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Evolution of the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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ABSTRACT

Objectives To describe the epidemiology of human brucellosis in the past decade and provide the evidence of disease control in Tongliao city, located in eastern Inner Mongolia province, which is one of the highest-risk areas of human brucellosis in China.

Design Cross-sectional study.

Participants Clinically and bacteriologically confirmed human brucellosis cases.

Primary and secondary outcome measures The reported cases and incidence rates of human brucellosis cases from 2007 to 2017 were carried out to describe the age, sex and occupational distributions of human brucellosis. The time series analysis model was explored to describe the seasonality. Geographic information system was used to identify the spatio-temporal distribution at county level.

Results A total of 13, 938 cases of human brucellosis occurred in Tongliao from 2007 to 2017. Most of patients were agriculturalists (81.9%) or pastoralists (12.4%), with the majority age from 25 to 59 years old (85.4%) and a male-to female ratio of 2.64:1. The reported incidence rate increased dramatically from 9.22/100, 000 in 2007 to 69.16/100, 000 in 2011 with an annual increase of 14.99%, followed a decrease during 2012-2016 (annual decrease of 8.37%) and then recovery in 2017 (44.32/100, 000). Human brucellosis cases peaked during the months from March to July, with a clear periodicity and a trend of monthly anterior displacement since 2012. Jarud Banner, located in the northwestern Tongliao, had the highest accumulated incidence rate (130.1/100, 000) accounting for 32.3% of the total cases (4501/13938). High-risk counties spread from the northwest to southward and eastward of Tongliao city during the past decade.

Conclusions The human brucellosis epidemic in Tongliao was aggravated during the past decade and peaked during the months from March to July with clear seasonality. High-risk areas were concentrated in the counties with extensive prairies and livestock.

Strengths and limitations of this study

1. This is the first study focusing on the epidemiological characteristic at county level of human brucellosis during the past 11-year period in Tongliao city, one of the highest-risk areas in Inner Mongolia province, China.

2. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for adjusting disease control strategies in Tongliao city.

3. The data in the present study may be influenced by the underreporting, laboratory misdiagnosis and incomplete information over the years as they were collected through passive public health surveillance.

4. The data of the density of livestock, meat yield, slaughter amount, environment and pathogen types in the study were not available, which should be taken into account for brucellosis transmission and prediction as risk factors.

INTRODUCTION

Brucellosis is a highly contagious zoonotic diseases caused by *Brucella spp.* and posing great

challenges to public health in the world, particularly in developing countries[1, 2]. It is rarely fatal, but has important impacts on the livestock economy due to production losses in international markets[3]. Human brucellosis is commonly transmitted from infected livestock directly or indirectly, and characterized by acute febrile illness, inflammation of the genitals, sterility, spontaneous miscarriage and lymphatic system lesions, which remains more than half a million new cases annually worldwide[4]. It is hyperendemic in China, and the incidence and prevalence of human brucellosis was severe since the first report in 1905[5]. A nationwide reporting of human brucellosis in China was established in 1960s, and the incidence was decreased in 1980s due to the domestic animal brucellosis control and eradication programs[6]. However, the epidemic situation of the disease was risen again since 2000 due to various kinds of factors, as 20 to 50 thousand new cases per year with the annual increase of 7.8% during the recent 10 years in China as reported[7]. The increased livestock trading, growing demands for meat consumption, lack of livestock products quarantine or pasteurization, and rapid movement of people in the past decade give rise to the increased risk of infections in population who have direct or indirect contact with livestock[8].

Inner Mongolia is the most important livestock husbandry province in the northeast of China, and contributes about 40% of new annually cases of human brucellosis for the nation in recent years[9]. New foci of human brucellosis spreads all over Inner Mongolia and is rapidly worsening, and the incidence was increased from 0.34 per million in 2002 to 3.33 per million in 2006[4, 10]. Most of the cases in Inner Mongolia are farmers and herdsmen, and commonly transmitted from *Brucella melitensis* infected sheep (92%)[11]. Besides, Tongliao, a city with a population of more than 3 million, is a semi-agricultural and semi-pastoral area in eastern Inner Mongolia. It is also one of the most high-risk areas of human brucellosis in Inner Mongolia with an incidence 10 to 100 per 100,000 over 2006-2010[9]. It has been reported that the incidence rate of human brucellosis among the high risk groups (population engaged in agricultural cultivation, grazing, slaughtering, etc.) in Tongliao city was as high as 11.4 to 49.8‰ from 2010 to 2014[12]. Previous researches have been expounded the spatio-temporal distribution of human brucellosis in Inner Mongolia, however, few studies have explored high-risk areas at the county level in recent years. In addition, since human brucellosis has a strong association with the work, and the variation features of seasonality, the new epidemic characteristics of human brucellosis should be revealed, so as to provide evidence for adjusting disease control strategies.

In the present study, the reported cases of human brucellosis at the county level in Tongliao, Inner Mongolia province, China from 2007 to 2017 was collected, and the epidemiological features were analyzed.

METHODS

Study areas

Tongliao (42°15′-45°41′N and 119°15′-123°43′E) is located in the equatorial zone in the eastern region of Inner Mongolia in China, with an altitude of 120-1400 m above sea level, and has a continental area of 59, 835 km^2. It is divided into 8 counties (the principal administrative areas in Tongliao are labeled in figure 3) with a total population of 3.16 million. It has an annual precipitation of 305-485 mm, and its average annual temperature is 0-6 °C. The region is a major foodstuff and livestock (mainly sheep, cattle and pigs) production zone in the country, and these husbandries contribute to 42.4% of total revenue of Tongliao. The communities of the area are mainly pastoralists and agriculturalists.

Data collection

Data for this retrospective, non-experimental study was obtained from the National Disease Prevention Information System, and was supplied by the First Institute of Endemic Diseases Prevention in Jilin Province, China. The information of human brucellosis cases in Tongliao city was collected during January 2007 to December 2017 according from the monthly reports of nationwide surveillance. Human brucellosis cases were diagnosed by clinically according to the clinical manifestations and confirmed by serologic test or isolation of the organism. All the data in the current study were publicly open and supplied in an anonymous format, without any personal privacy violation.

Statistical analysis

The data was entered into a Microsoft Excel spreadsheet, and the demographic data was analyzed using simple descriptive statistics. The cumulative incidence was explored to describe the prevalence and frequency of the disease during the study period. The spatio-temporal distribution maps of human brucellosis based on county were plotted using a geographic information system through R-Project software (MathSoft, Auckland, New Zealand). The monthly number of human brucellosis were drawn on a thermography to analyze the seasonality. All the further statistical analyses were conducted by

SPSS version 18.0 (SPSS Inc., Chicago, USA).

Patient and public involvement

Patients were not involved in the present study. The results of the main study were presented to study participants at the National Disease Prevention Information System of China and by reported monthly.

RESULTS

Demographic data of human brucellosis in Tongliao

A total of 13, 938 cases of human brucellosis during January 2007 to December 2017 were reported in Tongliao, with the average of 1268±555 cases per year. The median age of all the cases was 42 (1-85) years old (average of 41.81±12.22 years). The age distribution was shown in figure 1A and table S1, and the most of cases was aged from 25 to 59 years old with a percentage of 85.44%, although the susceptibility of human brucellosis was generally considered equally in all population. The proportions of children (<15 years old) and elderly (≥60 years old) were 1.43% and 7.21% respectively. The number of male patients (n=10, 114) was much more than female patients (n=3824) with a sex ratio of 2.64. The occupational distribution of human brucellosis over the 11-year period in Tongliao was also analyzed. As shown in figure 1B, the majority occupations of patients were agriculturalists and pastoralists, which were accounted for 81.9% and 12.4% of cases respectively (table S2).

The average of annual incidence rate of human brucellosis was 38.56 per 100, 000 in Tongliao over 2007-2017. The bottom of annual reported incidence rate was 9.22/100, 000, which appeared in 2007 with 351 cases of the disease, and the peak was 69.16/100, 000, which appeared in 2011 with 2270 cases. The epidemic trend of human brucellosis was sharply increased during 2007-2011, and the annual increase of incidence rate was 14.99%, whereas it was decreased during 2012-2016 with an average annual decrease in incidence rate of 8.37%. However, the incidence rate of human brucellosis tends to recovery in recent year which was reached 44.32/100, 000 in 2017 with 1402 reported cases (figure 1C).

Seasonality of reported brucellosis cases

A thermal table of monthly cases was carried out to describe the seasonality of human brucellosis during the 11 years in Tongliao city (figure 2A). The top of monthly cases was appeared in May 2011

with 323 cases of the disease, and the minimum was 11 cases, which presented in November and December 2007. There was an apparent seasonality of human brucellosis, and the high incidence month was during from March to July as reported in almost all of the years of the study with a total of 8162 reported cases and accounting for 58.6% of the total cases. The peak of monthly reported cases was appeared in April with the total number of 1891 cases. However, it trended to monthly anterior displacement since 2012, as a great quantity of cases (14.0% to 25.6% of annual cases) were appeared in January and February during 2012 to 2017. The time series analysis model indicated that a periodic trend of monthly reported cases was found in nearly all of the years, and there was a trend of rising first, then falling, and rising again from 2007 to 2017 (figure 2B).

Geographic distribution

Figure 3 examined the spatial distribution of accumulated cases and average incidence rates over the 2007-2017 period on the county level. There were 7 of 8 counties had accumulated incidence rate over 20/100, 000. The highest incidence rate (130.1 per 100, 000) was found in Jarud Banner among all 8 counties during the study period, which is located in the northwestern Tongliao, accounting for 32.3% of the total cases (4501/13938). The fewest reported cases was appeared in Holingol (with 413 cases) as its population totals are much lower than other counties, while the lowest incidence rate (13.1%) was reported in Horqin through 2007-2017 (talbe S3 and S4).

The yearly incidence rates and number of reported cases were further mapped in figure 4 and figure S1. The annual rates were continuous increased from 56.8 to 212.9 per 100, 000 in the years of 2007 to 2011 (with cases increased from 188 to 688) in Jrud Banner, which was the highest accumulated rates area, while it decreased to 55.8/100, 000 (with 168 cases) in 2016 followed by a slightly elevation in 2017 (87.11/100, 000 and 253 cases). However, Hure Banner, which is located in the southwestern of Tongliao, was subjected to an outbreak of human brucellosis and had a highest incidence rate (213.8/100, 000 with 369 cases) in 2011, although that was constantly low during 2007 to 2010 (2.2 to 75.6 per 100, 000), and it maintained higher incidence rates during 2012-2017 (81.9 to 114.9 per 100, 000) compared to other counties. The incidence rates and number of cases in nearly all of the counties were decreased since 2012 except for a slightly restoration in 2017. In 2007, only two counties had incidence rates over 30.0/100, 000 (Jrud Banner and Holingol), which are located in the northwestern Tongliao. However, the high risk areas were shifted to southward and eastward, and the

counties with incidence rates greater than 30.0/100,000 were increased to 7 in 2011 (talbe S3 and S4). The difference of incidence rate between western and eastern gradually lessened over the study period.

DISCUSSION

The transmission of human brucellosis has been received extensive attention in China, especially in Inner Mongolia[13]. However, the epidemiological characteristic of human brucellosis in Tongliao city, one of the high-risk areas in Inner Mongolia, has not been well-studied. In the present study, data accumulated in Tongliao were extracted to describe the demographic characteristics, seasonality and spatio-temporal distribution of reported human brucellosis at the county level from 2007 to 2017. The work might provide some enlightenments for the allocation of the brucellosis-related healthcare resources and the exploitation of control strategies for the brucellosis.

Based on the result of this study, a total of 13, 938 cases of human brucellosis over the past 11-year period were occurred in Tongliao, which were contributed to approximately 11.5% of all the cases in Inner Mongolia as reported[4]. The overall trend of the epidemic of human brucellosis in Tongliao was on the rise over the past decade, which was consistent with the trend of the nationwide and Inner Mongolia[6, 9, 14]. However, there was a bit inconsistent in the epidemic characteristics of the disease in Tongliao compared to other areas in China[8, 15], as the annual incidence rates were sharply increased during 2007-2011 while it was moderately decreased during 2012-2016. The speedy development of livestock trading, especially goat and sheep breeding in the past decade, might be attributed to the increase of cases in Tongliao[16, 17], as more than 90% of human brucellosis in China were transmitted from infected goat and sheep directly or indirectly[18]. Whereas, from the view of historical variations, the increasing of accessibility sanitation facilities, as well as the development of diagnostic and reporting networks since 2003, might be partly responsible for the visual increase of human brucellosis cases during the past decade[9, 19]. Some control strategies such as vaccination in livestock and the health-prevention education in population had been achieved through the government, which might be contributed to the decreased of human brucellosis cases during 2012-2016. However, human brucellosis in Tongliao and even in Inner Mongolia is hardly eliminated, as the researcher has predicted that the brucellosis will be gradually increased in the next decades and reaches a peak at about 2030[4]. Therefore, the policymakers should take a new sight in the comprehensive control strategies based on the optimal principle and find the right balance amongst several objectives, such as policy, resource

and technique, to prevent the disease spread.

It is well-known that occupational features, such as agriculture workers, herdsmen, abattoir workers and livestock dealers, were highly correlated with the occurrence of human brucellosis[20, 21]. In the present study, agriculture worker was the major occupation in human brucellosis cases (accounting for 81.9% of total cases), and the herdsmen occupied second (12.4%), which was consistent with previous reports in Inner Mongolia[22]. About 70% of Tongliao's population are rural farmers and mainly live by grazing or agriculture. It is common for them to share the living space with their livestock without effective personal protection, which leading to the easily exposure to the infected livestock[23, 24]. Numerous reports indicated that human brucellosis occurred in a specific gender and age range[25]. In the present study, we expounded that human brucellosis could happen in any age stage (range from 1 to 85 years old) in Tongliao, but most of them were aged from 25 to 59 years old (85.44%) with a sex ratio of 2.64 (male/female). The age and gender trends seem to be related to occupation, as most of the high-risk crowds are the primary money earners in rural families and likely participating in risky practices.

Human brucellosis seems to can happen in any season or month during a year. However, a clear seasonality of human brucellosis cases was found in our study, and the epidemic season in Tongliao was late spring and the whole summer, consistent with the reports in Inner Mongolia and the entire nation[4, 14]. This season coincides with the cultivation and lambing time in Tongliao, which may indicate more opportunities of contact between individual and infected livestock. The climate, such as the temperature, length of sunshine and rainfall have been demonstrated highly correlating with brucellosis transmission in China[16]. The warmer temperature and higher humidity during March to July in Tongliao may be also suitable for the spread of pathogens[4, 26]. However, we also found a monthly anterior displacement of the high incidence of human brucellosis since 2012, which could be attributed to the climate change in these years. Therefore, it is necessary for posting warnings before the epidemic season, which may be effective to protect risk group from infection and seek medical assistance in time when infected.

The geographic distribution analyzed at the county level during the study period indicated that the highest risk area of human brucellosis was Jarud Banner, located in the northwestern of Tongliao. This area is well-known for its extensive prairies and livestock, contained approximately 40.2% of total

cattle and sheep population in Tongliao during 2009-2015, larger than any other counties, which are often the carriers for the bacteria *Brucella*. However, only a little half of sheep and cattle in Tongliao were vaccinated previously[27]. Furthermore, it is hardly eradicating the brucellosis in sheep and cattle, based on the hypothesis that *Brucella* could persist for a long period of time in vaccinated adult livestock[28]. The infected cases were still common across Tongliao and had spread from northwest to southward and eastward during the study period, even the government began to require vaccinations for all sheep twice per year since 2012. In our opinion, the living habit, medical condition and education level might be also affected the distribution of the disease. Most of the patients were living in the rural areas with lower prevention awareness and far from the CDCs, the most important of disease prevention and monitoring units in China[8], leading to the increased risk of infection and inaccessible treatment service. Otherwise, the annual incidence rates were maintained lower levels during the study period in Horqin (2.7 to 22.3 per 100, 000), the administration center of Tongliao, which had a higher degree of modernization and medical education level. More research should be executed to explore the impacting factors of this spatial spread of the disease.

Strengths and limitations of this study

This is the first study focusing on the epidemiological characteristic at county level of human brucellosis during the past 11-year period in Tongliao city. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for adjusting disease control strategies. However, there are several limitations in this study. Firstly, the data were collected through passive public health surveillance. Due to the untypical symptoms of some human brucellosis and inaccessibility of health facilities for some patients, data may be influenced by the underreporting, laboratory misdiagnosis and incomplete information over the years[29, 30]. Secondly, as human brucellosis is a zoonotic disease which is affected by many factors, such as the density of livestock, meat yield, slaughter amount and environment, a dynamic model including the abovementioned factors should be taken into account for brucellosis transmission and prediction, but these data could not be obtained in the present study. Lastly, the data of the pathogen types in the study were not available.

CONCLUSIONS

In conclusion, the human brucellosis epidemic in Tongliao was aggravated during the past decade and peaked during the months from March to July with clear seasonality. High-risk areas were concentrated in the counties with extensive prairies and livestock. More research is required to clarify the burden of human brucellosis and to mobilize greater resources to combat the disease. The human brucellosis can be controlled by reducing breeding size of livestock or enhancing the culling rate of infectious livestock. However, government should find the right balance amongst several control problems in epidemics, although the Quarantine-Slaughter-Immunization strategy had been proven effective in past decades.

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Contributors All authors all took part in the design and planning of the study. DL and BZ collected the data. DL, LL, JZ and LW analyzed the data. DL drafted the manuscript. BZ conceived and designed the study.

Competing interests None declared.

Ethics approval Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Details of the monthly reported human brucellosis cases (anonymize) in Tongliao city during the last decade can be available for research on reasonable request (binz361@126.com).

Supporting Information Additional tables of annual age distribution, occupational distribution, yearly incidence rates, the number of reported human brucellosis cases, and figure of Annual distribution of reported cases of human brucellosis in Tongliao at county level during 2007 to 2017 are available free of charge via the http://.

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FIGURES

Figure 1 Demographic data of human brucellosis in Tongliao during 2007 to 2017. (A) The age distribution of the total reported cases. (B) The career distribution of human brucellosis over the 11-year period. (C) Annual reported cases and incidence rate of human brucellosis in Tongliao, 2007-2017.

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.

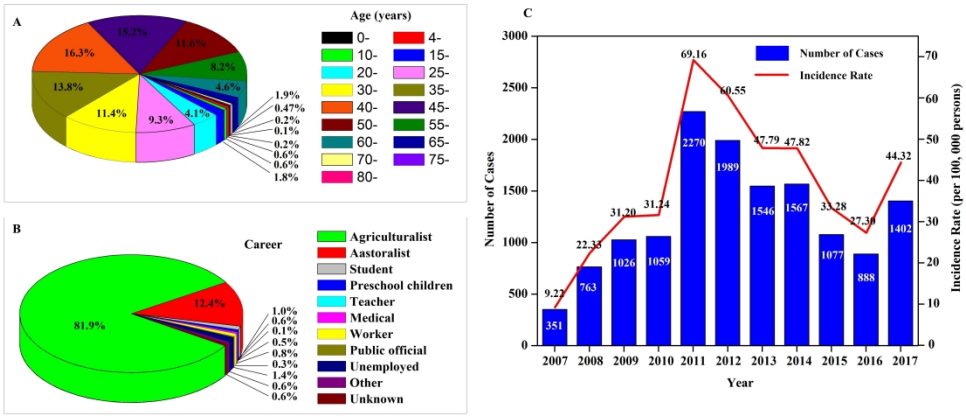

Figure 1 Demographic data of human brucellosis in Tongliao during 2007 to 2017. (A) The age distribution of the total reported cases. (B) The career distribution of human brucellosis over the 11-year period. (C) Annual reported cases and incidence rate of human brucellosis in Tongliao, 2007-2017.

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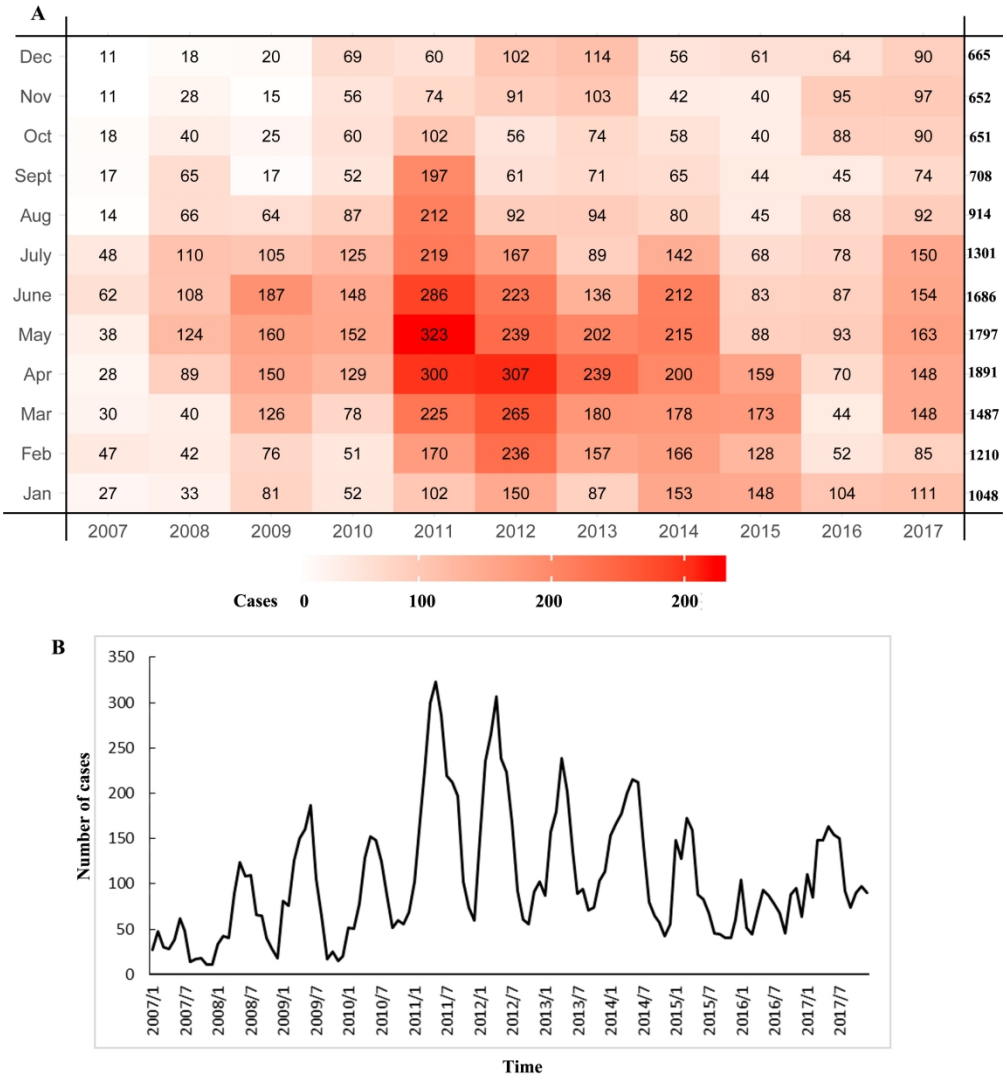

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

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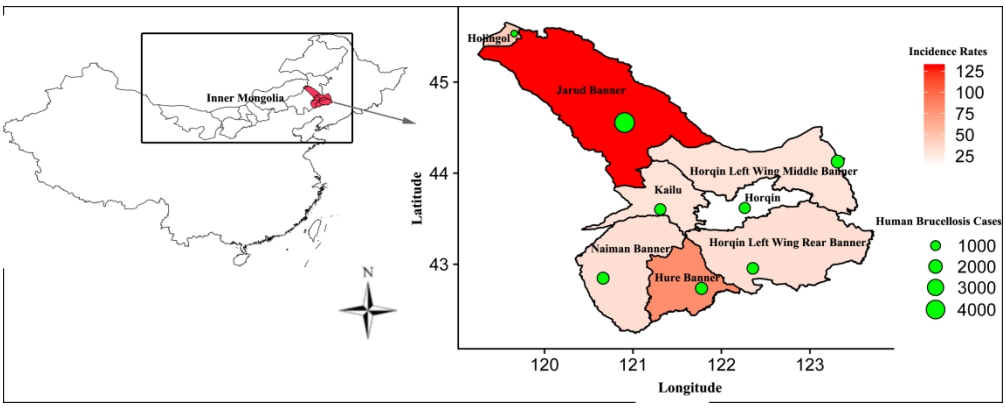

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

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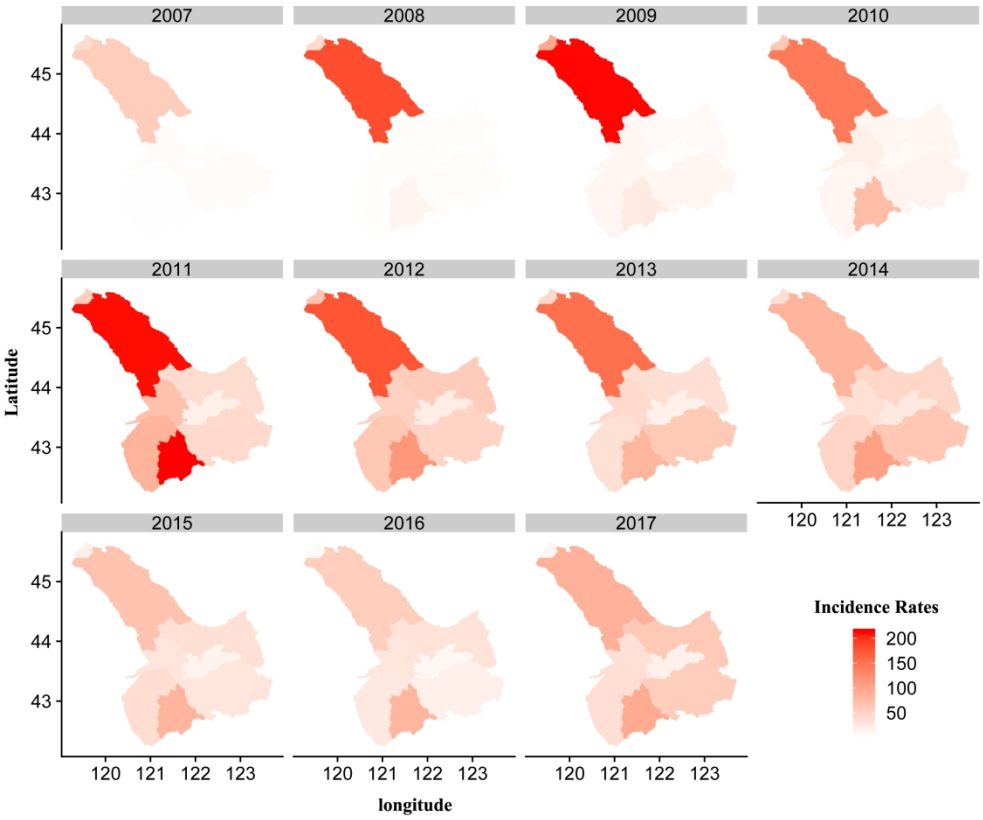

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.

228x186mm (300 x 300 DPI)

Supplementary materials

for

Evolution of the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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Table S1 The annual age distribution of human brucellosis in Tongliao during 2007-2017.

Age stage	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
0-	1	4	1	1	4	5	3	2	3	3	5	32
4-	4	10	11	4	14	11	9	5	4	5	6	83
10-	7	5	14	7	17	7	6	10	1	2	8	84
15-	5	21	33	29	46	39	19	25	8	5	21	251
20-	13	44	63	52	102	86	59	68	32	23	33	575
25-	49	96	123	101	208	170	133	141	84	67	86	1258
30-	46	123	128	132	272	234	179	168	115	80	114	1591
35-	53	127	169	173	341	285	203	206	119	102	140	1918
40-	49	132	162	165	374	352	264	228	184	145	217	2272
45-	39	79	132	158	328	311	244	248	184	153	238	2114
50-	38	59	77	96	245	216	183	214	150	138	200	1616
55-	29	33	62	74	192	153	145	129	102	72	148	1139
60-	6	17	31	41	87	78	63	88	56	54	115	636
65-	8	9	11	14	28	30	27	28	27	30	56	268
70-	2	3	7	8	7	7	6	6	5	4	10	65
75-	1	1	1	4	3	4	3	1	2	3	2	25
80-	1	0	1	0	2	1	0	0	1	2	3	11
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S2 Occupational distribution of annual reported human brucellosis over the 11-year period in Tongliao.

Occupation	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Agriculturalists	264	528	769	745	1837	1633	1249	1409	961	818	1201	11414
Pastoralist	62	168	181	256	311	236	241	96	78	34	62	1725
Student	11	19	28	12	10	15	9	19	5	2	11	141
Preschool children	3	7	5	5	13	11	9	5	5	7	9	79
Teacher	1	0	1	1	1	2	2	0	2	1	0	11
Medical	1	2	4	2	43	5	2	1	2	1	2	65
Worker	3	16	30	21	4	9	6	8	2	8	3	110
Public official	2	4	2	1	6	2	2	9	2	1	4	35
Unemployed	0	14	3	5	10	11	17	16	12	16	94	198
Other	3	5	3	11	28	11	6	4	2	0	4	77
Unknown	1	0	0	0	7	54	3	0	6	0	12	83
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S3 The yearly incidence rates of human brucellosis in Tongliao at county level during 2007 to 2017 (per 100, 000 population).

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Average
Horqin	2.72	2.59	2.46	8.85	18.91	22.27	17.11	26.27	14.10	10.41	17.80	13.05
Horqin Left Wing Middle Banner	1.11	4.23	8.74	12.63	40.21	57.70	36.87	46.27	35.28	32.82	60.76	30.60
Horqin Left Wing Rear Banner	6.12	4.86	12.30	14.84	43.24	49.17	61.63	63.60	30.00	18.56	57.02	32.85
Kailu	5.24	2.73	11.59	18.88	69.92	51.83	42.86	36.12	29.97	28.68	35.54	30.31
Hure Banner	2.22	13.24	24.66	75.67	213.75	114.94	81.93	105.46	83.05	81.89	93.94	80.98
Naiman Banner	2.04	3.15	10.72	12.42	85.68	62.45	36.07	47.61	38.52	27.30	37.32	33.03
Jurud Banner	56.78	181.38	212.85	143.48	211.90	176.61	153.03	84.54	67.86	55.80	87.11	130.12
Holingol	40.98	42.39	96.35	62.70	55.77	66.13	43.97	37.20	20.50	7.87	10.82	44.06
Average	9.22	22.33	31.20	31.24	69.16	60.55	47.79	47.82	33.28	27.30	44.32	38.56

Table S4 The number of reported human brucellosis cases in Tongliao at county level during 2007 to 2017.

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Horqin	42	22	22	76	170	200	154	244	130	94	159	1313
Horqin Left Wing Middle Banner	10	25	53	81	216	301	197	247	183	171	311	1795
Horqin Left Wing Rear Banner	35	20	51	66	169	187	249	249	114	72	217	1429
Kailu	28	11	51	81	284	209	179	146	121	118	140	1368
Hure Banner	5	30	45	158	369	195	137	187	141	143	159	1569
Naiman Banner	15	18	50	65	358	261	157	192	157	114	152	1539
Jurud Banner	188	608	688	489	647	569	428	264	210	168	253	4512
Holingol	28	29	66	43	57	67	45	38	21	8	11	413
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

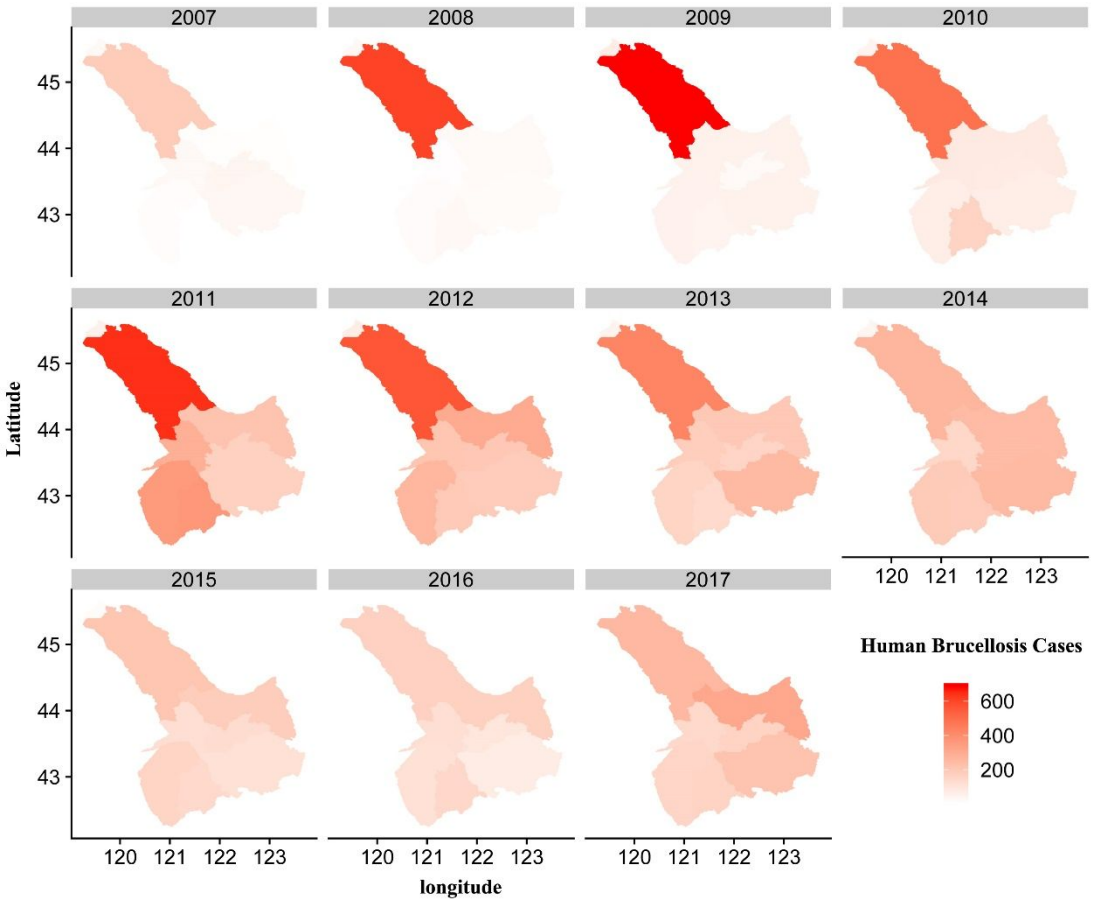

Figure S1 Annual distribution of reported cases of human brucellosis in Tongliao city, based on county (2007-2017).

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A cross-sectional study on the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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A cross-sectional study on the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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ABSTRACT

Objectives To describe the epidemiology of human brucellosis in the past decade and provide evidence of disease control in Tongliao city, where is one of the highest-risk areas of human brucellosis in Inner Mongolia province, China.

Design Cross-sectional study.

Participants Clinically and bacteriologically confirmed human brucellosis cases.

Primary and secondary outcome measures The reported cases of human brucellosis during 2007 to 2017 were carried out to describe the age, sex and occupational distributions. The time series analysis model and geographic information system were explored to describe the seasonality and spatio-temporal distribution at county level, respectively.

Results A total of 13, 938 cases of human brucellosis were collected in Tongliao from 2007 to 2017,

with the majority age from 25 to 59 years old (85.4%) and a male-to female ratio of 2.64:1, and most of them were agriculturalists (81.9%) and pastoralists (12.4%). The incidence rates were increased dramatically from 9.22/100, 000 in 2007 to 69.16/100, 000 in 2011 with an annual increase of 14.99%. They were decreased during 2012-2016 (annual decrease of 8.37%) and rose again in 2017 (44.32/100, 000). The disease was peaked during the months from March to July, with a clear periodicity and trend of monthly anterior displacement since 2012. Jarud Banner, the region located in the northwestern of Tongliao, had the highest accumulated incidence rate (130.1/100, 000) compared to other counties. The high-risk regions were spread from the northwest to southward and eastward of Tongliao during the past decade.

Conclusions The prevalence of human brucellosis in Tongliao was aggravated during the past decade and was peaked during the months from March to July. High-risk areas were mainly concentrated in the counties with extensive prairies and livestock.

Strengths and limitations of this study

1. This is the first study that was focused on the epidemiological characteristic of human brucellosis during the past 11-year period in Tongliao, a place where is one of the highest-risk areas in Inner Mongolia, China.

2. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for the strategies of disease control in Tongliao.

3. The data used in the present study might be influenced by underreporting, misdiagnosis and incomplete information due to the passive public health surveillance.

4. The density of livestock, meat yield, slaughter amount, environment and pathogen types were not available in the present study, and these data should be taken into account for brucellosis transmission and prediction as risk factors.

INTRODUCTION

Brucellosis is a highly contagious zoonotic diseases caused by *Brucella spp.* and poses great challenges to public health in the world, particularly in developing countries.[1 2] It is rarely fatal, but has important impacts on the livestock economy due to the loss of production in international

markets.[3] Human brucellosis is commonly transmitted from infected livestock directly or indirectly, and is characterized by acute febrile illness, inflammation of the genitals, sterility, spontaneous miscarriage and lymphatic system lesions, which remains more than half a million new cases annually worldwide.[4] It is a huge problem for hyperendemic northern China since the first report in 1905.[5] A nationwide reporting of human brucellosis in China was established in 1960s, and the incidence was quite severe before 1980s, followed by a decrease for 15 years due to the domestic animal brucellosis control and eradication programs.[6] However, the epidemic situation of the disease was increased sharply since 1995, and about 20 to 50 thousand new cases per year with the annual increase of 7.8% during the recent 10 years in China as reported.[7] The increased livestock trading, growing demands for meat consumption, lack of livestock products quarantine or pasteurization, and rapid movement of people in the past decade give rise to the increased risk of infection among population who have direct or indirect contacted with livestock.[8]

Inner Mongolia is the most important livestock husbandry province in the northeast of China, and contributes about 40% of new annually cases of human brucellosis for the nation in recent years.[9] New focus on human brucellosis has been spread all over Inner Mongolia, and the incidence was increased from 0.34 per million in 2002 to 3.33 per million in 2006.[4 10] Most of the patients in Inner Mongolia are farmers or herdsmen, and are commonly transmitted from *Brucella melitensis* infected sheep (92%).[11] Besides, Tongliao is a semi-agricultural and semi-pastoral area located in eastern Inner Mongolia, where is one of the most high-risk areas of human brucellosis with an incidence of 10 to 100 per 100,000 over 2006-2010.[9] It was reported that the incidence rate of human brucellosis among the high risk groups (population engaged in agricultural cultivation, grazing, slaughtering, etc.) in Tongliao city was as high as 11.4-49.8‰ from 2010 to 2014.[12] Previous researches have been expounded the spatio-temporal distribution of human brucellosis in Inner Mongolia, however, few studies have been explored the high-risk areas at county level in recent years. In addition, since human brucellosis is strong associated with work and seasonality, the new epidemic characteristics of human brucellosis should be revealed in Tongliao, so as to provide evidence for disease control strategies.

In the present study, the reported cases of human brucellosis at the county level in Tongliao, Inner Mongolia province, China from 2007 to 2017 was collected, and the epidemiological features were

analyzed.

METHODS

Study area

Tongliao (42°15′-45°41′N and 119°15′-123°43′E) is located in the equatorial zone in eastern Inner Mongolia in China, with an altitude of 120-1400 m and continental area of 59, 835 km^2. It is divided into 8 counties with a total population of 3.16 million. It has an annual precipitation of 305-485 mm, and its average annual temperature is 0-6 °C. The region is a major foodstuff and livestock (mainly sheep, cattle and pigs) production zone in China, and the husbandry contributes to 42.4% of total revenue of Tongliao. The communities of the area are mainly pastoralists and agriculturalists.

Data collection

Data for this retrospective, non-experimental study was obtained from the National Disease Prevention Information System, and was supplied by the First Institute of Endemic Diseases Prevention in Jilin Province, China. The information of human brucellosis cases in Tongliao city was collected during January 2007 to December 2017 according to the monthly reports of surveillance, a period that the complete data could be available and was consistent with the national conditions of China's ten-year statistics for the formulation of next decade control strategies. All the data in the current study were publicly open and supplied in an anonymous format, without any personal privacy violation.

Human brucellosis was diagnosed through combination of epidemiologic exposure (contact history of Brucella or living in endemic areas) and clinical manifestations (undulant fever, fatigue, sweats, arthritis, arthralgia, myalgia, splenomegaly, hepatomegaly, etc.), and confirmed by positive results of presumptive laboratory tests (plate agglutination test (PAT), rose Bengal plate test (RBPT), serum agglutination test (SAT), bacterial isolation, etc.), according to the "2007 Diagnostic Criteria of Brucellosis (WS268-2007)"of Chinese Ministry of Health.

Statistical analysis

The data was entered into a Microsoft Excel spreadsheet, and the demographic data was analyzed using a simple descriptive statistics. The cumulative incidence was explored to describe the

prevalence and frequency of the disease during the study period. The spatio-temporal distribution maps of human brucellosis based on county were plotted using a geographic information system through R-Project software (MathSoft, Auckland, New Zealand). The monthly number of human brucellosis was drawn on a thermography to analyze the seasonality. All the further statistical analyses were conducted by SPSS version 18.0 (SPSS Inc., Chicago, USA).

Patient and public involvement

Patients were not involved in the present study. The results of the main study were presented to study participants at the National Disease Prevention Information System of China by month report.

RESULTS

Demographic data of human brucellosis in Tongliao

A total of 13, 938 cases of human brucellosis during January 2007 to December 2017 were reported in Tongliao, with the average of 1268±555 cases per year. For all of the diagnosed cases, 72.9% (n=10162) and 30.2% (n=4214) of patients were confirmed by serological tests and bacterial culture, respectively. The median age of the cases was 42 (1-85) years old (average of 41.81±12.22 years). The age distribution was shown in figure 1A and table S1, and most of the cases were aged from 25 to 59 years old with a percentage of 85.44%, although the susceptibility of human brucellosis was generally considered equally in all population. The proportions of children (<15 years old) and elderly (≥60 years old) were 1.43% and 7.21%, respectively. The numbers of male patients (n=10, 114) were much more than female patients (n=3824) with a sex ratio of 2.64. The occupational distribution of human brucellosis over the 11-year period in Tongliao was also analyzed. As shown in figure 1B, the majority occupations of patients were agriculturalists and pastoralists, which were accounted for 81.9% and 12.4% of cases respectively (table S2). No death report ascribed to the disease was observed during the study period.

The average of annual incidence rate of human brucellosis was 38.56 per 100, 000 in Tongliao over 2007-2017. The bottom of annual incidence rate was 9.22/100, 000, which was appeared in 2007 with 351 cases of the disease, and the peak was 69.16/100, 000, appeared in 2011 with 2270 cases. The epidemic trend of human brucellosis was sharply increased during 2007-2011, and the annual

increase of incidence rate was 14.99%, whereas it was decreased during 2012-2016 with an average annual decrease of 8.37%. However, the incidence rate of human brucellosis tends to recovery in recent years as it was reached 44.32/100, 000 in 2017 with 1402 reported cases (figure 1C).

Seasonality of reported brucellosis cases

A thermal table of monthly cases was carried out to describe the seasonality of human brucellosis (figure 2A). The top of the monthly cases was appeared in May 2011 with 323 cases of the disease, and the minimum was 11 cases, which was presented in November and December 2007. There was an apparent seasonality of human brucellosis, and the highest incidence was occurred across from March to July as reported with accounting for 58.6% (n=8162) of the total cases during the study period. The peak of monthly cases reported was appeared in April with the total number of 1891. However, it trended to monthly anterior displacement since 2012, with a huge number of cases (14.0%-25.6%) were appeared in January and February during 2012-2017. The time series analysis model indicated that a periodic trend of monthly cases reported was found in nearly all of the study years, and there was a trend of rising first, then falling, and rising again from 2007 to 2017 (figure 2B).

Geographic distribution

Figure 3 showed the spatial distribution of the accumulated cases and average incidence rates over 2007-2017 at county level. There were 7 of 8 counties had accumulated incidence rate over 20/100, 000. The highest incidence rate (130.1/100, 000) was found in Jarud Banner during the study period, the area located in the northwestern Tongliao, accounting for 32.3% of total cases (n=4501). The fewest reported cases was appeared in Holingol (n=413) as its population totals are much lower than other counties, while the lowest incidence rate (13.1%) was reported in Horqin during 2007-2017 (talbe S3 and S4).

The incidence rates and cases were further mapped in figure 4 and figure S1. The annual rates were continuous increased from 56.8 to 212.9 per 100, 000 in the period of 2007 to 2011 (with cases increased from 188 to 688) in Jrud Banner, the region had the highest accumulated rates. While the incidence was decreased to 55.8/100, 000 (n=168) in 2016 followed by a slightly elevation in 2017 (87.11/100, 000, n=253). However, Hure Banner, the area located in the southwestern Tongliao, was

subjected to an outbreak of human brucellosis and had the highest incidence rate (213.8/100, 000 with 369 cases) in 2011, although that was constantly low during 2007 to 2010 (2.2 to 75.6 per 100, 000), and it maintained higher incidence rates during 2012-2017 (81.9 to 114.9 per 100, 000) compared to other counties. The incidence rates and number of cases in nearly all of the counties were decreased since 2012 except for a slightly restoration in 2017. In 2007, only two counties had incidence rates over 30.0/100, 000 (Jrud Banner and Holingol), the areas located in the northwestern Tongliao. However, the high risk areas were shifted to southward and eastward, and the counties with incidence rates greater than 30.0/100,000 were increased to 7 in 2011 (talbe S3 and S4). The difference of the incidence rate between western and eastern gradually lessened over the study period.

DISCUSSION

The transmission of human brucellosis has been received extensive attention in China, especially in Inner Mongolia.[13] However, the epidemiological characteristic of human brucellosis in Tongliao city, one of the high-risk areas in Inner Mongolia, has not been well-studied. In the present study, data accumulated in Tongliao were extracted to describe the demographic characteristics, seasonality and spatio-temporal distribution of reported human brucellosis at county level from 2007 to 2017. This study may provide some inspirations for the allocation of brucellosis-related healthcare resources and the exploitation of control strategies.

Based on the result of this study, a total of 13, 938 cases of human brucellosis over the past 11-year period were occurred in Tongliao, which were contributed to approximately 11.5% of all the cases in Inner Mongolia as reported.[4] The general trend of temporal variations in Tongliao during 2007-2011 showed an increase over time, especially in counties located in northwestern regions, which was similar with neighbor cities such as Shilingol, Chifeng and Hinggan in Inner Mongolia.[6 9 14] The rapid development of livestock trading, especially goat and sheep breeding in this period might be attributed to the increase of cases.[8 15] as more than 90% of human brucellosis in China were transmitted from infected goat and sheep directly or indirectly.[16-18] Whereas, from the view of historical variations, the increase of accessibility sanitation facilities, as well as the development of diagnostic and reporting networks since 2003, might be partly responsible for the visual increase of

human brucellosis during 2007-2011.[9 19]

The annual incidence rates were moderately decreased during 2012-2016. Some control strategies like systematic examination of livestock, disinfection of milk, control of animal trade and slaughter, and quarantine measures were conducted in Tongliao and other regions in Inner Mongolia in this period. Besides, the comprehensive health education program might also contribute to the decrease of the incidence rates, and it was reported that the awareness rate of brucellosis among high risk population apparent increased in Inner Mongolia (from 73.2% to 87.4% during 2010-2014) as reported.[20] More importantly, a mass vaccination with Rev 1 live strain vaccine twice per year of all sexually mature sheep was required by the government since 2011, resulting in reduced case of the disease during this period. However, human brucellosis in Tongliao and even in Inner Mongolia is hardly eliminated, as it concluded that Brucellosis could persist for a long period of time even though all sheep were supposedly vaccinated.[21] A sustainable strategy for continued implementation of the planned measures is still lack, and the infected sheep are still common across Tongliao. The procedure surveillance was also affected by misdiagnosis, reporting bias and imprecise symptoms. Finally, the insufficient strengthen of eradication strategy might be contributed to the slight upswing of human brucellosis in 2017, which could not completely be ascribed to the change of the climate. Researchers have predicted that the brucellosis will be gradually increased in the next decades and reaches a peak at about 2030, using an available dynamic model of brucellosis transmission taking into account of sheep population, vaccination and health education.[4] Therefore, the policymakers should take a new sight in the comprehensive control strategies based on the optimal principle and find the right balance amongst several objectives, such as policy, resource and technique, to prevent the disease spread. In suggesting, simultaneous disinfection, vaccination and regular sheep surveillance, as well as health education and economic compensation for slaughtered animals should be implemented.

It is well-known that the occupational features, such as agriculture workers, herdsmen, abattoir workers and livestock dealers, were highly correlated with the occurrence of human brucellosis.[22 23] In the present study, agriculture was the major occupation in human brucellosis cases (accounting for 81.9% of total cases), and the herdsman was occupied second (12.4%), which was consistent with previous reports in Inner Mongolia.[24] About 70% of Tongliao's population are rural farmers and

mainly live by grazing or agriculture. It is common for them to share the living space with their livestock without effective personal protection, leading to the easily exposure to the infected livestock.[25 26] Numerous reports indicated that human brucellosis occurred in a specific gender and age range.[27] In the present study, we expounded that human brucellosis could happen in any age stage (range from 1 to 85 years old) in Tongliao, but most of them were aged from 25 to 59 years old (85.44%) with a sex ratio of 2.64 (male/female). The age and gender trends seem to be related to the occupation, as most of the population participating in risky practices are the primary money earners in rural families.

Human brucellosis can happen in any season or month during a year. However, a clear seasonality of human brucellosis was found in our study, and the epidemic seasons in Tongliao were late spring and the whole summer, and were consistent with the reports in Inner Mongolia and other places.[4 14] These seasons are coincided with the cultivation and lambing time in Tongliao, indicating more opportunities for exposure to the infected livestock. The climates, such as temperature, length of sunshine and rainfall have been demonstrated highly correlating with brucellosis transmission in China[16]. The warmer temperature and higher humidity during March to July in Tongliao are also suitable for the spread of infection.[4 28] However, we also found a monthly anterior displacement of the high incidence of human brucellosis since 2012, which could be ascribed to the climate change in these years. Therefore, it is necessary for posting warnings before the epidemic season, which may be effective to protect risk group from infection and seek medical assistance in time.

The geographic distribution analyzed at county level during the study period indicated that the highest risk area of human brucellosis was Jarud Banner, located in northwestern Tongliao. This area is well-known for its extensive prairies and livestock, containing approximately 40.2% of total cattle and sheep in Tongliao during 2009-2015, and is larger than any other counties. In our opinion, the living habit, medical condition and education level might affect the distribution of the disease. Most of the patients were living in the rural areas with lower prevention awareness and far from the CDCs, the most important of disease prevention and monitoring units in China, leading to the increased risk of infection and inaccessible treatment service. Otherwise, the annual incidence rates were maintained lower levels during the study period in Horqin (2.7 to 22.3 per 100, 000), the administration center of Tongliao, a region had a higher degree of modernization and medical

education level. More research should be executed to explore the impacting factors of this spatial spread of the disease.

Strengths and limitations of this study

This is the first study focusing on the epidemiological characteristic at county level of human brucellosis during the past 11-year period in Tongliao city. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for control strategies. However, there are several limitations in this study. Firstly, the data were collected through passive public health surveillance. Regarding to the untypical symptoms of some human brucellosis and inaccessible health facilities for some patients, data may be influenced by the underreporting, laboratory misdiagnosis and incomplete information.[29 30] Secondly, as human brucellosis is a zoonotic disease which is affected by many factors, such as the density of livestock, meat yield, slaughter amount and environment, a dynamic model including the abovementioned factors should be taken into account for brucellosis transmission and prediction, but these data could not be obtained in the present study. Lastly, the data of the pathogen types in the study were not available.

CONCLUSIONS

In conclusion, the epidemic of human brucellosis in Tongliao was aggravated during the past decade and peaked during the months from March to July with clear seasonality. High-risk areas were concentrated in the counties with extensive prairies and livestock. More researches are required to clarify the burden of human brucellosis and to mobilize greater resources for the disease elimination. Human brucellosis can be controlled by reducing breeding size of livestock or enhancing the culling rate of infectious livestock. However, government should find the right balance amongst several control problems in epidemics, although the Quarantine-Slaughter-Immunization strategy had been proven effective in past decades.

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Contributors All authors all took part in the design and planning of the study. DL and BZ collected

the data. DL, LL, JZ and LW analyzed the data. DL drafted the manuscript. BZ conceived and designed the study.

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Competing interests None declared.

Ethics approval Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Details of the monthly reported human brucellosis cases (anonymize) in Tongliao city during the last decade can be available for research on reasonable request (binz361@126.com).

Supporting Information Additional tables of annual age distribution, occupational distribution, yearly incidence rates, the number of reported human brucellosis cases, and figure of Annual distribution of reported cases of human brucellosis in Tongliao at county level during 2007 to 2017 are available free of charge via the http://.

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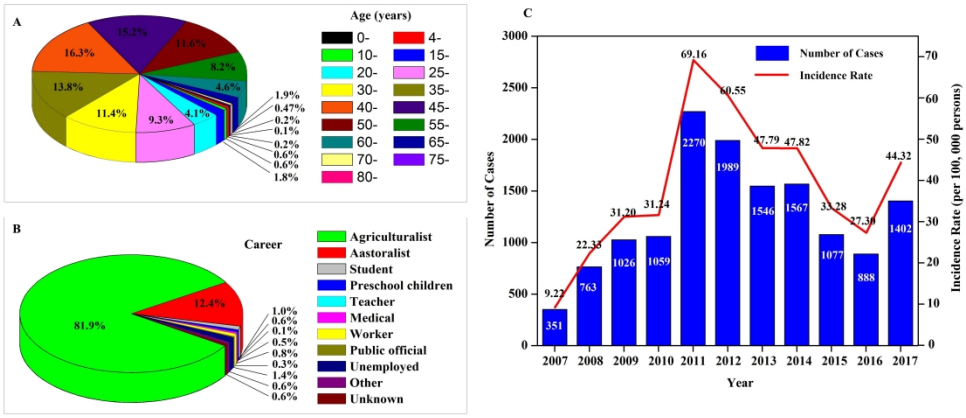
FIGURES

Figure 1 Demographic data of human brucellosis in Tongliao during 2007 to 2017. (A) The age distribution of the total reported cases. (B) The career distribution of human brucellosis over the 11-year period. (C) Annual reported cases and incidence rate of human brucellosis in Tongliao, 2007-2017.

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.



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500x230mm (300 x 300 DPI)

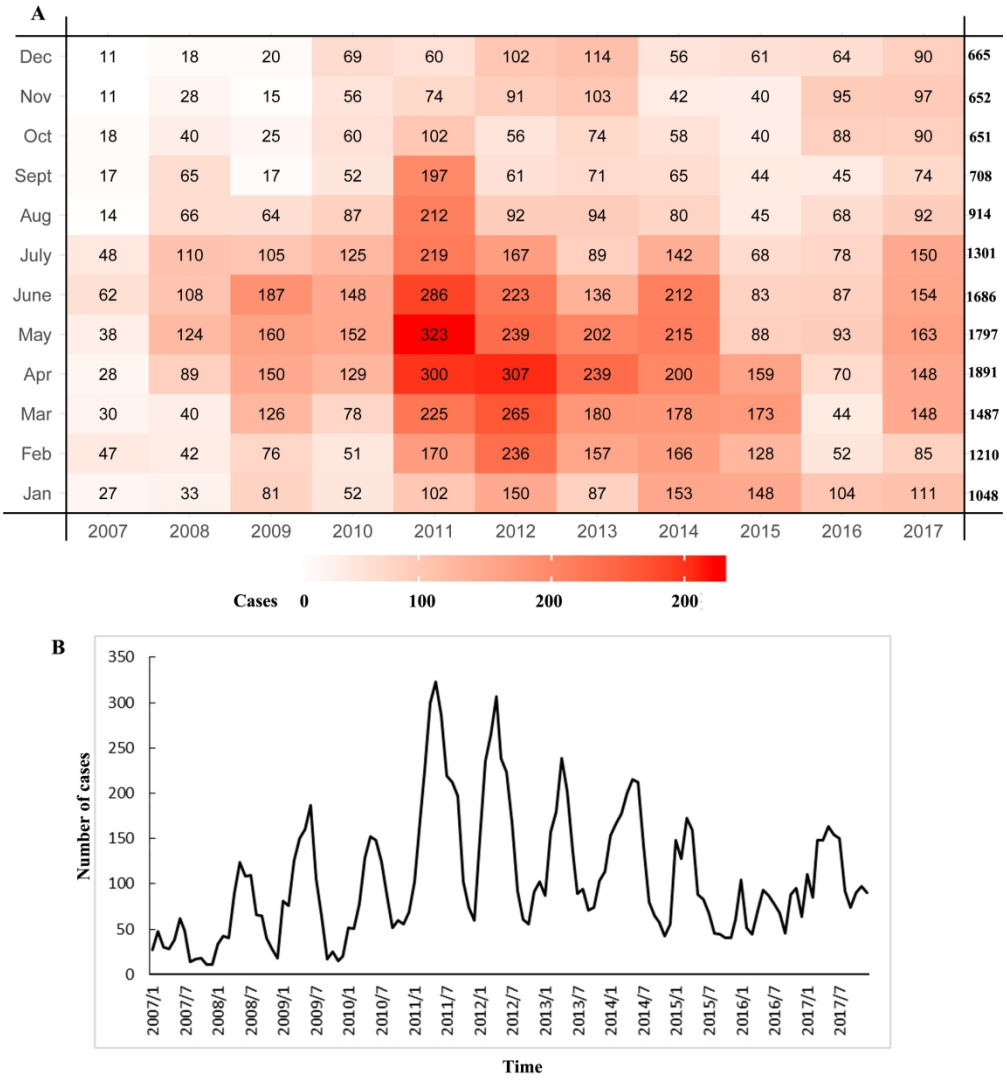

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

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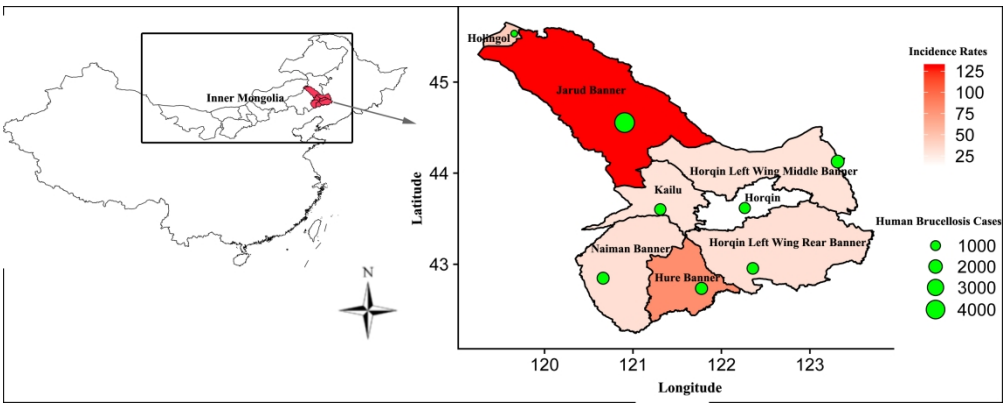

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

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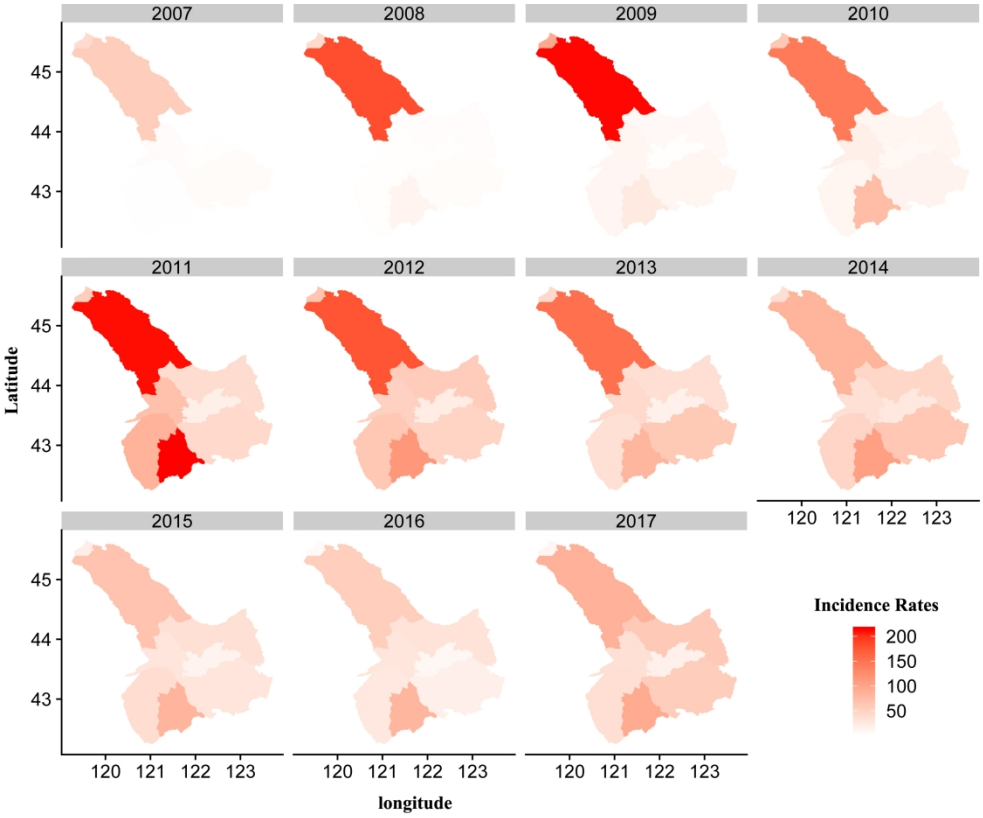

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.

228x186mm (300 x 300 DPI)

Supplementary materials

for

Evolution of the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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Table S1 The annual age distribution of human brucellosis in Tongliao during 2007-2017.

Age stage	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
0-	1	4	1	1	4	5	3	2	3	3	5	32
4-	4	10	11	4	14	11	9	5	4	5	6	83
10-	7	5	14	7	17	7	6	10	1	2	8	84
15-	5	21	33	29	46	39	19	25	8	5	21	251
20-	13	44	63	52	102	86	59	68	32	23	33	575
25-	49	96	123	101	208	170	133	141	84	67	86	1258
30-	46	123	128	132	272	234	179	168	115	80	114	1591
35-	53	127	169	173	341	285	203	206	119	102	140	1918
40-	49	132	162	165	374	352	264	228	184	145	217	2272
45-	39	79	132	158	328	311	244	248	184	153	238	2114
50-	38	59	77	96	245	216	183	214	150	138	200	1616
55-	29	33	62	74	192	153	145	129	102	72	148	1139
60-	6	17	31	41	87	78	63	88	56	54	115	636
65-	8	9	11	14	28	30	27	28	27	30	56	268
70-	2	3	7	8	7	7	6	6	5	4	10	65
75-	1	1	1	4	3	4	3	1	2	3	2	25
80-	1	0	1	0	2	1	0	0	1	2	3	11
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S2 Occupational distribution of annual reported human brucellosis over the 11-year period in Tongliao.

Occupation	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Agriculturalists	264	528	769	745	1837	1633	1249	1409	961	818	1201	11414
Pastoralist	62	168	181	256	311	236	241	96	78	34	62	1725
Student	11	19	28	12	10	15	9	19	5	2	11	141
Preschool children	3	7	5	5	13	11	9	5	5	7	9	79
Teacher	1	0	1	1	1	2	2	0	2	1	0	11
Medical	1	2	4	2	43	5	2	1	2	1	2	65
Worker	3	16	30	21	4	9	6	8	2	8	3	110
Public official	2	4	2	1	6	2	2	9	2	1	4	35
Unemployed	0	14	3	5	10	11	17	16	12	16	94	198
Other	3	5	3	11	28	11	6	4	2	0	4	77
Unknown	1	0	0	0	7	54	3	0	6	0	12	83
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S3 The yearly incidence rates of human brucellosis in Tongliao at county level during 2007 to 2017 (per 100, 000 population).

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Average
Horqin	2.72	2.59	2.46	8.85	18.91	22.27	17.11	26.27	14.10	10.41	17.80	13.05
Horqin Left Wing Middle Banner	1.11	4.23	8.74	12.63	40.21	57.70	36.87	46.27	35.28	32.82	60.76	30.60
Horqin Left Wing Rear Banner	6.12	4.86	12.30	14.84	43.24	49.17	61.63	63.60	30.00	18.56	57.02	32.85
Kailu	5.24	2.73	11.59	18.88	69.92	51.83	42.86	36.12	29.97	28.68	35.54	30.31
Hure Banner	2.22	13.24	24.66	75.67	213.75	114.94	81.93	105.46	83.05	81.89	93.94	80.98
Naiman Banner	2.04	3.15	10.72	12.42	85.68	62.45	36.07	47.61	38.52	27.30	37.32	33.03
Jurud Banner	56.78	181.38	212.85	143.48	211.90	176.61	153.03	84.54	67.86	55.80	87.11	130.12
Holingol	40.98	42.39	96.35	62.70	55.77	66.13	43.97	37.20	20.50	7.87	10.82	44.06
Average	9.22	22.33	31.20	31.24	69.16	60.55	47.79	47.82	33.28	27.30	44.32	38.56

Table S4 The number of reported human brucellosis cases in Tongliao at county level during 2007 to 2017.

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Horqin	42	22	22	76	170	200	154	244	130	94	159	1313
Horqin Left Wing Middle Banner	10	25	53	81	216	301	197	247	183	171	311	1795
Horqin Left Wing Rear Banner	35	20	51	66	169	187	249	249	114	72	217	1429
Kailu	28	11	51	81	284	209	179	146	121	118	140	1368
Hure Banner	5	30	45	158	369	195	137	187	141	143	159	1569
Naiman Banner	15	18	50	65	358	261	157	192	157	114	152	1539
Jurud Banner	188	608	688	489	647	569	428	264	210	168	253	4512
Holingol	28	29	66	43	57	67	45	38	21	8	11	413
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

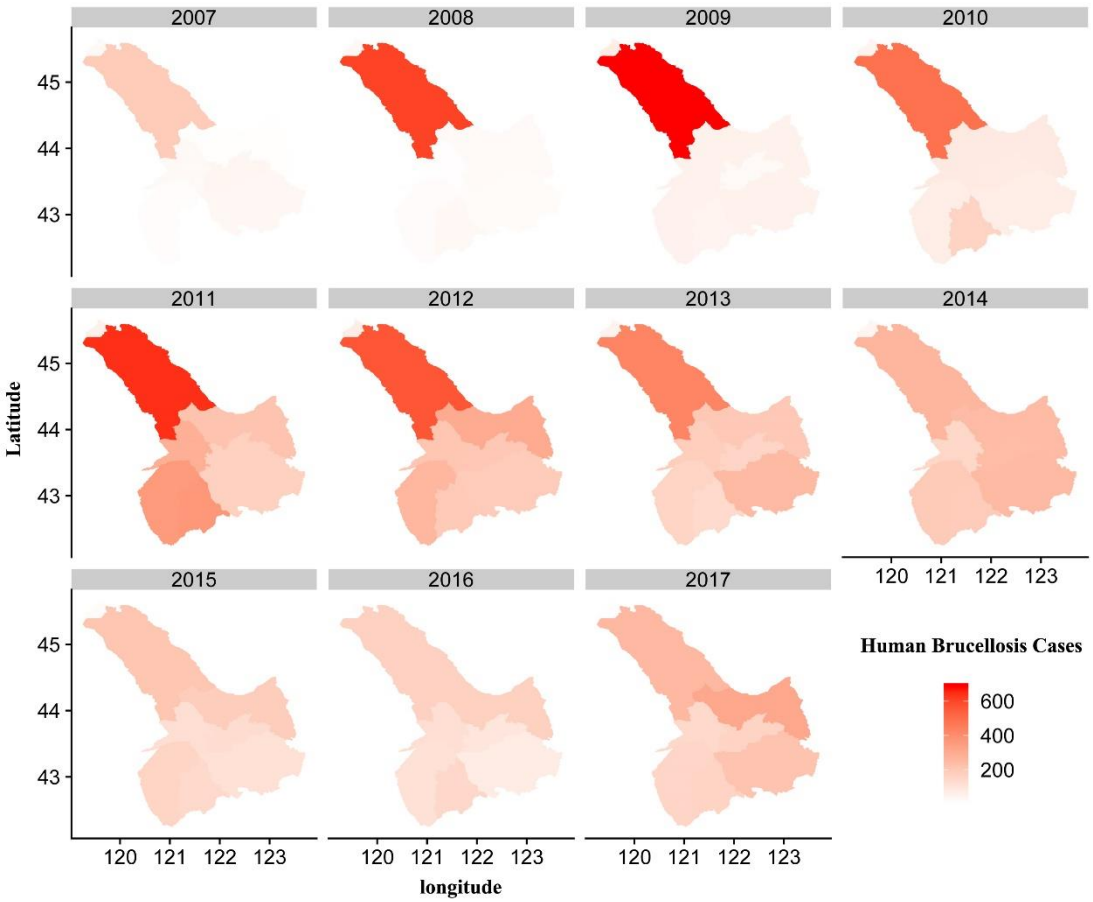

Figure S1 Annual distribution of reported cases of human brucellosis in Tongliao city, based on county (2007-2017).

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (Page1)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found (Page1 and 2)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page2 and 3)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 3)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 4, line12)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 4, line4-19)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants (Page 5, line7-10)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 4, line20-25)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 4, line12-19)
Bias	9	Describe any efforts to address potential sources of bias (Page 2, line21-23)
Study size	10	Explain how the study size was arrived at (Page 5, line12-13)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses (Page 5, line1-6)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 5, line12-15)
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 5, line12-24)
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures (Page 5-7)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized (Page 5-7)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives (Page 7-9)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 9, line 5-16)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 7-9)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 9, line 18-25)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

A cross-sectional study on the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	Human brucellosis, Epidemiology < TROPICAL MEDICINE, Tongliao city, Seasonality, High-risk areas

A cross-sectional study on the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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ABSTRACT

Objectives To describe the epidemiology of human brucellosis in the past decade and provide evidence of disease control in Tongliao city, where is one of the highest-risk areas of human brucellosis in Inner Mongolia province, China.

Design Cross-sectional study.

Participants Clinically and bacteriologically confirmed human brucellosis cases.

Primary and secondary outcome measures The reported cases of human brucellosis during 2007 to 2017 were carried out to describe the age, sex and occupational distributions. The time series analysis model and geographic information system were explored to describe the seasonality and spatio-temporal distribution at county level, respectively.

Results A total of 13, 938 cases of human brucellosis were collected in Tongliao from 2007 to 2017,

with the majority age from 25 to 59 years old (85.4%) and a male-to female ratio of 2.64:1, and most of them were agriculturalists (81.9%) and pastoralists (12.4%). The incidence rates were increased dramatically from 9.22/100, 000 in 2007 to 69.16/100, 000 in 2011 with an annual increase of 14.99%. They were decreased during 2012-2016 (annual decrease of 8.37%) and rose again in 2017 (44.32/100, 000). The disease was peaked during the months from March to July, with a clear periodicity and trend of monthly anterior displacement since 2012. Jarud Banner, the region located in the northwestern of Tongliao, had the highest accumulated incidence rate (130.1/100, 000) compared to other counties. The high-risk regions were spread from the northwest to southward and eastward of Tongliao during the past decade.

Conclusions The prevalence of human brucellosis in Tongliao was aggravated during the past decade and was peaked during the months from March to July. High-risk areas were mainly concentrated in the counties with extensive prairies and livestock.

Strengths and limitations of this study

1. This is the first study that was focused on the epidemiological characteristic of human brucellosis during the past 11-year period in Tongliao, a place where is one of the highest-risk areas in Inner Mongolia, China.

2. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for the strategies of disease control in Tongliao.

3. The data used in the present study might be influenced by underreporting, misdiagnosis and incomplete information due to the passive public health surveillance.

4. The density of livestock, meat yield, slaughter amount, environment and pathogen types were not available in the present study, and these data should be taken into account for brucellosis transmission and prediction as risk factors.

INTRODUCTION

Brucellosis is a highly contagious zoonotic diseases caused by *Brucella spp.* and poses great challenges to public health in the world, particularly in developing countries.[1 2] It is rarely fatal, but has important impacts on the livestock economy due to the loss of production in international

markets.[3] Human brucellosis is commonly transmitted from infected livestock directly or indirectly, and is characterized by acute febrile illness, inflammation of the genitals, sterility, spontaneous miscarriage and lymphatic system lesions, which remains more than half a million new cases annually worldwide.[4] It is a huge problem for hyperendemic northern China since the first report in 1905.[5] A nationwide reporting of human brucellosis in China was established in 1960s, and the incidence was quite severe before 1980s, followed by a decrease for 15 years due to the domestic animal brucellosis control and eradication programs.[6] However, the epidemic situation of the disease was increased sharply since 1995, and about 20 to 50 thousand new cases per year with the annual increase of 7.8% during the recent 10 years in China as reported.[7] The increased livestock trading, growing demands for meat consumption, lack of livestock products quarantine or pasteurization, and rapid movement of people in the past decade give rise to the increased risk of infection among population who have direct or indirect contacted with livestock.[8]

Inner Mongolia is the most important livestock husbandry province in the northeast of China, and contributes about 40% of new annually cases of human brucellosis for the nation in recent years.[9] New focus on human brucellosis has been spread all over Inner Mongolia, and the incidence was increased from 0.34 per million in 2002 to 3.33 per million in 2006.[4 10] Most of the patients in Inner Mongolia are farmers or herdsmen, and are commonly transmitted from *Brucella melitensis* infected sheep (92%).[11] Besides, Tongliao is a semi-agricultural and semi-pastoral area located in eastern Inner Mongolia, where is one of the most high-risk areas of human brucellosis with an incidence of 10 to 100 per 100,000 over 2006-2010.[9] It was reported that the incidence rate of human brucellosis among the high risk groups (population engaged in agricultural cultivation, grazing, slaughtering, etc.) in Tongliao city was as high as 11.4-49.8‰ from 2010 to 2014.[12] Previous researches have been expounded the spatio-temporal distribution of human brucellosis in Inner Mongolia, however, few studies have been explored the high-risk areas at county level in recent years. In addition, since human brucellosis is strong associated with work and seasonality, the new epidemic characteristics of human brucellosis should be revealed in Tongliao, so as to provide evidence for disease control strategies.

In the present study, the reported cases of human brucellosis at the county level in Tongliao, Inner Mongolia province, China from 2007 to 2017 was collected, and the epidemiological features were

analyzed.

METHODS

Study area

Tongliao (42°15′-45°41′N and 119°15′-123°43′E) is located in the equatorial zone in eastern Inner Mongolia in China, with an altitude of 120-1400 m and continental area of 59, 835 km^2. It is divided into 8 counties with a total population of 3.16 million. It has an annual precipitation of 305-485 mm, and its average annual temperature is 0-6 °C. The region is a major foodstuff and livestock (mainly sheep, cattle and pigs) production zone in China, and the husbandry contributes to 42.4% of total revenue of Tongliao. The communities of the area are mainly pastoralists and agriculturalists.

Data collection

Data for this retrospective, non-experimental study was obtained from the National Disease Prevention Information System, and was supplied by the First Institute of Endemic Diseases Prevention in Jilin Province, China. The information of human brucellosis cases in Tongliao city was collected during January 2007 to December 2017 according to the monthly reports of surveillance, a period that the complete data could be available and was consistent with the national conditions of China's ten-year statistics for the formulation of next decade control strategies. All the data in the current study were publicly open and supplied in an anonymous format, without any personal privacy violation.

Human brucellosis was diagnosed through combination of epidemiologic exposure (contact history of Brucella or living in endemic areas) and clinical manifestations (undulant fever, fatigue, sweats, arthritis, arthralgia, myalgia, splenomegaly, hepatomegaly, etc.), and confirmed by positive results of presumptive laboratory tests (plate agglutination test (PAT), rose Bengal plate test (RBPT), serum agglutination test (SAT), bacterial isolation, etc.), according to the "2007 Diagnostic Criteria of Brucellosis (WS268-2007)"of Chinese Ministry of Health.

Statistical analysis

The data was entered into a Microsoft Excel spreadsheet, and the demographic data was analyzed using a simple descriptive statistics. The cumulative incidence was explored to describe the

prevalence and frequency of the disease during the study period. The spatio-temporal distribution maps of human brucellosis based on county were plotted using a geographic information system through R-Project software (MathSoft, Auckland, New Zealand). The monthly number of human brucellosis was drawn on a thermography to analyze the seasonality. All the further statistical analyses were conducted by SPSS version 18.0 (SPSS Inc., Chicago, USA).

Patient and public involvement

Patients were not involved in the present study. The results of the main study were presented to study participants at the National Disease Prevention Information System of China by month report.

RESULTS

Demographic data of human brucellosis in Tongliao

A total of 13, 938 cases of human brucellosis during January 2007 to December 2017 were reported in Tongliao, with the average of 1268±555 cases per year. For all of the diagnosed cases, 72.9% (n=10162) and 30.2% (n=4214) of patients were confirmed by serological tests and bacterial culture, respectively. The median age of the cases was 42 (1-85) years old (average of 41.81±12.22 years). The age distribution was shown in figure 1A and table S1, and most of the cases were aged from 25 to 59 years old with a percentage of 85.44%, although the susceptibility of human brucellosis was generally considered equally in all population. The proportions of children (<15 years old) and elderly (≥60 years old) were 1.43% and 7.21%, respectively. The numbers of male patients (n=10, 114) were much more than female patients (n=3824) with a sex ratio of 2.64. The occupational distribution of human brucellosis over the 11-year period in Tongliao was also analyzed. As shown in figure 1B, the majority occupations of patients were agriculturalists and pastoralists, which were accounted for 81.9% and 12.4% of cases respectively (table S2). No death report ascribed to the disease was observed during the study period.

The average of annual incidence rate of human brucellosis was 38.56 per 100, 000 in Tongliao over 2007-2017. The bottom of annual incidence rate was 9.22/100, 000, which was appeared in 2007 with 351 cases of the disease, and the peak was 69.16/100, 000, appeared in 2011 with 2270 cases. The epidemic trend of human brucellosis was sharply increased during 2007-2011, and the annual

increase of incidence rate was 14.99%, whereas it was decreased during 2012-2016 with an average annual decrease of 8.37%. However, the incidence rate of human brucellosis tends to recovery in recent years as it was reached 44.32/100, 000 in 2017 with 1402 reported cases (figure 1C).

Seasonality of reported brucellosis cases

A thermal table of monthly cases was carried out to describe the seasonality of human brucellosis (figure 2A). The top of the monthly cases was appeared in May 2011 with 323 cases of the disease, and the minimum was 11 cases, which was presented in November and December 2007. There was an apparent seasonality of human brucellosis, and the highest incidence was occurred across from March to July as reported with accounting for 58.6% (n=8162) of the total cases during the study period. The peak of monthly cases reported was appeared in April with the total number of 1891. However, it trended to monthly anterior displacement since 2012, with a huge number of cases (14.0%-25.6%) were appeared in January and February during 2012-2017. The time series analysis model indicated that a periodic trend of monthly cases reported was found in nearly all of the study years, and there was a trend of rising first, then falling, and rising again from 2007 to 2017 (figure 2B).

Geographic distribution

Figure 3 showed the spatial distribution of the accumulated cases and average incidence rates over 2007-2017 at county level. There were 7 of 8 counties had accumulated incidence rate over 20/100, 000. The highest incidence rate (130.1/100, 000) was found in Jarud Banner during the study period, the area located in the northwestern Tongliao, accounting for 32.3% of total cases (n=4501). The fewest reported cases was appeared in Holingol (n=413) as its population totals are much lower than other counties, while the lowest incidence rate (13.1%) was reported in Horqin during 2007-2017 (table S3 and S4).

The incidence rates and cases were further mapped in figure 4 and figure S1. The annual rates were continuous increased from 56.8 to 212.9 per 100, 000 in the period of 2007 to 2011 (with cases increased from 188 to 688) in Jrud Banner, the region had the highest accumulated rates. While the incidence was decreased to 55.8/100, 000 (n=168) in 2016 followed by a slightly elevation in 2017 (87.11/100, 000, n=253). However, Hure Banner, the area located in the southwestern Tongliao, was

subjected to an outbreak of human brucellosis and had the highest incidence rate (213.8/100, 000 with 369 cases) in 2011, although that was constantly low during 2007 to 2010 (2.2 to 75.6 per 100, 000), and it maintained higher incidence rates during 2012-2017 (81.9 to 114.9 per 100, 000) compared to other counties. The incidence rates and number of cases in nearly all of the counties were decreased since 2012 except for a slightly restoration in 2017. In 2007, only two counties had incidence rates over 30.0/100, 000 (Jrud Banner and Holingol), the areas located in the northwestern Tongliao. However, the high risk areas were shifted to southward and eastward, and the counties with incidence rates greater than 30.0/100,000 were increased to 7 in 2011 (table S3 and S4). The difference of the incidence rate between western and eastern gradually lessened over the study period.

DISCUSSION

The transmission of human brucellosis has been received extensive attention in China, especially in Inner Mongolia.[13] However, the epidemiological characteristic of human brucellosis in Tongliao city, one of the high-risk areas in Inner Mongolia, has not been well-studied. In the present study, data accumulated in Tongliao were extracted to describe the demographic characteristics, seasonality and spatio-temporal distribution of reported human brucellosis at county level from 2007 to 2017. This study may provide some inspirations for the allocation of brucellosis-related healthcare resources and the exploitation of control strategies.

Based on the result of this study, a total of 13, 938 cases of human brucellosis over the past 11-year period were occurred in Tongliao, which were contributed to approximately 11.5% of all the cases in Inner Mongolia as reported.[4] The general trend of temporal variations in Tongliao during 2007-2011 showed an increase over time, especially in counties located in northwestern regions, which was similar with neighbor cities such as Shilingol, Chifeng and Hinggan in Inner Mongolia.[6 9 14] The rapid development of livestock trading, especially goat and sheep breeding in this period might be attributed to the increase of cases,[8 15] as more than 90% of human brucellosis in China were transmitted from infected goat and sheep directly or indirectly.[16-18] Whereas, from the view of historical variations, the increase of accessibility sanitation facilities, as well as the development of diagnostic and reporting networks since 2003, might be partly responsible for the visual increase of

human brucellosis during 2007-2011.[9 19]

The annual incidence rates were moderately decreased during 2012-2016. Some control strategies like systematic examination of livestock, disinfection of milk, control of animal trade and slaughter, and quarantine measures were conducted in Tongliao and other regions in Inner Mongolia in this period. Besides, the comprehensive health education program might also contribute to the decrease of the incidence rates, and it was reported that the awareness rate of brucellosis among high risk population apparent increased in Inner Mongolia (from 73.2% to 87.4% during 2010-2014) as reported.[20] More importantly, a mass vaccination with Rev 1 live strain vaccine twice per year of all sexually mature sheep was required by the government since 2011, resulting in reduced case of the disease during this period. However, human brucellosis in Tongliao and even in Inner Mongolia is hardly eliminated, as it concluded that Brucellosis could persist for a long period of time even though all sheep were supposedly vaccinated.[21] A sustainable strategy for continued implementation of the planned measures is still lack, and the infected sheep are still common across Tongliao. The procedure surveillance was also affected by misdiagnosis, reporting bias and imprecise symptoms. Finally, the insufficient strengthen of eradication strategy might be contributed to the slight upswing of human brucellosis in 2017, which could not completely be ascribed to the change of the climate. Researchers have predicted that the brucellosis will be gradually increased in the next decades and reaches a peak at about 2030, using an available dynamic model of brucellosis transmission taking into account of sheep population, vaccination and health education.[4] Therefore, the policymakers should take a new sight in the comprehensive control strategies based on the optimal principle and find the right balance amongst several objectives, such as policy, resource and technique, to prevent the disease spread. In suggesting, simultaneous disinfection, vaccination and regular sheep surveillance, as well as health education and economic compensation for slaughtered animals should be implemented.

It is well-known that the occupational features, such as agriculture workers, herdsmen, abattoir workers and livestock dealers, were highly correlated with the occurrence of human brucellosis.[22 23] In the present study, agriculture was the major occupation in human brucellosis cases (accounting for 81.9% of total cases), and the herdsman was occupied second (12.4%), which was consistent with previous reports in Inner Mongolia.[24] About 70% of Tongliao's population are rural farmers and

mainly live by grazing or agriculture. It is common for them to share the living space with their livestock without effective personal protection, leading to the easily exposure to the infected livestock.[25 26] Numerous reports indicated that human brucellosis occurred in a specific gender and age range.[27] In the present study, we expounded that human brucellosis could happen in any age stage (range from 1 to 85 years old) in Tongliao, but most of them were aged from 25 to 59 years old (85.44%) with a sex ratio of 2.64 (male/female). The age and gender trends seem to be related to the occupation, as most of the population participating in risky practices are the primary money earners in rural families.

Human brucellosis can happen in any season or month during a year. However, a clear seasonality of human brucellosis was found in our study, and the epidemic seasons in Tongliao were late spring and the whole summer, and were consistent with the reports in Inner Mongolia and other places.[4 14] These seasons are coincided with the cultivation and lambing time in Tongliao, indicating more opportunities for exposure to the infected livestock. The climates, such as temperature, length of sunshine and rainfall have been demonstrated highly correlating with brucellosis transmission in China[16]. The warmer temperature and higher humidity during March to July in Tongliao are also suitable for the spread of infection.[4 28] However, we also found a monthly anterior displacement of the high incidence of human brucellosis since 2012, which could be ascribed to the climate change in these years. Therefore, it is necessary for posting warnings before the epidemic season, which may be effective to protect risk group from infection and seek medical assistance in time.

The geographic distribution analyzed at county level during the study period indicated that the highest risk area of human brucellosis was Jarud Banner, located in northwestern Tongliao. This area is well-known for its extensive prairies and livestock, containing approximately 40.2% of total cattle and sheep in Tongliao during 2009-2015, and is larger than any other counties. In our opinion, the living habit, medical condition and education level might affect the distribution of the disease. Most of the patients were living in the rural areas with lower prevention awareness and far from the CDCs, the most important of disease prevention and monitoring units in China, leading to the increased risk of infection and inaccessible treatment service. Otherwise, the annual incidence rates were maintained lower levels during the study period in Horqin (2.7 to 22.3 per 100, 000), the administration center of Tongliao, a region had a higher degree of modernization and medical

education level. More research should be executed to explore the impacting factors of this spatial spread of the disease.

Strengths and limitations of this study

This is the first study focusing on the epidemiological characteristic at county level of human brucellosis during the past 11-year period in Tongliao city. The demographic data, seasonality and spatio-temporal distribution of reported brucellosis cases were explored to provide evidence for control strategies. However, there are several limitations in this study. Firstly, the data were collected through passive public health surveillance. Regarding to the untypical symptoms of some human brucellosis and inaccessible health facilities for some patients, data may be influenced by the underreporting, laboratory misdiagnosis and incomplete information.[29 30] Secondly, as human brucellosis is a zoonotic disease which is affected by many factors, such as the density of livestock, meat yield, slaughter amount and environment, a dynamic model including the abovementioned factors should be taken into account for brucellosis transmission and prediction, but these data could not be obtained in the present study. Lastly, the data of the pathogen types in the study were not available.

CONCLUSIONS

In conclusion, the epidemic of human brucellosis in Tongliao was aggravated during the past decade and peaked during the months from March to July with clear seasonality. High-risk areas were concentrated in the counties with extensive prairies and livestock. More researches are required to clarify the burden of human brucellosis and to mobilize greater resources for the disease elimination. Human brucellosis can be controlled by reducing breeding size of livestock or enhancing the culling rate of infectious livestock. However, government should find the right balance amongst several control problems in epidemics, although the Quarantine-Slaughter-Immunization strategy had been proven effective in past decades.

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Contributors All authors all took part in the design and planning of the study. DL and BZ collected

the data. DL, LL, JZ and LW analyzed the data. DL drafted the manuscript. BZ conceived and designed the study.

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Competing interests None declared.

Ethics approval Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Details of the monthly reported human brucellosis cases in Tongliao city during the last decade can be available for research on reasonable request (binz361@126.com).

Supporting Information Additional tables of annual age distribution, occupational distribution, yearly incidence rates, the number of reported human brucellosis cases, and figure of Annual distribution of reported cases of human brucellosis in Tongliao at county level during 2007 to 2017 are available free of charge via the http://.

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FIGURES

Figure 1 Demographic data of human brucellosis in Tongliao during 2007 to 2017. (A) The age distribution of the total reported cases. (B) The career distribution of human brucellosis over the 11-year period. (C) Annual reported cases and incidence rate of human brucellosis in Tongliao, 2007-2017.

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.

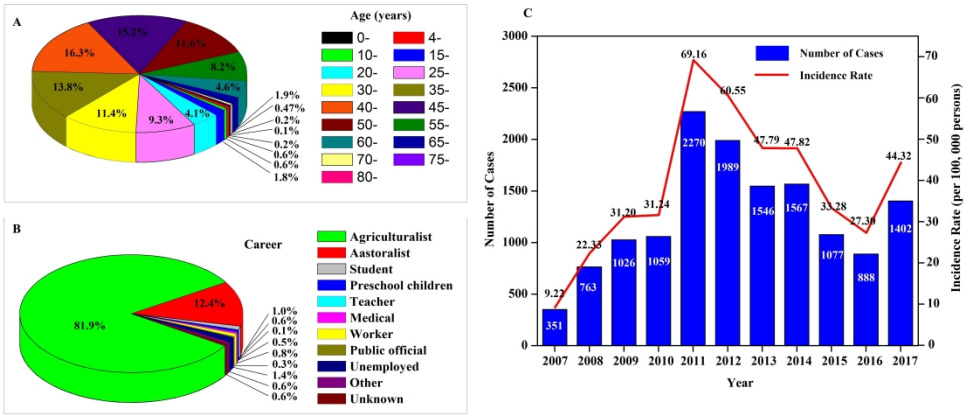

Figure 1 Demographic data of human brucellosis in Tongliao during 2007 to 2017. (A) The age distribution of the total reported cases. (B) The career distribution of human brucellosis over the 11-year period. (C) Annual reported cases and incidence rate of human brucellosis in Tongliao, 2007-2017.

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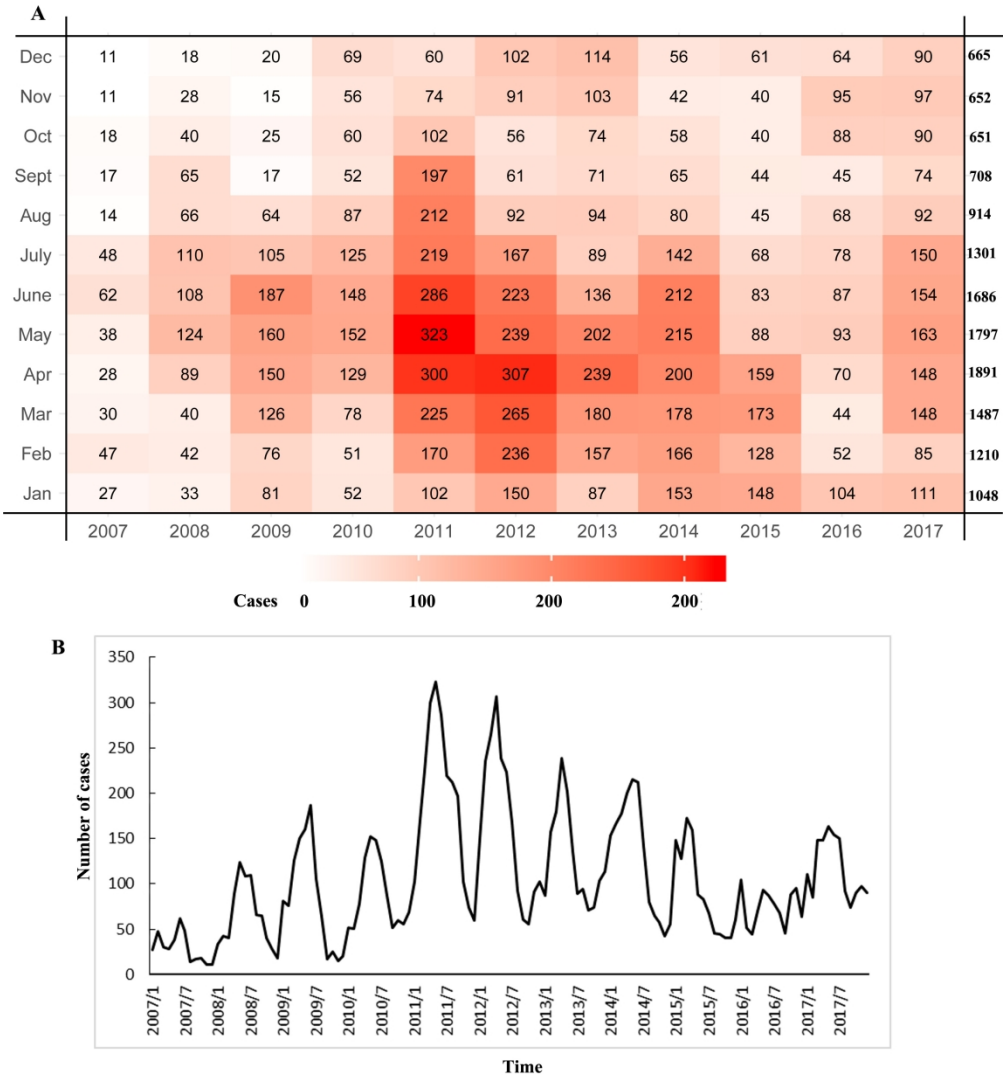

Figure 2 The analysis of the seasonal features of reported brucellosis cases during 2007 to 2017. (A) The thermal map of monthly reported cases of human brucellosis in Tongliao city. (B) The time series analysis model of the cycle and trend of the monthly reported cases.

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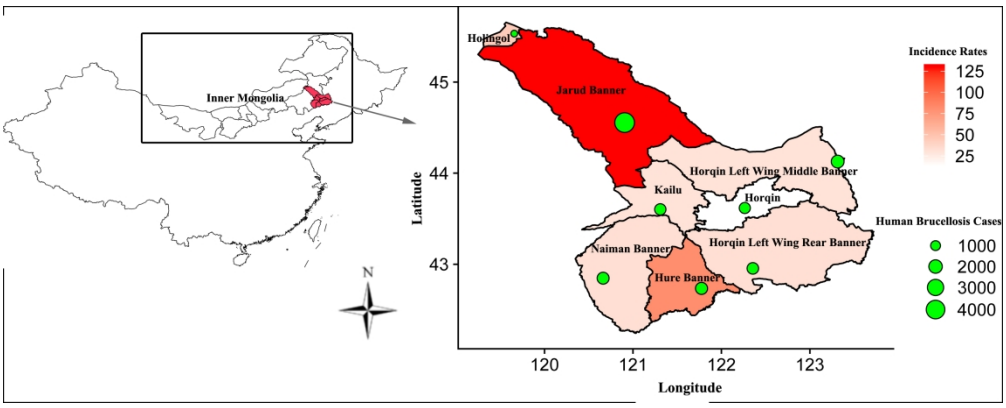

Figure 3 County level spatial distribution of reported cases and incidence rates (cases per 100,000 population) of human brucellosis over 2007-2017.

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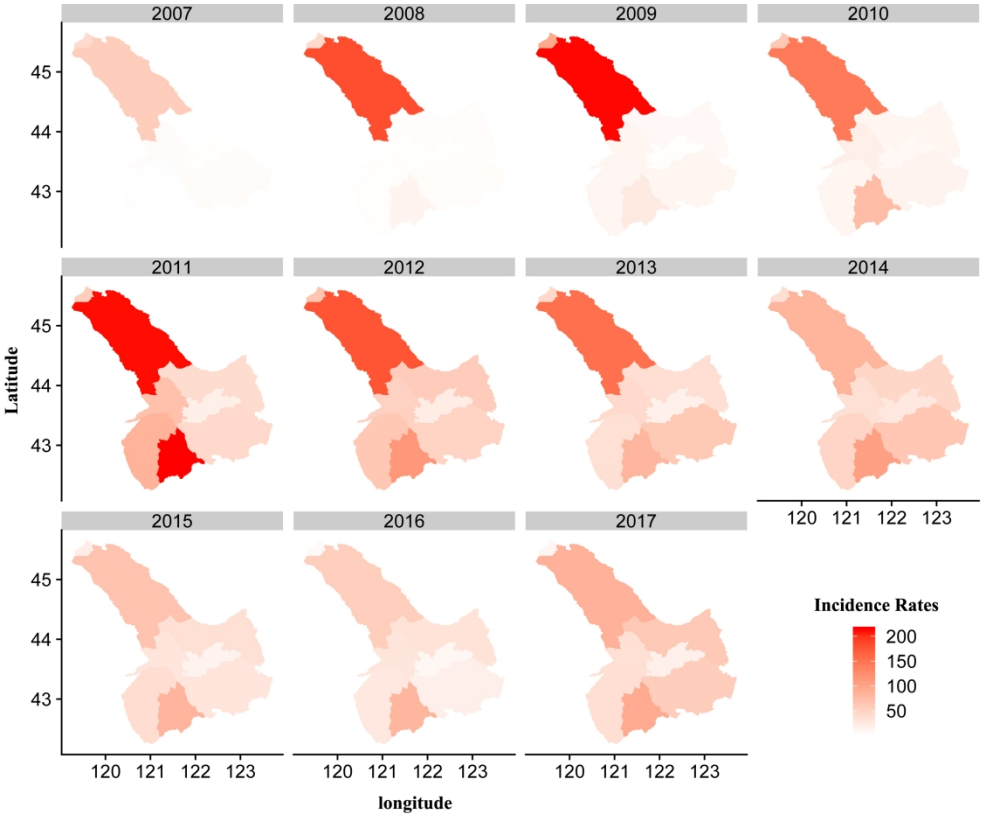

Figure 4 The annual incidence rates of human Brucellosis cases in Tongliao city.

228x186mm (300 x 300 DPI)

Supplementary materials

for

A cross-sectional study on the epidemiological features of human brucellosis in Tongliao city, Inner Mongolia province, China, over a 11-year period (2007-2017)

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Table S1 The annual age distribution of human brucellosis in Tongliao during 2007-2017.

Age stage	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
0-	1	4	1	1	4	5	3	2	3	3	5	32
4-	4	10	11	4	14	11	9	5	4	5	6	83
10-	7	5	14	7	17	7	6	10	1	2	8	84
15-	5	21	33	29	46	39	19	25	8	5	21	251
20-	13	44	63	52	102	86	59	68	32	23	33	575
25-	49	96	123	101	208	170	133	141	84	67	86	1258
30-	46	123	128	132	272	234	179	168	115	80	114	1591
35-	53	127	169	173	341	285	203	206	119	102	140	1918
40-	49	132	162	165	374	352	264	228	184	145	217	2272
45-	39	79	132	158	328	311	244	248	184	153	238	2114
50-	38	59	77	96	245	216	183	214	150	138	200	1616
55-	29	33	62	74	192	153	145	129	102	72	148	1139
60-	6	17	31	41	87	78	63	88	56	54	115	636
65-	8	9	11	14	28	30	27	28	27	30	56	268
70-	2	3	7	8	7	7	6	6	5	4	10	65
75-	1	1	1	4	3	4	3	1	2	3	2	25
80-	1	0	1	0	2	1	0	0	1	2	3	11
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S2 Occupational distribution of annual reported human brucellosis over the 11-year period in Tongliao.

Occupation	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Agriculturalists	264	528	769	745	1837	1633	1249	1409	961	818	1201	11414
Pastoralist	62	168	181	256	311	236	241	96	78	34	62	1725
Student	11	19	28	12	10	15	9	19	5	2	11	141
Preschool children	3	7	5	5	13	11	9	5	5	7	9	79
Teacher	1	0	1	1	1	2	2	0	2	1	0	11
Medical	1	2	4	2	43	5	2	1	2	1	2	65
Worker	3	16	30	21	4	9	6	8	2	8	3	110
Public official	2	4	2	1	6	2	2	9	2	1	4	35
Unemployed	0	14	3	5	10	11	17	16	12	16	94	198
Other	3	5	3	11	28	11	6	4	2	0	4	77
Unknown	1	0	0	0	7	54	3	0	6	0	12	83
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

Table S3 The yearly incidence rates of human brucellosis in Tongliao at county level during 2007 to 2017 (per 100, 000 population).

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Average
Horqin	2.72	2.59	2.46	8.85	18.91	22.27	17.11	26.27	14.10	10.41	17.80	13.05
Horqin Left Wing Middle Banner	1.11	4.23	8.74	12.63	40.21	57.70	36.87	46.27	35.28	32.82	60.76	30.60
Horqin Left Wing Rear Banner	6.12	4.86	12.30	14.84	43.24	49.17	61.63	63.60	30.00	18.56	57.02	32.85
Kailu	5.24	2.73	11.59	18.88	69.92	51.83	42.86	36.12	29.97	28.68	35.54	30.31
Hure Banner	2.22	13.24	24.66	75.67	213.75	114.94	81.93	105.46	83.05	81.89	93.94	80.98
Naiman Banner	2.04	3.15	10.72	12.42	85.68	62.45	36.07	47.61	38.52	27.30	37.32	33.03
Jurud Banner	56.78	181.38	212.85	143.48	211.90	176.61	153.03	84.54	67.86	55.80	87.11	130.12
Holingol	40.98	42.39	96.35	62.70	55.77	66.13	43.97	37.20	20.50	7.87	10.82	44.06
Average	9.22	22.33	31.20	31.24	69.16	60.55	47.79	47.82	33.28	27.30	44.32	38.56

Table S4 The number of reported human brucellosis cases in Tongliao at county level during 2007 to 2017.

County	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
Horqin	42	22	22	76	170	200	154	244	130	94	159	1313
Horqin Left Wing Middle Banner	10	25	53	81	216	301	197	247	183	171	311	1795
Horqin Left Wing Rear Banner	35	20	51	66	169	187	249	249	114	72	217	1429
Kailu	28	11	51	81	284	209	179	146	121	118	140	1368
Hure Banner	5	30	45	158	369	195	137	187	141	143	159	1569
Naiman Banner	15	18	50	65	358	261	157	192	157	114	152	1539
Jurud Banner	188	608	688	489	647	569	428	264	210	168	253	4512
Holingol	28	29	66	43	57	67	45	38	21	8	11	413
Total	351	763	1026	1059	2270	1989	1546	1567	1077	888	1402	13938

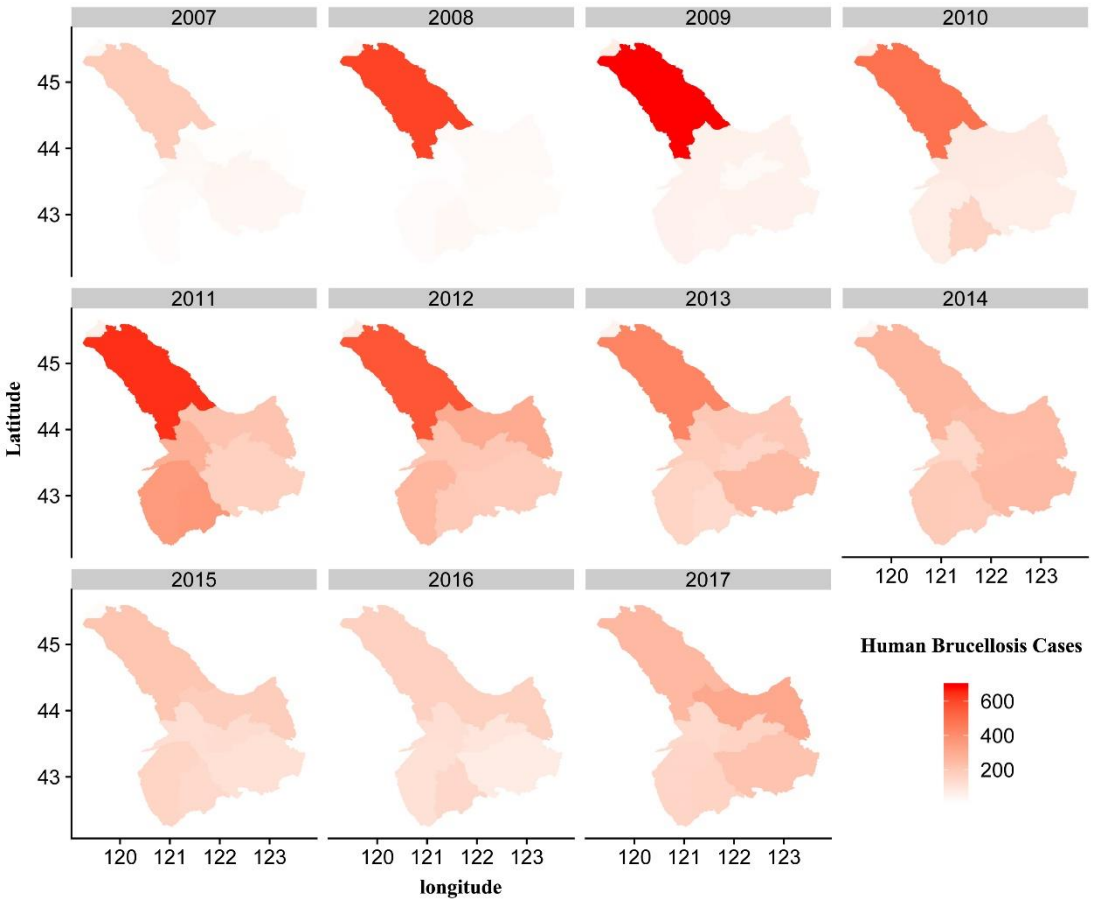

Figure S1 Annual distribution of reported cases of human brucellosis in Tongliao city, based on county (2007-2017).

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (Page1)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found (Page1 and 2)
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (Page2 and 3)
Objectives	3	State specific objectives, including any prespecified hypotheses (Page 3)
Methods		
Study design	4	Present key elements of study design early in the paper (Page 4, line12)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (Page 4, line4-19)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants (Page 5, line7-10)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (Page 4, line20-25)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (Page 4, line12-19)
Bias	9	Describe any efforts to address potential sources of bias (Page 2, line21-23)
Study size	10	Explain how the study size was arrived at (Page 5, line12-13)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses (Page 5, line1-6)

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (Page 5, line12-15)
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (Page 5, line12-24)
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures (Page 5-7)
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized (Page 5-7)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives (Page 7-9)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (Page 9, line 5-16)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (Page 7-9)
Generalisability	21	Discuss the generalisability (external validity) of the study results (Page 9, line 18-25)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.