Association between Antibiotic Resistance and Increasing Ambient Temperature in China: An Ecological Study with Nationwide Panel Data

Supplementary Material

Statistical modeling

Considering the existence of unobserved influencing factors, we conducted panel data analyses to address potential spatial-temporal heterogeneity. The F test (**Supplementary Table S1**) and Hausman test (**Supplementary Table S2**) indicate that a fixed effect model is more suitable for panel data analyses. We then established models with fixed individual effects (**Supplementary Table S3-1**), with fixed time effects (**Supplementary Table S3-2**) and with two-way fixed effects (**Supplementary Table S3-3**), respectively.

Supplementary Table S1.

Comparison of the within and the pooling model.

F test	CRAB				CRKP				CRPA			
	F	*df1*	*df2*	*p*	*F*	*df1*	*df2*	*p*	*F*	*df1*	*df2*	*p*
Individual effects	8.27	27	163	<0.001	5.25	27	165	<0.001	6.15	25	163	<0.001
Time effects	2.98	13	177	<0.001	1.08	13	179	0.378	1.67	13	175	0.072
Two-way effects	6.07	40	150	<0.001	3.57	40	152	<0.001	4.66	38	150	<0.001

Supplementary Table S2.

Specification test for panel models. The random effects models (REM) were found to be inconsistent with the alternative specification. A fixed-effects model (FEM) is more suitable for the panel data.

Hausman test	CRAB			CRKP			CRPA		
	χ^2	*df*	*p*	χ^2	*df*	*p*	χ^2	*df*	*p*
Regression-based Hausman test	54.22	10	<0.001	39.75	10	<0.001	23.51	10	0.009
Robust Hausman test with vcov supplied as a function	134.18	10	<0.001	252.18	10	<0.001	79.64	10	<0.001

Supplementary Table S3-1.

Rate ratios (RR) of predictors with fixed individual effects.

Predictor	CRAB		CRKP		CRPA	
	RR	*p*	*RR*	*p*	*RR*	*p*
Antibiotic consumption (DDDs)	1.003	0.512	1.018	0.079	1.004	0.302
Corruption Perceptions Index (CPI)	1.003	0.868	0.991	0.852	1.003	0.868
Population density (person/km^2)	1.000	0.563	1.004	<0.001	1.000	0.310
GDP per capita (Yuan)	14.794	<0.001	0.498	0.537	0.387	0.018
Health facilities per 10,000 population	1.069	0.508	0.493	0.007	1.131	0.193
Physicians per 10,000 population	0.978	0.002	1.026	0.163	1.006	0.370
Hospital beds per 10,000 population	0.972	0.017	1.076	0.015	1.017	0.126
Annual average humidity (%)	1.001	0.951	0.940	0.045	1.006	0.559
Annual average rainfall (mm)	1.000	0.893	1.000	0.174	1.000	0.682
Average ambient temperature (℃)	1.028	0.613	1.007	0.963	0.977	0.633

R^2	0.448	0.396	0.100
adj.-R^2	0.323	0.260	-0.093

Adj.-R^2: adjusted coefficient of determination.

Supplementary Table S3-2.

Rate ratios (RR) of predictors with fixed time effects.

Predictor	CRAB		CRKP		CRPA	
	RR	*p*	*RR*	*p*	*RR*	*p*
Antibiotic consumption (DDDs)	1.004	0.594	1.055	0.009	1.000	0.987
Population density (person/km^2)	1.000	0.173	1.000	0.499	1.000	0.145
GDP per capita (Yuan)	0.957	0.726	0.585	0.082	1.196	0.104
Health facilities per 10,000 population	0.958	0.052	0.756	<0.001	0.953	0.012
Physicians per 10,000 population	1.003	0.309	1.002	0.803	1.000	0.899
Hospital beds per 10,000 population	1.021	0.001	1.060	<0.001	1.025	0.000
Annual average humidity (%)	1.004	0.569	0.969	0.078	1.003	0.642
Annual average rainfall (mm)	1.000	0.240	1.000	0.329	1.000	0.008
Average ambient temperature (°C)	1.023	0.156	1.131	0.002	1.075	<0.001
R^2	0.151		0.330		0.340	
adj.-R^2	0.041		0.244		0.254	

Adj.-R^2: adjusted coefficient of determination.

Supplementary Table S3-3.

Rate ratios (RR) of predictors with two-way fixed effects model.

Predictor	CRAB		CRKP		CRPA	
	RR	*p*	*RR*	*p*	*RR*	*p*
Antibiotic consumption (DDDs)	0.997	0.679	1.030	0.109	0.997	0.616
Population density (person/km^2)	0.999	0.110	1.004	0.004	1.001	0.192
GDP per capita (Yuan)	4.631	0.063	0.660	0.850	0.337	0.148
Health facilities per 10,000 population	1.218	0.078	0.498	0.017	1.159	0.156
Physicians per 10,000 population	0.973	0.003	1.030	0.223	1.010	0.221
Hospital beds per 10,000 population	0.977	0.096	1.067	0.082	1.023	0.077
Annual average humidity (%)	1.013	0.314	0.947	0.118	1.001	0.919
Annual average rainfall (mm)	1.000	0.877	1.000	0.200	1.000	0.671
Average ambient temperature (°C)	1.129	0.099	1.013	0.948	0.939	0.343
R^2	0.129		0.141		0.065	
adj.-R^2	-0.161		-0.141		-0.234	

Adj.-R^2: adjusted coefficient of determination.

Model validation

We predicted the 2019 prevalence (and 95% confidence interval) of antibiotic resistance in all provinces/regions of the CHINET using the established regression models, and compared the predicting values with the published data extracted from the China Antimicrobial Resistance Surveillance System (CARSS).

CRAB was highly prevalent in Tibet, Guangxi, Hainan and Chongqing, compared with very low prevalence of CRKP and CRPA. The unstandardized estimations of modelling produced a higher prediction accuracy for CRAB as indicated by the Index of Estimation Deviation in comparison with CRKP and CRPA.

Supplementary Table S4.

Unstandardized estimations of antibiotic resistance prevalence

Region	CRAB			CRKP			CRPA		
	Published	Predicted	IED	Published	Predicted	IED	Published	Predicted	IED
Tibet	24.4	29.3	0.17	0.6	0.2	0.70	7.1	8.8	0.19
Guangxi	56.0	68.6	0.18	3.2	23.2	0.86	13.4	27.8	0.52
Hainan	45.9	68.0	0.32	3.8	35.2	0.89	11.8	36.3	0.67
Chongqing	59.6	88.9	0.33	5.5	46.5	0.88	11.8	37.9	0.69

Note: IED represents Index of Estimation Deviation, which is the gap between 1 and the smaller one of published/predicted and predicted/published, with a higher IED indicating higher deviation.

Unstandardized estimations and prediction intervals of antibiotic resistance prevalence in 2019 was shown in **Supplementary Table S5**.

Supplementary Table S5.

Unstandardized estimations and prediction intervals of antibiotic resistance prevalence in 2019.

Province	CRAB(%)			CRKP(%)			CRPA(%)		
	ABR	PRE	95%*CI*	ABR	PRE	95%*CI*	ABR	PRE	95%*CI*
Ningxia	82.5	75.8	(28.1, 204.5)	7.6	14.6	(1.5, 144.4)	17.4	21.7	(9.5, 49.7)
Tianjin	59.9	58.3	(21.4, 158.9)	14.5	7.9	(0.8, 80.0)	26.0	23.0	(9.9, 53.2)
Beijing	77.7	88.7	(31.7, 248.2)	23.7	20.1	(1.9, 217.9)	21.2	30.1	(12.7, 71.3)
Xinjiang	62.2	93.0	(34.7, 249.5)	4.6	18.0	(1.8, 177.0)	17.6	23.4	(10.2, 53.4)
Shanghai	61.7	76.3	(27.9, 208.9)	28.7	26.0	(2.5, 268.1)	32.5	32.3	(13.9, 75.0)
Inner Mongolia	59.7	63.8	(23.8, 171.0)	5.9	4.0	(0.4, 39.4)	19.8	16.6	(7.3, 38.0)
Gansu	64.4	76.0	(28.5, 202.6)	2.0	5.4	(0.6, 52.1)	15.6	17.9	(7.9, 40.7)
Jilin	60.8	70.5	(26.4, 187.9)	2.0	5.6	(0.6, 53.9)	13.8	16.8	(7.4, 38.2)
Shanxi	76.7	56.6	(21.1, 151.9)	4.6	3.4	(0.3, 33.0)	27.0	17.5	(7.6, 39.9)
Fujian	55.3	62.5	(23.3, 167.9)	6.2	12.0	(1.2, 117.9)	20.1	28.6	(12.5, 65.2)
Shaanxi	90.1	81.7	(30.5, 218.7)	27.1	15.6	(1.6, 152.4)	43.0	28.6	(12.5, 65.2)
Heilongjiang	86.6	92.1	(33.9, 250.5)	11.7	14.2	(1.4, 143.9)	20.9	19.7	(8.6, 45.6)
Liaoning	66.0	79.9	(29.8, 214.0)	11.2	16.2	(1.7, 158.5)	34.2	24.1	(10.6, 54.9)
Jiangxi	44.4	62.5	(23.4, 167.0)	8.0	15.6	(1.6, 151.4)	5.8	24.3	(10.7, 55.3)
Yunnan	75.3	88.7	(32.8, 239.7)	31.3	45.6	(4.6, 454.8)	44.5	30.8	(13.4, 70.8)
Zhejiang	65.4	78.5	(29.4, 209.6)	38.8	21.0	(2.2, 204.5)	31.0	28.9	(12.7, 65.7)
Hubei	80.5	94.2	(35.2, 252,0)	21.8	32.1	(3.3, 314.2)	16.0	34.0	(14.9, 77.6)
Anhui	65.6	85.9	(31.6, 233.7)	25.0	18.4	(1.8, 186.9)	17.1	29.5	(12.8, 68.2)
Hunan	92.4	89.6	(33.4, 240.5)	33.0	25.6	(2.6, 252.1)	38.1	32.1	(14.0, 73.4)
Hebei	84.5	52.4	(19.3, 142.2)	38.6	4.2	(0.4, 42.5)	34.8	20.0	(8.7, 46.2)
Jiangsu	65.7	93.9	(34.6, 254.8)	21.3	30.6	(3.0, 308.5)	18.9	37.6	(16.3, 86.6)
Sichuan	74.2	93.2	(34.2, 254.0)	22.4	14.3	(1.4, 144.9)	34.0	30.6	(13.2, 70.8)
Henan	96.5	74.0	(27.3, 201.1)	62.1	29.6	(2.9, 298.6)	36.2	29.6	(12.8, 68.2)
Shandong	60.0	69.6	(26.1, 185.5)	16.0	10.4	(1.1, 101.1)	14.2	26.2	(11.5, 59.4)
Guangdong	56.5	61.5	(22.8, 166.0)	16.5	22.3	(2.2, 221.9)	17.9	26.8	(11.7, 61.5)
Guizhou	60.4	100.4	(36.9, 272.6)	39.6	23.3	(2.3, 235.2)	12.9	28.1	(12.2, 65.1)
Qinghai	9.2	72.7	(27.1, 195.3)	1.8	3.6	(0.4, 35.5)	12.3	15.6	(6.8, 35.8)
Tibet	24.4	29.3	(9.6, 90.0)	0.6	0.2	(0, 2.4)	7.1	8.8	(3.4, 22.5)
Guangxi	56.0	68.6	(25.6, 183.5)	3.2	23.2	(2.4, 226.6)	13.4	27.8	(12.2, 63.3)
Hainan	45.9	68.0	(25.2, 183.6)	3.8	35.2	(3.5, 352.1)	11.8	36.3	(15.8, 83.3)
Chongqing	59.6	88.9	(32.8, 240.9)	5.5	46.5	(4.6, 467.7)	11.8	37.9	(16.5, 87.3)

Supplementary Figure S1.

The distribution of four administrative types of regions in China.
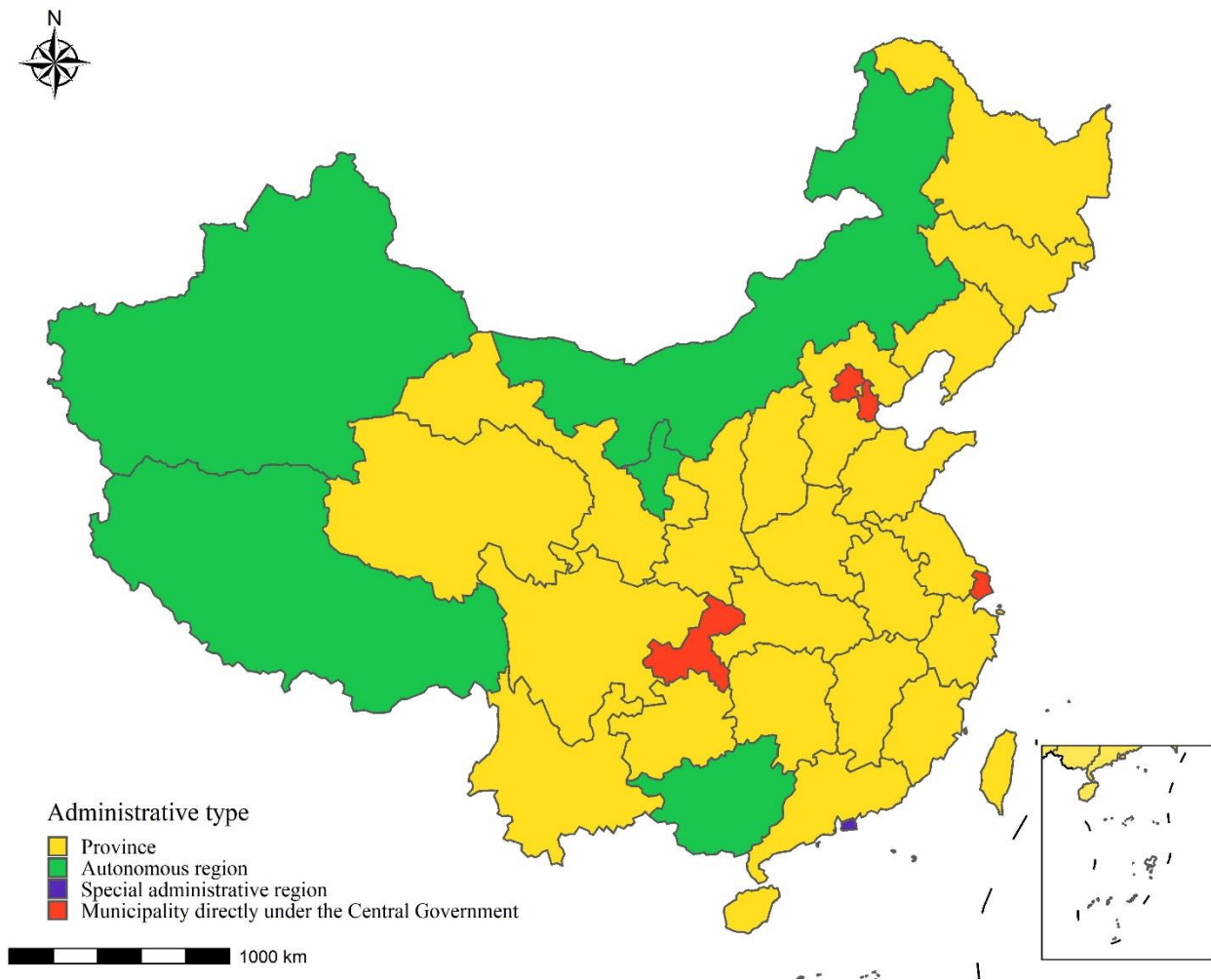
Supplementary Figure S2.

Simple division of northern (colder) and southern (warmer) regions in China.