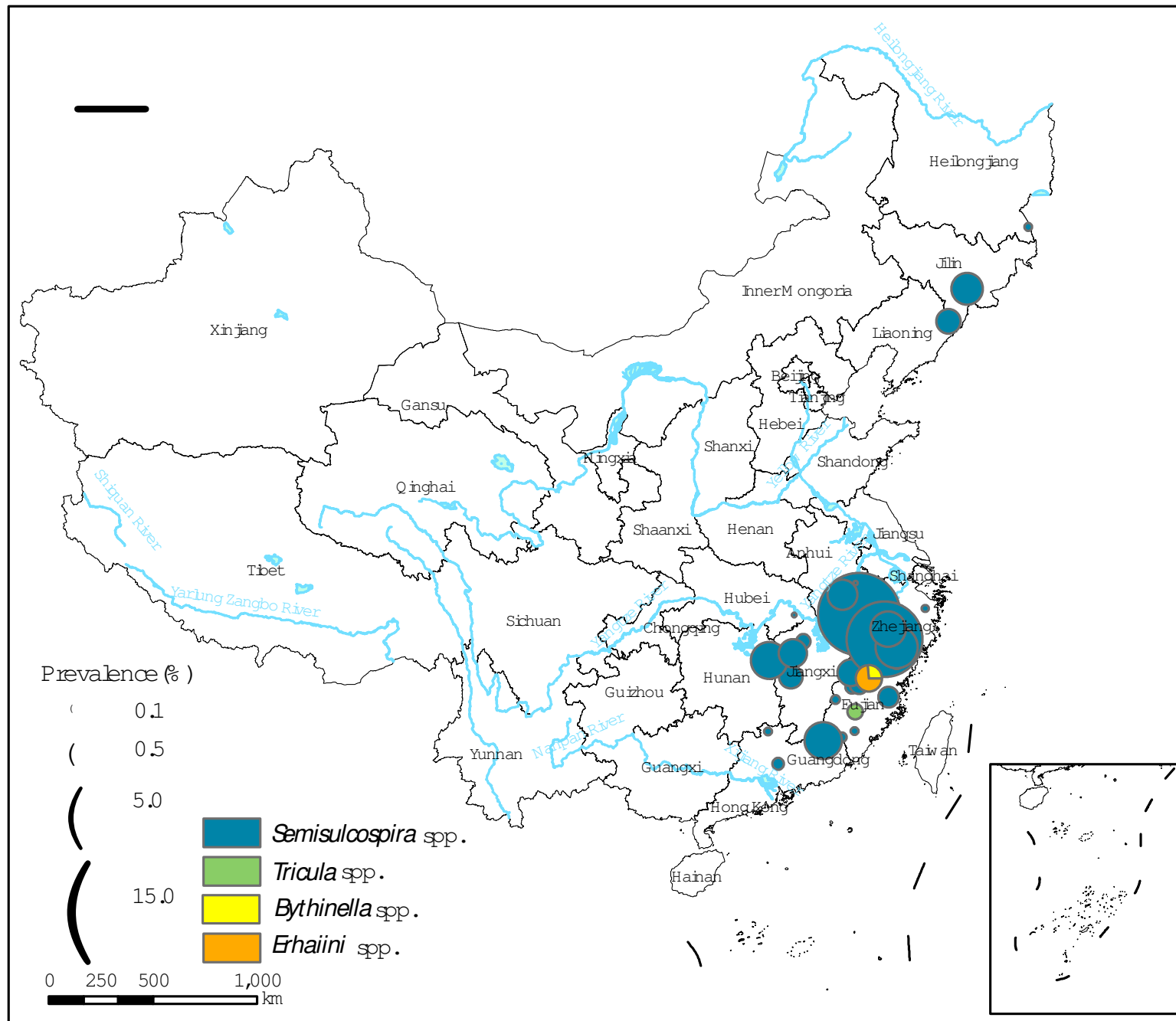


Fig 3b. Spatial distribution of *P. skrjabini* infection in the first intermediate hosts.

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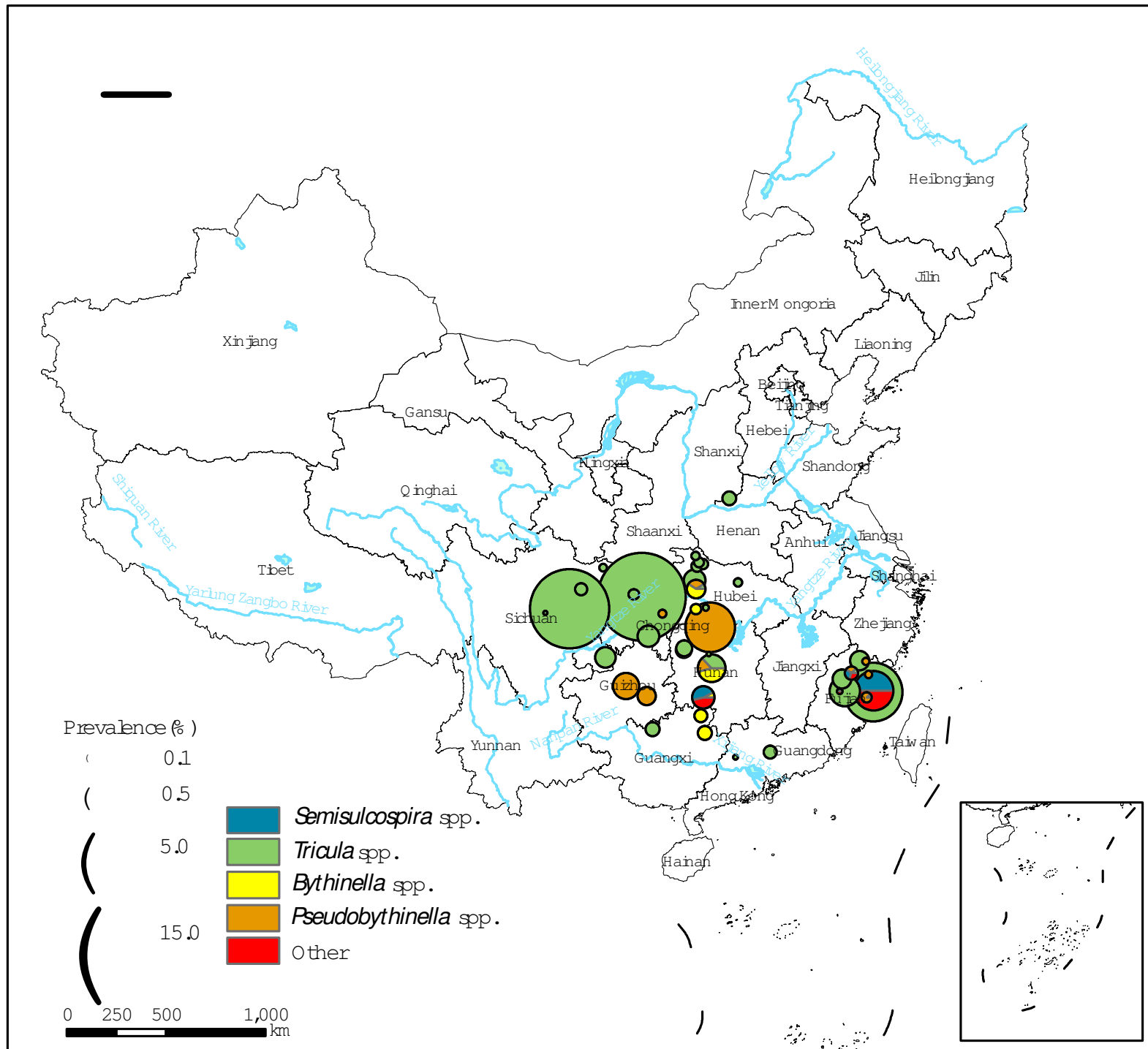


Fig 4a. Spatial distribution of *P. westermani* infection in the second intermediate hosts.

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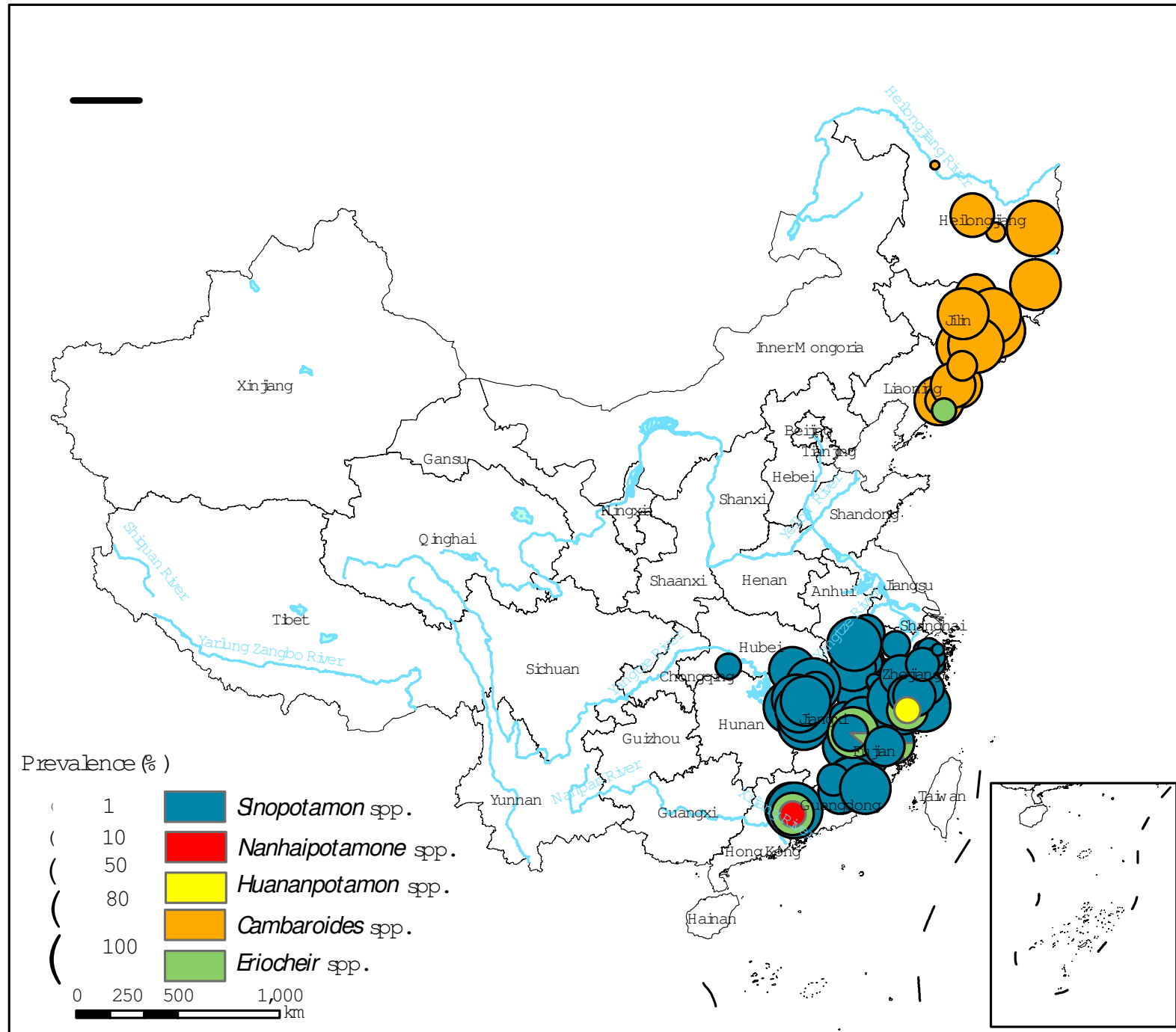


Fig 4b. Spatial distribution of *P. skrjabini* infection in the second intermediate hosts.

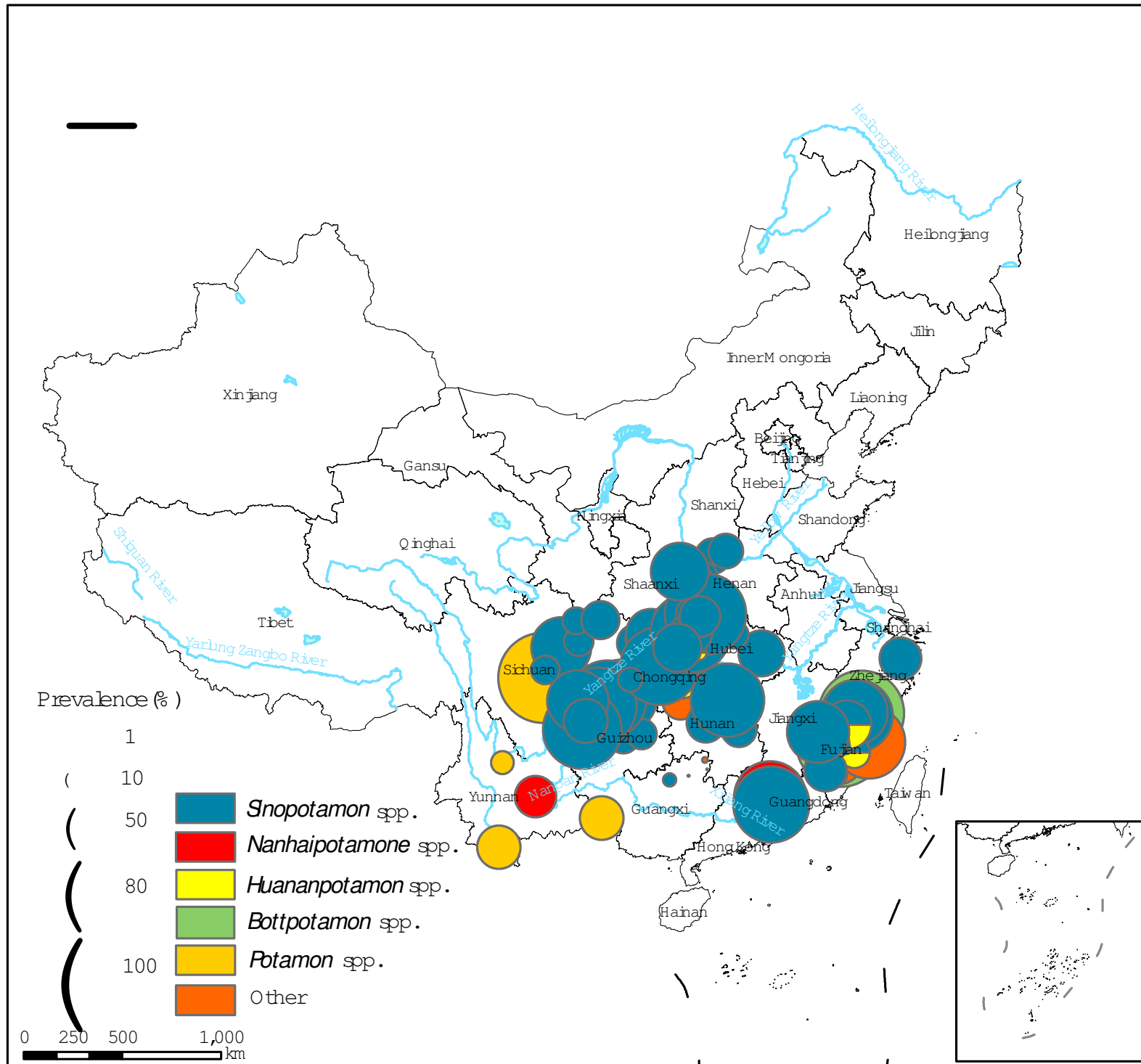
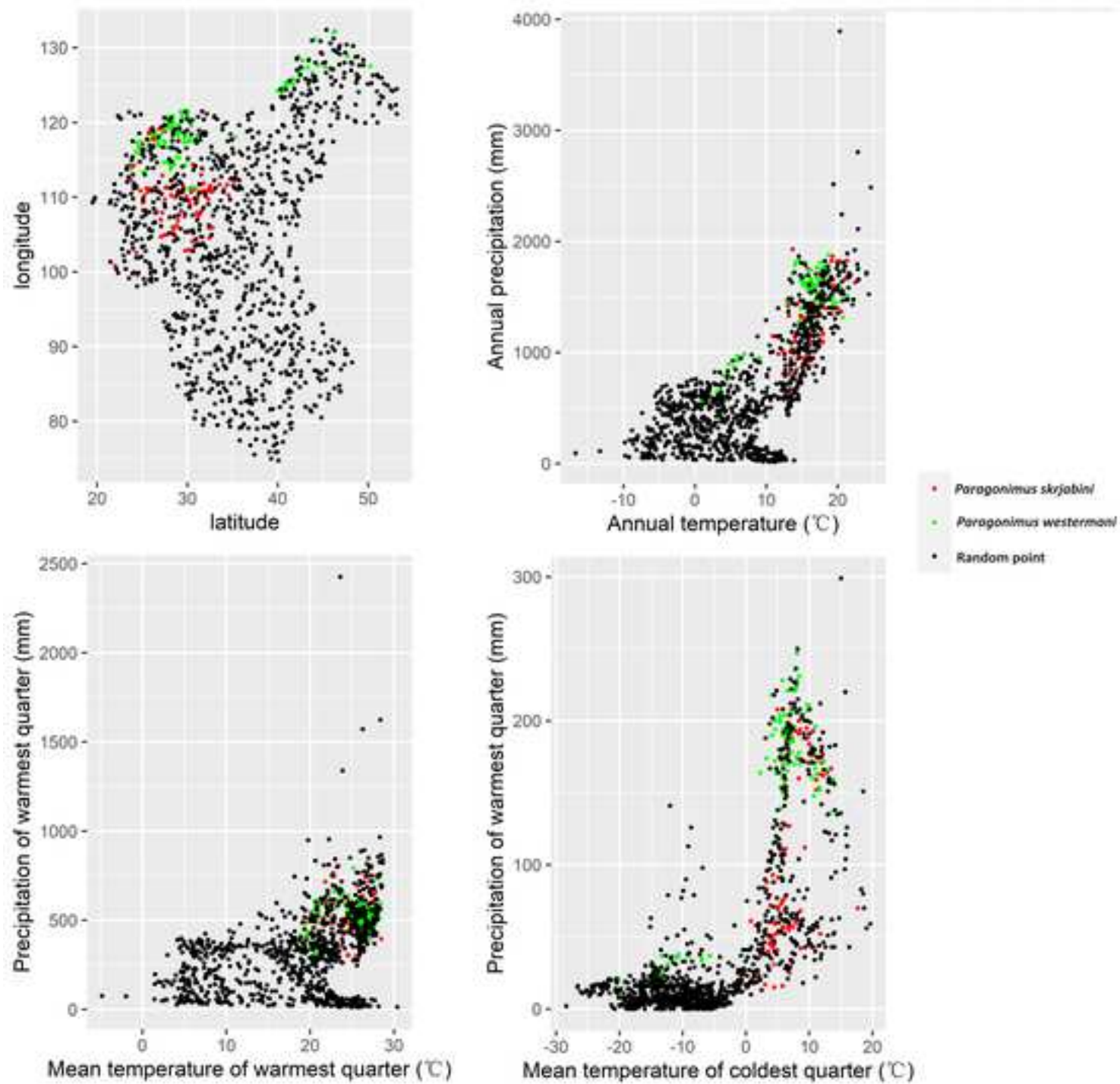


Fig 5. Environmental characteristics of areas with reported Paragonimus infections in China.

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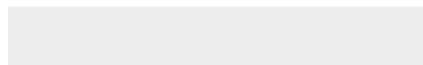




S1b Fig. Forest plots of prevalence of *P. westermani* in the first intermediate host.



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Supporting Information
S1b_Fig.tif



S1c Fig. Forest plots of prevalence of *P. skrjabini* in the first intermediate host.



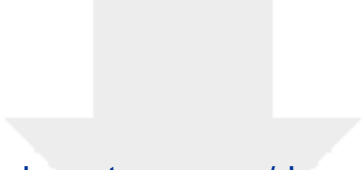
S1d Fig. Forest plots of prevalence of *P. westermani* in the second intermediate host.



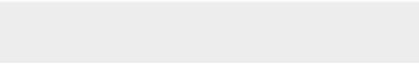

S1e Fig. Forest plots of prevalence of *P. skrjabini* in the second intermediate host.



S1f Fig. Forest plots of prevalence of *P. skrjabini* in animal reservoir.



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Supporting Information
S1f_Fig.tif



S1g Fig. Forest plots of prevalence of *P. westermani* in animal reservoir.



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S1g_Fig.tif

S2a Fig. Funnel plot for assessing publication bias in studies reporting prevalence of Paragonimus in humans.



S2b Fig. Funnel plot for assessing publication bias in studies reporting prevalence of *P. skrjabini* in the first intermediate host.







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S2d_Fig.tif



S2e Fig. Funnel plot for assessing publication bias in studies reporting prevalence of *P. westermani* in the second intermediate



S2f Fig. Funnel plot for assessing publication bias in studies reporting prevalence of *P. skrjabini* in animal reservoir.



S2g Fig. Funnel plot for assessing publication bias in studies reporting prevalence of *P. westermani* in animal reservoir.





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S1-S10 Tables.zip

