Preplanned Studies

Epidemiological and Spatiotemporal Clustering Analysis of Human Brucellosis — China, 2019–2023

Zhiguo Liu[1,&]; Yue Shi[2,&]; Chuizhao Xue[3]; Min Yuan[1]; Zhenjun Li[2,#]; Canjun Zheng[2,#]

Summary

What is already known about this topic?

The number of reported cases of human brucellosis significantly increased from 45,046 (3.25/100,000) in 2019 to 70,439 (4.99/100,000) in 2023.

What is added by this report?

Human brucellosis continued to spread and expand of in northern China, with the most cases reported in the Inner Mongolia Autonomous Region (*n*=87,961), Xinjiang Uygur Autonomous Region (*n*=27,845) and Shanxi Province (*n*=21,932). In southern China, reported cases increased substantially from 2,036 in 2019 to 5,128 in 2023. Joinpoint regression analysis revealed an upward trend in incidence rate across 29 provincial-level administrative divisions (PLADs), with an annual percent change (APC) of 12.86, (P<0.05), with particularly rapid increases observed in most southern PLADs. Spatiotemporal analysis identified high-risk clusters concentrated in the northwestern and northeastern regions.

What are the implications for public health practice?

With the continued worsening of human brucellosis over the past five years, implementing strict controls on the movement of infected animals is urgeent.

Brucellosis is a globally significant zoonotic disease that causes substantial economic losses and poses serious occupational health risks (*1*–*2*). Since 1995, brucellosis has reemerged in China, reaching a historic peak in 2014, with the affected areas expanding from northern to southern regions (*3*). Notably, in 2021, 69,767 cases were reported across 2,083 counties in China, representing a 47.7% increase from 2020 (47,425) (*4*). However, epidemiological evolution characteristics of human brucellosis from 2019 to 2023 remain unclear. Therefore, this study aims to analyze disease evolution patterns and to identify high-risk areas for human brucellosis in China from 2019 to 2023.

The case and incidence rates were obtained from the National Notifiable Disease Reporting System (NNDRS) for the period January 1, 2019 to December 31, 2023. The average annual growth rate was calculated according to previously reported methods (*5*). Average annual incidence growth rates (%) were calculated using power functions in Microsoft Excel 2021 (Microsoft Corporation, Redmond, Washington, United States).

The Qinling-Huaihe line served as the geographical boundary between northern and southern China. The northern region comprised 16 provincial-level administrative divisions (PLADs) [Heilongjiang, Jilin, Liaoning, Beijing, Tianjin, Inner Mongolia, Shaanxi, Hebei, Henan, Ningxia, Shanxi, Shandong, Gansu, Qinghai, Xinjiang (Xinjiang Production and Construction Corps, XPCC) and Xizang], while the southern region included 15 PLADs (Jiangsu, Shanghai, Zhejiang, Anhui, Hunan, Hubei, Sichuan, Chongqing, Guizhou, Yunnan, Guangxi, Guangdong, Hainan, Fujian and Jiangxi). Hong Kong Special Administrative Region (SAR); Macau SAR; and Taiwan, China were excluded due to data unavailability.

Joinpoint regression analyses were performed using Joinpoint Regression Program version 5.2.0 (https://surveillance.cancer.gov/joinpoint/) (National Cancer Institute, Bethesda, Maryland, USA) based on Poisson regression to estimate joinpoint positions and regression coefficients (*6*). Annual percentage changes (APCs) were calculated to quantify the year-over-year rate changes between successive joinpoints as percentages.

A retrospective space-time scan analysis using the discrete Poisson model was conducted using SaTScan v10.1.3 (National Cancer Institute, Bethesda, Maryland, USA) to identify spatiotemporal clusters of human brucellosis. Statistical significance was assessed through 999 Monte Carlo simulations. The log likelihood ratio (LLR) test statistic was constructed by comparing observed and expected case counts inside and outside the scanning window. Clusters were defined by scanning windows with statistically

significant LLR values (P<0.05).

From 2019 to 2023, human brucellosis cases and incidence rates demonstrated a fluctuating upward trend across 31 PLADs in China, with 304,668 total reported cases and an average annual incidence of 4.33/10,000 population (Figure 1).

The annual reported cases increased from 45,046 (3.25/100,000) in 2019 to 48,455 (3.45/100,000) in 2020, reaching a peak of 71,628 (5.06/100,000) in 2021. Subsequently, cases slightly decreased to 69,100 (4.89/10,000) in 2022 before rising again to 70,439 (4.99/10,000) in 2023 (Figure 1). Further, 87.78% (267,446/304,668) of cases occurred in northern PLADs, while 12.22% (37,222/304,668) were reported from southern PLADs. Notably, southern PLADs experienced a substantial increase in reported cases, from 4,310 in 2019 to 10,363 in 2023 (Figure 1 and Table 1).

From 2019 to 2023, Inner Mongolia accounted for the largest proportion (87,961 cases; 28.87% of all reports) with an average annual incidence of 71.88/100,000 (Table 1). Shanghai reported the lowest number of cases (22), followed by Hainan (257), with average annual incidence rates of 0.018/100,000 and 0.31/100,000, respectively. With the exception of Yunnan, all southern PLADs reported incidence rates below 1.0/100,000 (Table 1).

The average annual growth rate of incidence in China from 2019 to 2023 was 8.97% (Table 2). Notably, 13 southern PLADs and 5 northern PLADs reported average annual growth rates exceeding 10% (Table 2). Qinghai showed a marked upward trend, with annual incidence increasing from 2.45/100,000 in 2019 to 34.86/100,000 in 2023. Although most southern PLADs maintained incidence rates below 1.0/100,000, they showed consistent increases over time (Table 2).

Joinpoint regression analysis revealed APCs ranging from –0.70 to 97.97, with 29 PLADs demonstrating significant upward trends in incidence rates, except for Jilin and Xizang (Table 3). Notably, six PLADs — Qinghai, Guizhou, Yunnan, Sichuan, Jiangxi, and Guangxi (Table 3) — exhibited particularly significant increases, with five of these PLADs located in southern China.

Retrospective space-time analysis scanning for clusters with high rates using the discrete Poisson model identified 14 distinct zones of human brucellosis clusters. The largest cluster occurred between January 1, 2022, and December 31, 2023, encompassing 419 counties (Figure 2 and Table 3). This primary cluster demonstrated a relative risk of 8.95 with a LLR of 79,182.30 (P<0.001) (Figure 2 and Table 4).

The second largest cluster, comprising 33 counties across Inner Mongolia, Jilin, and Liaoning, was identified between January 1, 2020, and December 31, 2021, with a relative risk of 20.75 and LLR of 40,377.28 (P<0.001) (Figure 2). The third largest cluster included 19 counties in Henan Province during January 1, 2022, to December 31, 2023, exhibiting a relative risk of 3.73 and LLR of 2,140.47 (P<0.001). The remaining 11 clusters each contained 1 to 3 counties, distributed across Henan, Shandong, Yunnan, and Sichuan (Figure 2 and Table 4).

DISCUSSION

Our analysis reveals that human brucellosis continued to spread and expand, the majority of cases remain concentrated in northern China, with PLADs in the northwestern and northeastern region. Inner Mongolia's cases, accounting for 28.87% of the national total, indicate ineffective control measures and inadequate containment of animal brucellosis (*7*). In

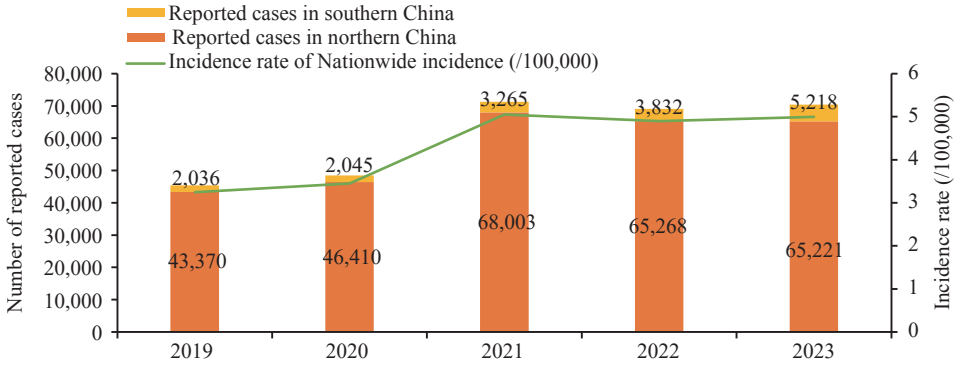

FIGURE 1. Evolution trend of human brucellosis in northern and southern China, from 2019 to 2023.

TABLE 1. Number of reported cases in 31 PLADs in China from 2019 to 2023.

Areas	PLADs	Number of reported cases, 2019-2023					Total cases
		2019	2020	2021	2022	2023	
Northern	Inner Mongolia	14,148	16,406	21,910	19,088	16,409	87,961
	Xinjiang	4,135	3,079	4,828	6,469	9,334	27,845
	Shanxi	3,465	3,498	4,962	4,876	5,131	21,932
	Ningxia	2,242	2,988	5,049	6,295	4,505	21,079
	Henan	2,274	3,121	5,032	5,254	5,145	20,826
	Gansu	1,787	3,003	4,601	5,229	5,569	20,189
	Hebei	3,407	3,158	4,777	3,970	4,196	19,508
	Liaoning	2,298	3,000	5,483	3,916	3,162	17,859
	Heilongjiang	4,326	2,956	4,119	2,849	3,387	17,637
	Shandong	2,534	2,427	3,370	3,218	3,311	14,860
	Shaanxi	1,138	1,116	1,419	1,705	1,543	6,921
	Jilin	1,191	1,151	1,311	847	1,093	5,593
	Qinghai	148	259	772	1,159	2,074	4,412
	Tianjin	136	136	238	258	209	977
	Beijing	86	54	83	115	131	469
	Xizang	55	58	49	20	22	204
Southern	Yunnan	321	383	701	1,039	1,519	3,963
	Guangdong	456	361	479	490	612	2,398
	Anhui	142	229	353	347	414	1,485
	Hunan	212	167	239	248	349	1,215
	Jiangsu	142	165	284	284	299	1,174
	Sichuan	114	130	206	267	417	1,134
	Guangxi	153	125	229	248	367	1,122
	Fujian	151	111	195	207	238	902
	Zhejiang	108	127	181	209	195	820
	Hubei	80	73	107	175	254	689
	Guizhou	33	54	92	140	207	526
	Jiangxi	58	53	103	80	177	471
	Chongqing	49	54	72	49	94	318
	Hainan	15	9	21	41	71	157
	Shanghai	2	4	3	8	5	22
Nationwide		45,406	48,455	71,268	69,100	70,439	304,668

Abbreviation: PLAD=provincial-level administrative division.

agricultural and livestock farming regions facilitate *Brucella* strain transmission through close human-animal interaction, where livestock farming represents the sole livelihood, complicated by nomadic lifestyles and low socioeconomic conditions.

In southern China, reported cases have increased markedly from 2.0% of national cases in 2019 to 5.38% in 2023, with total cases rising from 4,310 to 10,363. All 15 southern PLADs show upward trends in both case numbers and incidence rates. Molecular epidemiological investigation of *Brucella* in Guizhou from 2009 to 2021 confirms strain importation from northern areas such as Inner Mongolia and Xinjiang (*8*).

The high-risk clusters were predominantly concentrated in the northwestern and northeastern regions, with additional clusters in two southern PLADs, Yunnan and Sichuan. This distribution differs

TABLE 2. Average annual growth rate (%) of incidence (/100,000) in 31 PLADs from 2019 to 2023.

Areas	PLADs	2019–2023, incidence (/100,000)					Average annual incidence (/100,000)	Average annual growth rate (%)
		2019	2020	2021	2022	2023		
Northern	Qinghai	2.45	4.26	13.03	19.51	34.86	14.82	70.02
	Gansu	6.78	11.34	18.39	21.00	22.34	15.97	26.95
	Henan	2.37	3.24	5.06	5.32	5.21	4.24	17.10
	Xinjiang	16.63	12.20	18.68	24.99	36.08	21.71	16.76
	Ningxia	32.59	43.01	70.10	86.83	61.85	58.88	13.67
	Tianjin	0.87	0.87	1.72	1.88	1.53	1.37	11.96
	Shanxi	9.32	9.38	14.21	14.01	14.74	12.33	9.61
	Beijing	0.40	0.25	0.38	0.53	0.60	0.43	8.48
	Liaoning	5.27	6.89	12.87	9.26	7.53	8.37	7.40
	Shaanxi	2.94	2.88	3.59	4.31	3.90	3.53	5.78
	Shandong	2.52	2.41	3.32	3.16	3.26	2.93	5.25
	Hebei	4.51	4.16	6.40	5.33	5.66	5.21	4.63
	Inner Mongolia	55.83	64.60	91.11	79.53	68.34	71.88	4.12
	Jilin	4.40	4.28	5.45	3.57	4.66	4.47	1.12
	Heilongjiang	11.47	7.88	12.93	9.12	10.93	10.46	−0.95
	Xizang	1.60	1.65	1.34	0.55	0.60	1.15	−17.69
Southern	Guizhou	0.09	0.15	0.24	0.36	0.54	0.28	42.39
	Yunnan	0.66	0.79	1.48	2.22	3.24	1.68	37.25
	Hainan	0.16	0.10	0.21	0.40	0.69	0.31	33.93
	Sichuan	0.14	0.16	0.25	0.32	0.50	0.27	29.51
	Hubei	0.14	0.12	0.19	0.30	0.43	0.24	26.31
	Jiangxi	0.12	0.11	0.23	0.18	0.39	0.21	25.65
	Anhui	0.22	0.36	0.58	0.57	0.68	0.48	24.64
	Shanghai	0.01	0.02	0.01	0.03	0.02	0.02	19.47
	Guangxi	0.31	0.25	0.46	0.49	0.73	0.45	18.54
	Jiangsu	0.18	0.20	0.34	0.33	0.35	0.28	14.76
	Chongqing	0.16	0.17	0.22	0.15	0.29	0.20	13.11
	Hunan	0.31	0.24	0.36	0.37	0.53	0.36	11.45
	Zhejiang	0.19	0.22	0.28	0.32	0.30	0.26	9.51
	Fujian	0.38	0.28	0.47	0.49	0.57	0.44	8.20
	Guangdong	0.40	0.31	0.38	0.39	0.48	0.39	3.77
Nationwide		3.25	3.45	5.06	4.90	5.00	4.33	8.97

Abbreviation: PLAD=provincial-level administrative division.

from the 2004–2019 pattern, where significant spatial correlations of high incidence were primarily confined to northern China, particularly Inner Mongolia, Shanxi, and Heilongjiang (*9*). In Jiangsu, the disease progression from 2006 to 2021 showed gradual expansion from northern and southern regions toward central areas. This situation necessitates urgent enhancement of local outbreak response capabilities in high-incidence regions.

The control of human brucellosis is fundamentally dependent on effective animal brucellosis surveillance and control measures. However, the ongoing development of animal husbandry presents significant challenges to animal brucellosis prevention and control (*10*). Strict enforcement of regulations prohibiting the movement of infected animals from northern to southern areas is crucial, including systematic screening and isolation of diseased animals from herds, and

TABLE 3. Joinpoint regression analysis of human brucellosis in 31 PLADs from 2019 to 2023.

Areas	PLADs	Period	APC	95% *CI*	*P*
Northern	Qinghai	2019–2023	97.97	69.82, 129.00	<0.001
	Gansu	2019–2023	35.02	−0.79, 82.97	0.063
	Xinjiang	2019–2023	25.44	−1.55, 58.41	0.070
	Henan	2019–2023	23.05	1.99, 47.46	0.024
	Ningxia	2019–2023	21.95	−20.49, 86.16	0.320
	Tianjin	2019–2023	20.91	−14.88, 71.26	0.266
	Beijing	2019–2023	16.81	−6.27, 44.65	0.188
	Shanxi	2019–2023	14.09	1.60, 27.52	0.020
	Liaoning	2019–2023	10.62	−19.40, 49.80	0.472
	Shaanxi	2019–2023	10.14	−5.45, 27.97	0.206
	Shandong	2019–2023	8.16	−0.29, 16.88	0.061
	Hebei	2019–2023	7.26	−3.07, 18.19	0.180
	Inner Mongolia	2019–2023	6.31	−9.43, 24.12	0.419
	Heilongjiang	2019–2023	0.50	−24.41, 32.65	0.971
	Jilin	2019–2023	−0.70	−14.26, 14.34	0.891
	Xizang	2019–2023	−26.32	−45.07, −1.92	0.035
Southern	Guizhou	2019–2023	55.67	48.68, 62.84	<0.001
	Hainan	2019–2023	54.66	9.50, 115.38	0.008
	Yunnan	2019–2023	52.19	41.92, 62.91	<0.001
	Sichuan	2019–2023	39.18	23.83, 56.00	<0.001
	Hubei	2019–2023	38.07	6.19, 78.88	0.011
	Jiangxi	2019–2023	31.36	8.88, 57.77	<0.001
	Anhui	2019–2023	30.46	9.96, 53.80	0.001
	Shanghai	2019–2023	27.69	−3.12, 66.00	0.080
	Guangxi	2019–2023	26.76	10.13, 45.20	<0.001
	Jiangsu	2019–2023	20.53	6.08, 36.22	0.003
	Hunan	2019–2023	16.45	−2.44, 38.56	0.103
	Fujian	2019–2023	14.56	−0.73, 31.89	0.068
	Zhejiang	2019–2023	13.82	−1.66, 31.38	0.088
	Chongqing	2019–2023	11.71	−9.84, 37.80	0.334
	Guangdong	2019–2023	5.96	−15.45, 32.30	0.499
Nationwide		2019–2023	12.86	1.33, 25.09	0.028

Abbreviation: PLAD=provincial-level administrative division; *CI*=confidence interval; APC=annual percent change.

continued vaccination programs. Remarkably, resource and financial investment in brucellosis control must be continuously increased to curb its spread, even after achieving initial control (*11*).

This study has several limitations. Brucellosis is frequently underreported due to its nonspecific clinical presentation, and our analysis relies on surveillance system data that may be influenced by regional variations in physician awareness of the disease.

Our analysis demonstrates that the disease has not only persisted in northern China but has also established significant presence in southern PLADs. The proportion of total reported cases in southern regions has increased markedly from 2.0% before 2019 to 5.38% after 2019. These findings underscore the urgent need to implement more stringent control strategies to prevent further deterioration of the situation.

Conflicts of interest: No conflicts of interest.

Acknowledgements: We acknowledge the

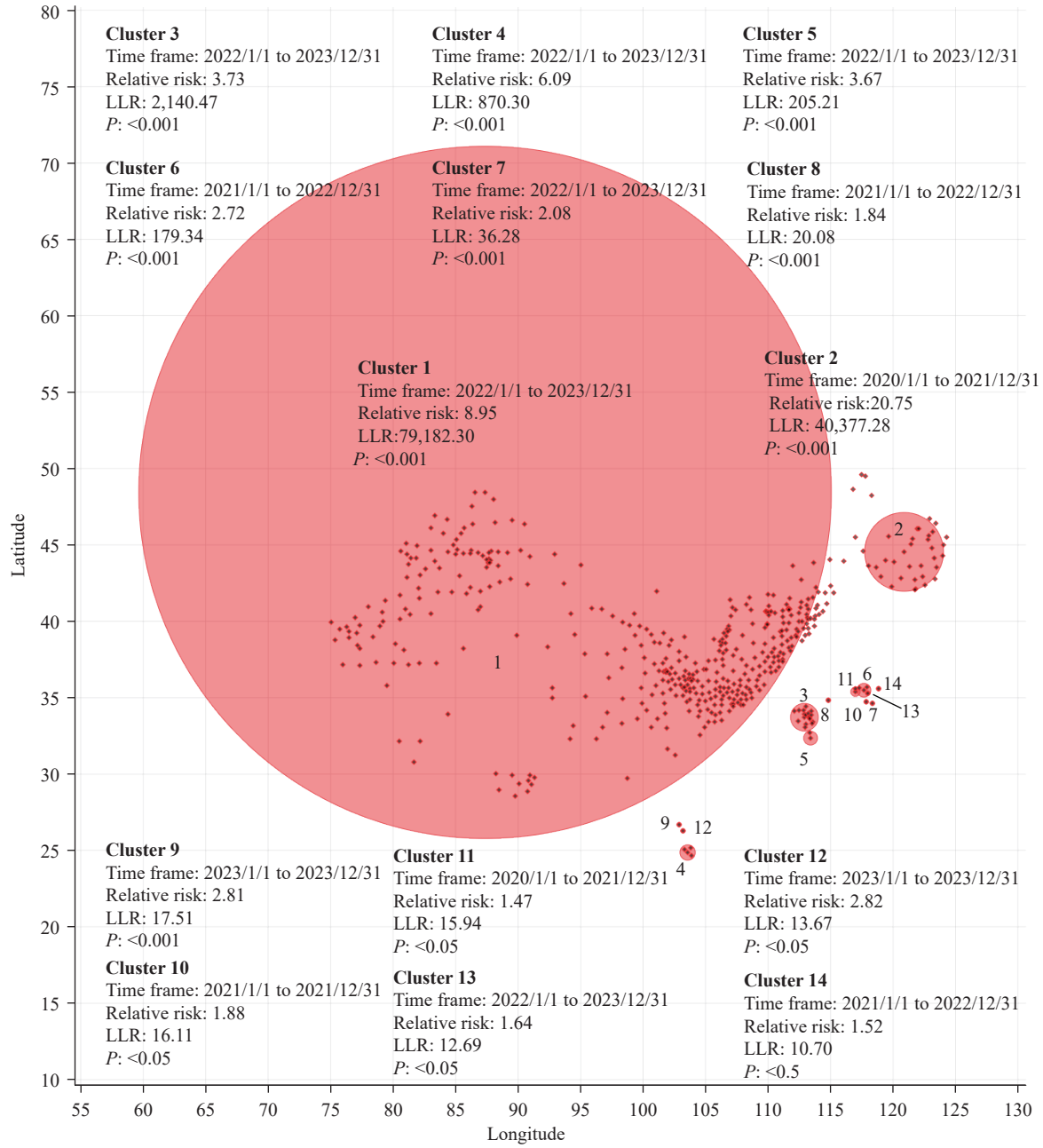

FIGURE 2. Spatial-temporal feature of human brucellosis in China, from 2019 to 2023.
Note: Retrospective space-time analysis scanning for clusters with high rates using the Discrete Poisson model; numbers (1–14) in figures indicates location of 14 clusters zones.
Abbreviation: LLR=log likelihood ratio.

dedication of healthcare staff at provincial, prefecture, and county-level CDCs across the 31 PLADs and XPCC in China for their contributions to brucellosis surveillance and control efforts.

Funding: Supported by the National Natural Science Foundation of China (No. L2124006, Institute Number: 90100). The funding body had no role in study design, data collection and analysis, decision to publish, or manuscript preparation.

doi: 10.46234/ccdcw2025.020

[#] Corresponding authors: Zhenjun Li, lizhenjun@icdc.cn; Canjun Zheng, zhengcj@chinacdc.cn.

[1] National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; [2] Chinese Center for Disease Control and Prevention, Beijing, China; [3] National Institute of Parasitic Diseases,

TABLE 4. Distribution profile of high-high clusters of human brucellosis from 2019 to 2023.

Clusters	Time frame	Relative risk	LLR	Number of counties	PLADs
1	2022/1/1 to 2023/12/31	8.95	79182.30	419	Xinjiang, Inner Mongolia, Gansu, Qinghai, Ningxia, Xizang, Sichuan, Shanxi, Shaanxi, Hebei
2	2020/1/1 to 2021/12/31	20.75	40377.28	33	Inner Mongolia, Jilin, Liaoning, Heilongjiang
3	2022/1/1 to 2023/12/31	3.73	2140.47	19	Henan
4	2022/1/1 to 2023/12/31	6.09	870.29	4	Yunnan
5	2022/1/1 to 2023/12/31	3.67	205.21	2	Henan
6	2021/1/1 to 2022/12/31	2.72	179.34	3	Shandong
7	2022/1/1 to 2023/12/31	2.08	36.28	1	Shandong
8	2021/1/1 to 2022/12/31	1.84	20.08	1	Henan
9	2023/1/1 to 2023/12/31	2.81	17.51	1	Sichuan
10	2021/1/1 to 2021/12/31	1.88	16.11	1	Shandong
11	2020/1/1 to 2021/12/31	1.47	15.94	2	Shandong
12	2023/1/1 to 2023/12/31	2.82	13.67	1	Yunnan
13	2022/1/1 to 2023/12/31	1.64	12.69	1	Shandong
14	2021/1/1 to 2022/12/31	1.52	10.70	1	Shandong

Note: Number of counties: total of counties involved in the high-risk clusters zone.
Abbreviation: LLR=log likelihood ratio; PLAD=provincial-level administrative division.

Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research), Shanghai, China.
[&] Joint first authors.

Submitted: September 13, 2024
Accepted: December 03, 2024
Issued: January 24, 2025

REFERENCES

1. Xu QG. Knowledge, attitude and practice associated with brucellosis in occupational risk groups in China [dissertation]. Bangkok, Thailand: Chulalongkorn University; 2021. https://digital.car.chula.ac.th/chulaetd/4950/.
2. Dutkiewicz J, Cisak E, Sroka J, Wójcik-Fatla A, Zając V. Biological agents as occupational hazards-selected issues. Ann Agric Environ Med 2011;18(2):286-93. https://www.aaem.pl/Biological-agents-as-occupational-hazards-selected-issues,71702,0,2.html.
3. Lai SJ, Zhou H, Xiong WY, Yu HJ, Huang ZJ, Yu JX, et al. Changing epidemiology of human brucellosis, China, 1955-2014. Emerg Infect Dis 2017;23(2):184 – 94. https://doi.org/10.3201/eid2302.151710.
4. Yang HM, Chen QL, Li Y, Mu D, Zhang YP, Yin WW. Epidemic characteristics, high-risk areas and space-time clusters of human brucellosis — China, 2020–2021. China CDC Wkly 2023;5(1):17 – 22. https://doi.org/10.46234/ccdcw2023.004.
5. Tao ZF, Chen QL, Chen YS, Li Y, Mu D, Yang HM, et al. Epidemiological characteristics of human brucellosis - China, 2016-2019. China CDC Wkly 2021;3(6):114 – 9. https://doi.org/10.46234/ccdcw2021.030.
6. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19(3):335 – 51. https://doi.org/10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z.
7. Zhou LH, Fan M, Hou Q, Jin Z, Sun XD. Transmission dynamics and optimal control of brucellosis in Inner Mongolia of China. Math Biosci Eng 2018;15(2):543 – 67. https://doi.org/10.3934/mbe.2018025.
8. Tan QQ, Wang Y, Liu Y, Tao ZF, Yu C, Huang Y, et al. Molecular epidemiological characteristics of *Brucella* in Guizhou Province, China, from 2009 to 2021. Front Microbiol 2023;14:1188469. https://doi.org/10.3389/fmicb.2023.1188469.
9. Sun ZX, Wang Y, Li YJ, Yu SH, Wu W, Huang DS, et al. Socioeconomic, meteorological factors and spatiotemporal distribution of human brucellosis in China between 2004 and 2019-a study based on spatial panel model. PLoS Negl Trop Dis 2023;17(11):e0011765. https://doi.org/10.1371/journal.pntd.0011765.
10. Qureshi KA, Parvez A, Fahmy NA, Abdel Hady BH, Kumar S, Ganguly A, et al. Brucellosis: epidemiology, pathogenesis, diagnosis and treatment-a comprehensive review. Ann Med 2023;55(2):2295398. https://doi.org/10.1080/07853890.2023.2295398.
11. El-Sayed A, Awad W. Brucellosis: evolution and expected comeback. Int J Vet Sci Med 2018;6(Suppl):S31 – 5. https://doi.org/10.1016/j.ijvsm.2018.01.008.