GeoHealth

RESEARCH ARTICLE
10.1029/2022GH000721

Key Points:

- Climate, geographical landscape, demographic characteristics, and host infection integrally affect cystic echinococcosis (CE)
- The driving factors for CE in Qinghai-Tibet Plateau and other regions are distinguished
- The optimal generalized additive model model fits well with the correlation between CE and key risk factors

Supporting Information:

Supporting Information may be found in the online version of this article.

Correspondence to:

X. Wu,
wuxx@bnu.edu.cn

Citation:

Yin, J., Wu, X., Li, C., Han, J., & Xiang, H. (2023). The impact of environmental and host factors on human cystic echinococcosis: A county-level modeling study in Western China. *GeoHealth*, *7*, e2022GH000721. https://doi.org/10.1029/2022GH000721

Received 16 SEP 2022
Accepted 16 MAY 2023

Author Contributions:

Conceptualization: Jie Yin, Xiaoxu Wu
Data curation: Jie Yin, Jiatong Han
Formal analysis: Jie Yin
Funding acquisition: Xiaoxu Wu
Investigation: Jie Yin
Methodology: Jie Yin
Project Administration: Xiaoxu Wu
Resources: Jie Yin
Software: Jie Yin
Supervision: Xiaoxu Wu
Validation: Jie Yin, Chenlu Li

The Impact of Environmental and Host Factors on Human Cystic Echinococcosis: A County-Level Modeling Study in Western China

Jie Yin[1], Xiaoxu Wu[1], Chenlu Li[1], Jiatong Han[1], and Hongxu Xiang[1]

[1]State Key Laboratory of Remote Sensing Science, Faculty of Geographical Science, Beijing Normal University, Beijing, China

Abstract Human cystic echinococcosis (CE) is a parasitic disease caused by tapeworms from the *Echinococcus granulosus* genus, potentially affected by the environment and host animals. West China is one of the most endemic areas of human CE nation and worldwide. The current study identifies the crucial environmental and host factors of human CE prevalence in the Qinghai-Tibet Plateau and non-Qinghai-Tibet Plateau regions. An optimal county-level model was used to analyze the association between key factors and human CE prevalence within the Qinghai-Tibet Plateau. Geodetector analysis and multicollinearity tests identify key factors, and an optimal model is developed through generalized additive models. In the Qinghai-Tibet Plateau, four key factors were identified from the 88 variables, such as maximum annual precipitation (Pre), maximum summer normalized difference vegetation index (NDVI), Tibetan population rate (TibetanR), and positive rates of *Echinococcus* coproantigen in dogs (DogR). Based on the optimal model, a significant positive linear relationship was observed between maximum annual Pre and human CE prevalence. A probable U-shaped curve depicts the non-linear relationship between maximum summer NDVI and the human CE prevalence. Human CE prevalence possesses significant positive non-linear relationships with TibetanR and DogR. Human CE transmission is integrally affected by environmental and host factors. This explains the mechanism of human CE transmission based on the pathogen, host, and transmission framework. Therefore, the current study provides references and innovative ideas for preventing and controlling human CE in western China.

Plain Language Summary Western China is one of the most prevalent epidemic areas of human cystic echinococcosis (CE) worldwide. This region is closely associated with the natural environment, human society, and host animals. The relative contribution of the natural and human environments and host factors to human CE prevalence has been tremendously neglected. Here it was presented that natural, human, and host factors interactively affect human CE prevalence by impacting pathogens, hosts, and transmission. Thus climate, geographical landscape, demographic characteristics, and host infection status significantly affect human CE prevalence. This explains the mechanism of nature, humans, and the host on CE transmission and is instructive for monitoring, preventing, and controlling CE in the future.

1. Introduction

Echinococcosis is a zoonotic parasitic disease transmitted from animals to humans. *Echinococcus granulosus* causes Cystic echinococcosis (CE), primarily transmitted in a “dog-domestic animals-dog” cycle, where the dog is the end host and domestic animals (such as sheep, goats, cattle, yaks, and swine) become the intermediate hosts (WHO, 2021). Ingesting parasite eggs in a contaminated environment and direct contacting hosts become the leading causes of human CE infection (WHO, 2021). Annually, CE causes the loss of 1 million disability-adjusted life years worldwide (Budke et al., 2006). Human CE has a wide distribution across China, but 98% of these cases occur in seven provincial western regions, that is, Inner Mongolia Autonomous Region (Inner Mongolia), Sichuan Province, Tibet Autonomous Region (Tibet), Gansu Province (Gansu), Qinghai Province (Qinghai), Ningxia Hui Autonomous Region (Ningxia), and Xinjiang Uygur Autonomous Region (Xinjiang) (W. P. Wu et al., 2018). The Qinghai-Tibet Plateau is the most served area of human CE worldwide (Craig et al., 2019). Thus, human CE seriously threatens public health and socio-economic development across China (Zhang et al., 2015).

Human CE prevalence in China has distinct geographical heterogeneity, gradually decreasing from west to east (W. P. Wu et al., 2018), reflecting the impact of the ecological environment on human CE transmission.

Visualization: Jie Yin, Chenlu Li, Jiatong Han, Hongxu Xiang
Writing – original draft: Jie Yin
Writing – review & editing: Jie Yin, Xiaoxu Wu

Additionally, the widespread CE prevalence in economically disadvantaged agricultural and pastoral areas and Tibetan communities demonstrates that social economy, demographic structure, and host animals could be potential risk factors. Previous studies have analyzed the relationship between CE and certain risk factors (Huang et al., 2018; Ma et al., 2021; Paternoster et al., 2021; Possenti et al., 2016; Yuan et al., 2017). For instance, human CE prevalence positively correlates with the grassland area and Tibetan population ratio. Moreover, the prevalence negatively correlates with the gross domestic product (GDP) and land surface temperature across western China (Huang et al., 2018). Immunizing sheep is a protective CE factor, and encountering stray dogs increases the risk of CE infection in five western China provinces (Yuan et al., 2017). A study in Tibet also observed that annual average precipitation, elevation, and animal population were associated with human CE prevalence (Ma et al., 2021). A study in the Qinghai-Tibet Plateau regions found a negative correlation between human CE prevalence and altitude, land surface temperature, and socioeconomics (Zeng et al., 2020). Female, Tibetan, low-income, herdsman occupations, and livestock ownership are significant risk factors for human CE infection in Qinghai (Schantz et al., 2003). Human CE hospitalization rate is negatively correlated with annual average temperature and positively associated with goat density and intermediate precipitation in Chile (Colombe et al., 2017).

Many studies have analyzed risk factors affecting human CE prevalence, primarily focusing on one or a particular aspect of risk factors. Few studies have comprehensively screened the environmental and host risk factors affecting human CE. Moreover, several previous studies depended on correlation and regression analysis to determine the relationship between risk factors and human CE. However, a well-fitted quantitative model study to analyze this relationship is still lacking, especially in western China. The study summarized three risk factors affecting human CE in western China, including the natural environment, human environment, and host. Western China was divided into the Qinghai-Tibet and the non-Qinghai-Tibet Plateau regions, and key risk factors for human CE were selected separately. Finally, the models containing different covariates were compared to select the best model explaining the relationship between human CE prevalence and the key factors. This enables a theoretical basis and scientific guidance for preventing and controlling human CE.

2. Materials and Methods

2.1. Study Area

The study area included six provinces in western China: Inner Mongolia, Ningxia, Gansu, Qinghai, Xinjiang, and Tibet (Figure 1). Human CE is endemic in these six provinces, and its prevalence is high in the Qinghai-Tibet Plateau and decreases with prolonged distance, indicating spatial characteristics (Zhou, 2009). The natural environment in western China is diverse. The Qinghai-Tibet Plateau is a high-altitude ecosystem with intense solar radiation and low temperature, having mainly alpine meadow vegetation (Craig et al., 2019; Shang et al., 2014). In the non-Qinghai-Tibet Plateau regions, it is primarily temperate continental climate being arid and rainless, and temperate steppe and desert steppe are the primary vegetation type (Zeng et al., 2020). Agriculture and animal husbandry are the main product types in these provinces with abundant animal resources (Schaller, 1998; Smith & Xie, 2008). Animals constitute a relatively fixed food chain relationship, which favors echinococcosis transmission from animals to humans. For instance, a stable life cycle of *E. granulosus* is formed between the end hosts (dogs) and intermediate hosts (domestic animals), leading to endemic human CE (Craig et al., 2019). Additionally, these provinces have vast areas, sparse populations, and underdeveloped economies. Thus, local populations are more vulnerable to CE being affected by living environment conditions, education level, and religious customs (Yin et al., 2020).

2.2. Data Collection and Preprocessing

This study retrieved county-level data on human CE prevalence from updated and published scientific papers and reports (Huang et al., 2018; Yin et al., 2022). A total of 191 data from the counties was obtained. Among them, 53 Tibet counties were derived from the 2016 published epidemiological survey on echinococcosis (BaiMa et al., 2018; Bianba et al., 2018; CiRen et al., 2018; DanZhen et al., 2018; GongSang et al., 2018; D. M. Wang et al., 2018). The data from 138 other counties were derived from the 2012 epidemiological survey report on echinococcosis in China (G. Q. Wang, 2016). Human CE prevalence details per county are listed in Table S1 in Supporting Information S1. These were the first large-scale epidemiological surveys in the study area. The same

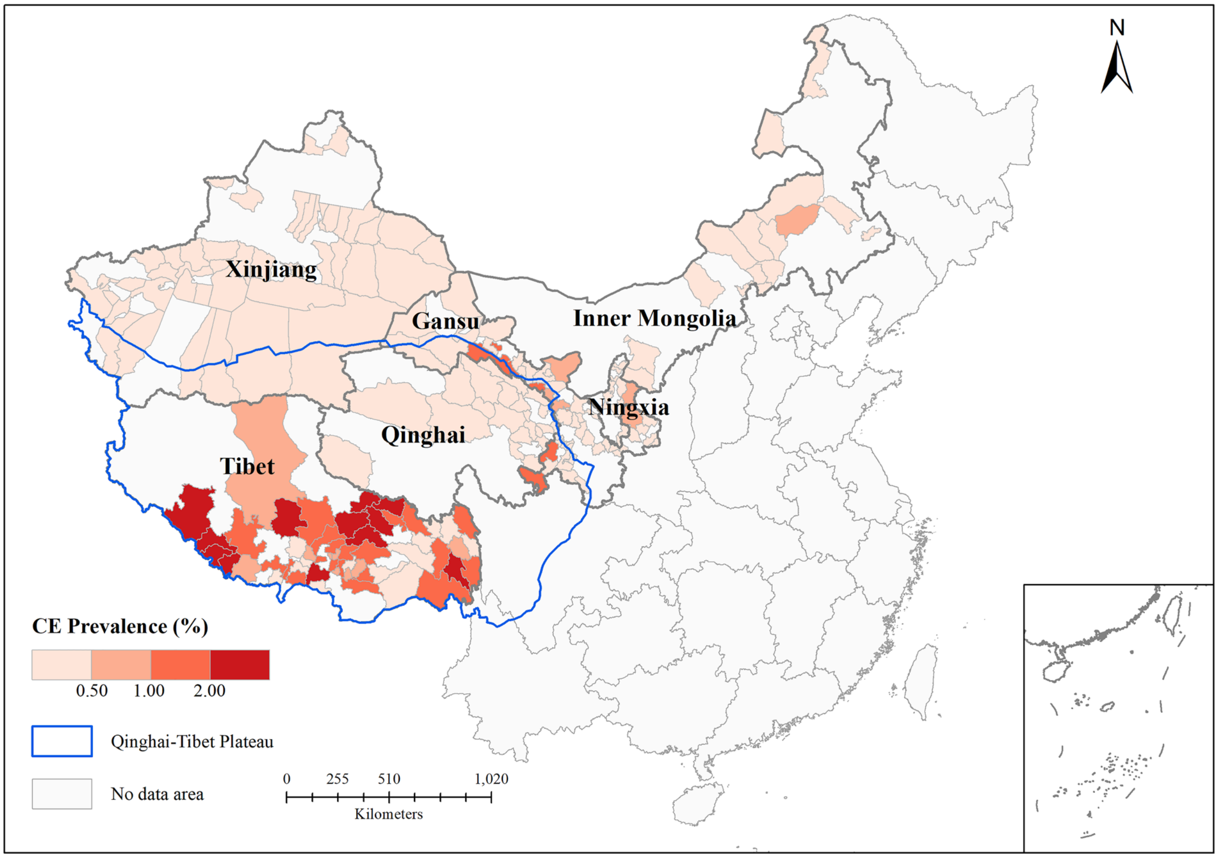

Figure 1. Distribution of the human cystic echinococcosis prevalence at county level in Western China.

survey strategies were used under the guidance of the National Institute of Parasitic Disease, Chinese Center for Disease Control and Prevention. B. Li et al. (2019) introduced the details of the case diagnosis and human prevalence estimate.

Based on the literature review, we considered 12 potential risk factors based on the complexity of the local environment and the life cycle of *E. granulosus* (Table 1). We classified them into natural, human, and host factors. Finally, 88 variables were used in the analysis, including 81 natural variables, five human variables, and two host variables. The time of factor data for each category has been listed in Table S2 in Supporting Information S1.

2.2.1. Natural Factors

Climate and geographical landscape were considered natural factors. Climate factors included precipitation (Pre), temperature (T), relative humidity (Rh), and sunshine duration (Sun). Geographical landscape factors included the digital elevation model (DEM), normalized difference vegetation index (NDVI), the area proportion of grassland in total land use (GrassR), the area proportion of forest in total land use (ForestR), and the area proportion of cultivated land in total land use (CultivatedR). The annual, spring (March to May), summer (June to August), autumn (September to November), and winter (December to February) indicators of climate factors and NDVI were also calculated. For example, we calculated the indicators for the factor precipitation, including maximum, minimum, and mean values of annual/spring/summer/autumn/winter precipitation.

2.2.2. Human Factors

Human factors involve economic and population factors. Economic factors have per capita GDP and beds of medical institutions (BMI), reflecting economic development and medical care capacity. Population factors include the agricultural population rate, illiterate population rate, and Tibetan population rate (TibetanR). This represents the local production type, education level, and ethnicity.

Table 1
Attributes of Natural, Human, and Host Factors

Category		Factor	Data source
Natural factors	Climate	Precipitation (mm)	National Earth System Science Data Center, National Science & Technology Infrastructure of China (http://www.geodata.cn)
		Temperature (°C)	
		Relative humidity (%)	
		Sunshine duration (hr)	
	Geographical landscape	Digital elevation model (m)	Resource and Environment Data Cloud Platform (http://www.resdc.cn/DataList.aspx)
		Normalized difference vegetation index (–)	
		Area proportion of grassland/forest/cultivated land in total land use (%)	
Human factors	Economy	Per capita gross domestic product (million RMB)	China Statistical Yearbook database (https://data.cnki.net/)
		Beds of medical institutions (–)	
	Population	Agricultural/illiterate/Tibetan population rate (%)	
Host factors	Animal	Positive rates of echinococcosis in livestock (%)	BaiMa et al. (2018), Bianba et al. (2018), CiRen et al. (2018), DanZhen et al. (2018), GongSang et al. (2018), G. Q. Wang (2016), and D. M. Wang et al. (2018)
		Positive rates of *Echinococcus* coproantigen in dogs (%)	

2.2.3. Host Factors

The host mainly refers to livestock and dogs closely associated with the life cycle of *E. granulosus*. The corresponding factors involve positive rates of echinococcosis in livestock and *Echinococcus* coproantigen in dogs (DogR). The host data source in each county is consistent with the human CE prevalence data source. The livestock diagnosis involves a clinical visual examination, veterinary palpation of the livestock organs (e.g., livers, lungs), and suspected cyst anatomization (B. Li et al., 2019; G. Q. Wang, 2016). The sandwich ELISA kit is used to test dog feces for *Echinococcus* coproantigens, with over 80% kit sensitivity and specificity (B. Li et al., 2019; G. Q. Wang, 2016). These two factors reflect the echinococcosis spread, prevention progress, and animal echinococcosis control.

2.3. Analysis Methods

In this study, the dependent variable is the human CE prevalence, and risk factors are the independent variables. Geodetector and multicollinearity tests helped select key factors. The generalized additive model (GAM) determines the significant key factors. Moreover, GAM assesses the quantitative relationship between natural, human, and host factors and human CE prevalence.

Geodetector (http://www.geodetector.cn) is used to detect stratified spatial heterogeneity and determine driving factors (J. F. Wang et al., 2010). The theoretical basis of the method is that the spatial distribution of X and Y should be similar if the independent variable X has a significant effect on the dependent variable Y (J. Wang & Xu, 2017). The factor detector calculates the contribution of each risk factor to human CE prevalence using the *q*-statistic value. This method requires that the independent variable is categorical. We discretize continuous data by setting the optional discretization parameters. The *q*-statistic is defined with the following equation:

$$q = 1 - \frac{\sum_{h=1}^{L} N_h \sigma_h^2}{N\sigma^2} \tag{1}$$

where N is the number of samples, L is the category number of the independent variable X, σ^2 is the total variance of the dependent variable Y, and σ_h^2 is the variance of Y in category h of X. The larger the q value, the greater X explains Y.

GAM is a flexible and convenient model specifying smooth functions (Wood, 2017) involving the covariate sum of smooth functions. This method allows for the flexible specification of the response dependence on the covariates. In this study, the human CE prevalence of each county was used as the response variable and the risk factors were used as covariates to develop the GAM model with the following expressions:

$$\text{prevalence}_i = \beta_0(i) + \sum\nolimits_{j=1}^{p} s\left(x_j(i), bs{=}''tp''\right) \tag{2}$$

where prevalence$_i$ is the human CE prevalence in the county i $(i = 1, \ldots n)$; $\beta_0(i)$ is the intercept of the county i; $x_j(i)$ is the jth key factor $(j = 1 \ldots p)$; $s(\cdot)$ indicates a spline function; bs specifies the penalty in smooth classes; and "*tp*" stands for thin plate regression splines.

The developed models were validated by determining the adjusted R square (R-sq.(adj)), deviance, and Akaike Information Criterion (AIC). The computing and graphical displays were performed with R 4.1.2.

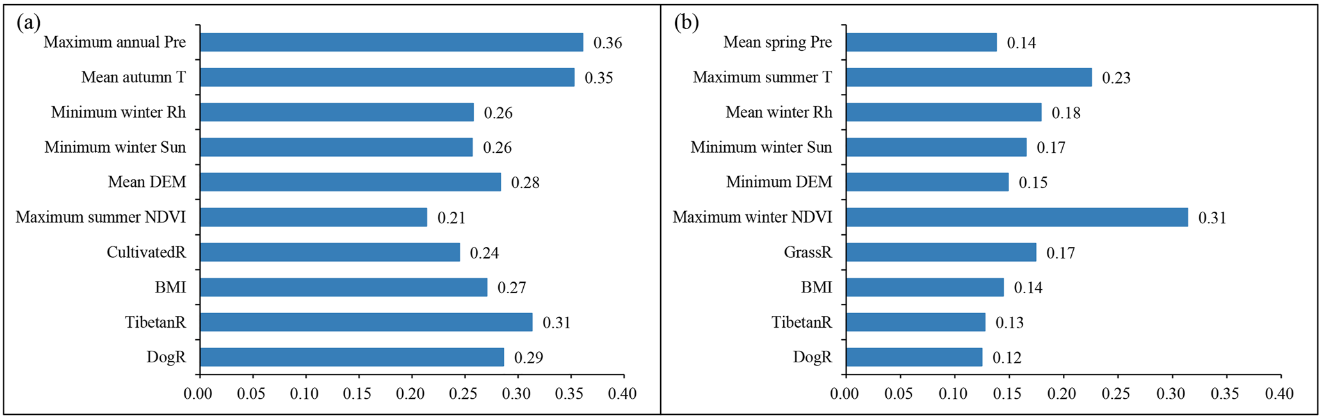

Figure 2. The q-values of variables based on the Geodetector analysis: (a) Qinghai-Tibet Plateau and (b) non-Qinghai-Tibet Plateau region.

3. Results

3.1. Identification of Key Factors

Since the Qinghai-Tibet and the non-Qinghai-Tibet Plateau regions have significant differences in the natural and human environment, the human CE risk factors were analyzed in these regions. Key factors are screened and determined based on Geodetector analysis (Figure 2). These selected variables have the largest q-value of each type. Therefore, these variables significantly contribute to the prevalence of human CE and can be used for further analysis. The contribution of natural, human, and host factors to human CE prevalence is more significant in the Qinghai-Tibet Plateau (Figure 2a) than in the non-Qinghai-Tibet Plateau regions (Figure 2b). Thus, the dominant factors differ in these two regions.

First, the Qinghai-Tibet Plateau has approximate q-value ranges for key natural, human, and host factors (Figure 2a). Among the natural factors, climate factors contribute more to human CE prevalence than geographic landscape factors. The q-value for maximum annual Pre is the highest ($q = 0.36$), followed by the mean autumn T ($q = 0.35$), mean DEM ($q = 0.28$), and other natural factors ($0.21 < q < 0.26$). Regarding human factors, the dominant power of population factors is higher than economic ones. The TibetaR ($q = 0.31$) is vital in the prevalence of human CE. The DogR ($q = 0.29$) contributes significantly to human CE prevalence. Second, the q-values of key natural factors are more prominent in the non-Qinghai-Tibet Plateau regions than those of key human and host factors (Figure 2b). Thus, the natural environment is dominant in human CE prevalence. The q-value of maximum winter NDVI is the largest ($q = 0.31$) among all the factors, followed by the maximum summer T ($q = 0.23$) and other factors ($0.12 < q < 0.18$).

The multicollinearity test can eliminate key risk factors with strong collinearity. Factors with tolerance <0.2 or variance inflation factor value >5 were excluded. In the Qinghai-Tibet Plateau, the mean DEM is eliminated; maximum summer T is eliminated in the non-Qinghai-Tibet Plateau regions. Finally, the key factors identified for modeling in the Qinghai-Tibet Plateau are maximum annual Pre, mean autumn T, minimum winter Rh, minimum winter Sun, maximum summer NDVI, CultivatedR, BMI, TibetanR, and DogR. In contrast, the key factors identified for modeling in the non-Qinghai-Tibet Plateau regions are mean spring Pre, mean winter Rh, minimum winter Sun, minimum DEM, maximum winter NDVI, GrassR, BMI, TibetanR, and DogR.

3.2. Modeling

These key factors are put into GAM models for the final selection. Then, based on the AIC values, the optimal model and significant risk factors are determined. In the Qinghai-Tibet Plateau, the identified key factors involve maximum annual Pre, maximum summer NDVI, TibetanR, and DogR, respectively, reflecting the climate, geographical landscape, demographic characteristics, and host infection. Table 2 represents the approximate significance of smooth terms and statistic diagnosis information of the model. Statistic diagnosis information demonstrates that the model fits well. R-sq.(adj) value is 0.462, the deviance explained is 71.90%, and the AIC is −626.099. The human CE prevalence possesses a significant linear relationship with the maximum annual

Table 2
Approximate Significance of Smooth Terms and Statistic Diagnosis Information of the Optimal Model in the Qinghai-Tibet Plateau

Smooth term	edf	Ref.df	*p*-Value
s(Maximum annual pre)	1.000	1.001	0.0495*
s(Maximum summer NDVI)	2.283	2.809	0.0402*
s(TibetanR)	2.302	2.822	1.41e−05***
s(DogR)	3.084	3.765	7.48e−06***
Statistic diagnosis attributes			
Family			Beta regression (154.944)
Link function			Logit
R-sq.(adj)			0.462
Deviance explained			71.90%
AIC			−626.099

Note. *** $p < 0.001$; * $p < 0.05$.

Pre and non-linear relationships with maximum summer NDVI, TibetanR, and DogR. In the non-Qinghai-Tibet Plateau regions, the statistic diagnosis information of the optimal model is bad (R-sq.(adj) = 0.13, deviance explained = 31.5%). Therefore, we did not analyze the relationship between human CE prevalence and risk factors.

3.3. Analysis of the Relationship Between Key Factors and Human CE

According to the optimal model in the Qinghai-Tibet Plateau, the impact of natural, human, and host factors on human CE prevalence is analyzed. The contribution of significant key factors is depicted in Figure 3. Human CE prevalence possesses a significant positive linear relationship with maximum annual Pre (Figure 3a). The human CE prevalence relationship with maximum summer NDVI depicts a U-shaped curve across all ranges and achieves a minimum when the maximum summer NDVI is 0.8 (Figure 3b). However, the maximum summer NDVI is greater than 0.8 in most counties. Thus, human CE prevalence increases with maximum summer NDVI in most parts of the Qinghai-Tibet Plateau. Figure 3c demonstrates that human CE prevalence increases with rising TibetanR. The increase rate is low when TibetanR is <50%, and it is fast after that. Thus, human CE is more prevalent among clustered Tibetan populations, consistent with the previous research results on vulnerable echinococcosis populations (Yin et al., 2020). Human CE prevalence shows a significant positive non-linear relationship with DogR (Figure 3d). An evident increase in human CE prevalence is observed when DogR rises from 0% to 8% and exceeds 18%. However, human CE prevalence remains stable when DogR is within 8%–18%.

4. Discussion

The impact of natural, human, and host factors on human CE prevalence in the Qinghai-Tibet Plateau can be explained based on the pathogen, host, and transmission framework. This is similar to the impact of climate change on human infectious diseases (X. Wu et al., 2016). Natural factors, such as maximum annual Pre and maximum summer NDVI, significantly affect human CE prevalence. Maximum annual Pre could affect CE transmission from two aspects. First, the release, survival, and infectivity of *E. granulosus* eggs could be sensitive to precipitation (Lawson & Gemmell, 1983; Veit et al., 1995). For example, soil moisture changes may affect the number of viable eggs in the environment (Wachira et al., 1991). Second, the precipitation affects the host and transmission route. Increased precipitation would favor the survival of eggs of *E. granulosus* in limited moisture environments and increases the possibility of eggs being washed into rivers and drinking reservoirs (Jenkins et al., 2011; Yin et al., 2023). Seasonal precipitation changes could affect intermediate host numbers of CE in drier periods (Previtali et al., 2010). NDVI reflects the vegetation coverage and is associated with the production type of residents. The vegetation type in the Qinghai-Tibet Plateau is primarily grassland, and the higher the maximum summer NDVI, the higher the grassland coverage. Therefore, animal husbandry is more developed in areas with high NDVI. Human CE is prevalent within pastoral regions (B. Li et al., 2019; Yin et al., 2020, 2022), associated with the environment and the living habits of herdsmen. In pastoral areas, there are more cattle, sheep, and dogs without clean drinking water, which is conducive to human CE transmission. Moreover, herdsmen always come in contact with dogs and cannot wash hands frequently, increasing the risk of human CE. Tibetans are more vulnerable to echinococcosis due to increased lifestyle susceptibility (Yin et al., 2020). They collect yak dung as fuel and feed dogs with infected livestock organs, promoting *E. granulosus* transmission to humans (Craig et al., 2019; T. Li et al., 2005). DogR has direct and indirect effects on CE infection risk in humans. On the one hand, it affects human exposure risk to *E. granulosus* eggs, which could be ingested through direct contact with infected dogs or from a contaminated environment of dog feces. On the other hand, the progress and importance of dog

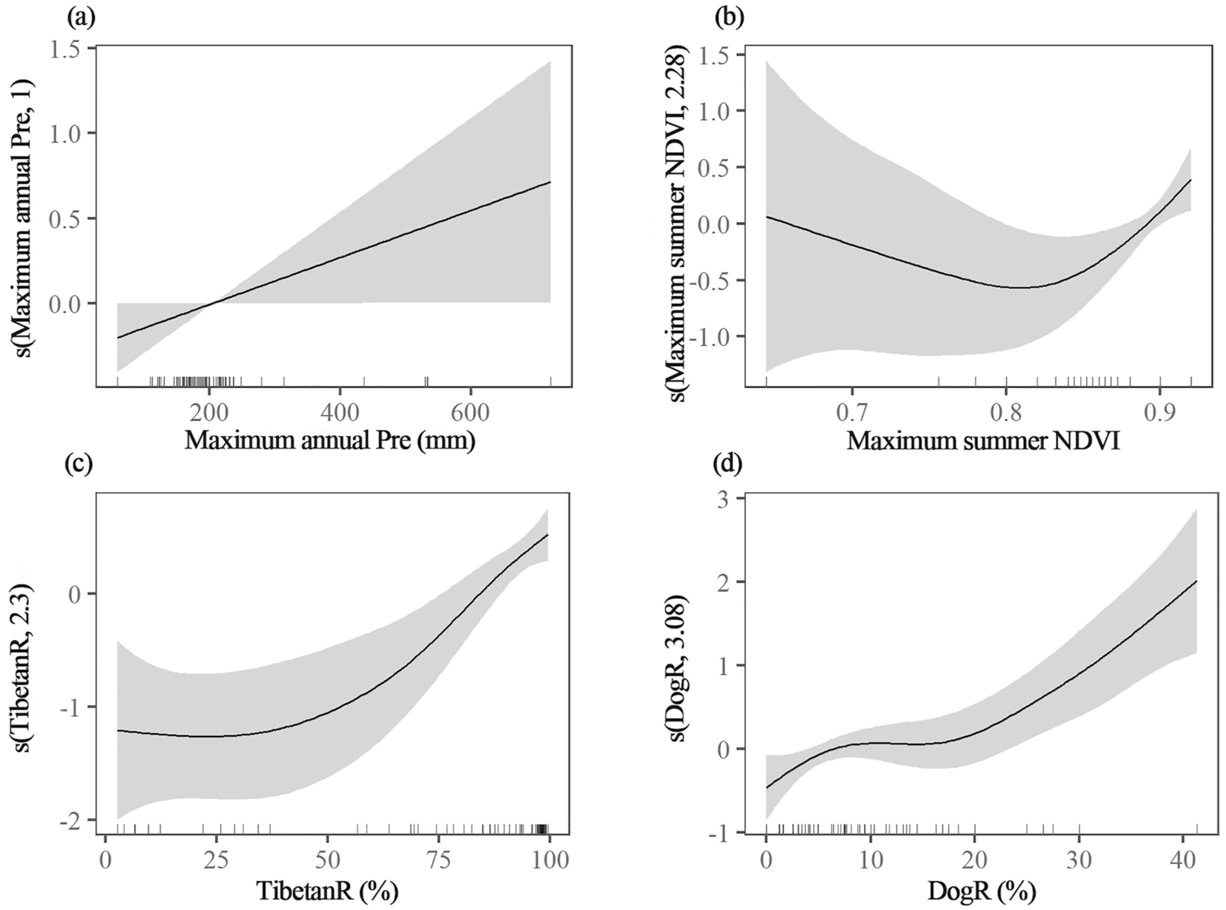

Figure 3. Relationship between key factors and human cystic echinococcosis prevalence: (a) maximum annual Pre; (b) maximum summer normalized difference vegetation index; (c) TibetanR; and (d) DogR. Smoothed functions are shown as solid lines, and 95% confidence intervals are represented by gray shading.

deworming are reflected. The management and regular deworming of dogs are crucial for controlling echinococcosis in endemic areas in China (Yu et al., 2020).

Our study comprehensively analyzes the relationship between human CE prevalence and natural, human, and host factors, with some relevant literature. One study investigates the relationship between human CE prevalence, the natural geography, and the human environment in western China. The results indicate that CE prevalence correlates positively with annual mean precipitation and the overall Tibetan population ratio (Huang et al., 2018). Human CE prevalence is also related to the altitude and number of hosts in Tibet (Ma et al., 2021). Contact with dogs can increase the human CE risk among herding families in western China (Yuan et al., 2017). Compared with previous literature, our research provides improvements in several respects. First, we identified the dominant human CE prevalence factors in the Qinghai-Tibet and non-Qinghai-Tibet Plateau regions. Second, this study considered the comprehensive effect of natural, human, and host factors on human CE worldwide in the most endemic areas. The study also quantitatively analyzed the mechanism of natural, human, and host factors affecting human CE prevalence. This is a comprehensive study to elucidate the complex mechanism of CE transmission in western China. Moreover, the study provides innovative ideas and methods for deciphering echinococcosis and other similar diseases in different regions.

However, the study had a few inevitable limitations. First, the analysis did not include some high-endemic areas with human CE due to data limitations, such as Ganzi and Aba prefectures in Sichuan, Yushu, and Guoluo prefectures of southern Qinghai. Second, some risk factors were not considered due to data unavailability, such as drinking water quality, human behavior, and host animal population. They are also crucial for human CE, but it is not easy to collect comprehensive factor data on such a large scale. Still, the factors considered in this study are very representative and critical. Future studies would develop a more comprehensive model integrating key factors from the most endemic areas of echinococcosis. Third, data on relative humidity and sunshine duration were not contemporaneous with prevalence data, for high quality of the available meteorological raster data. But this does not affect the modeling results since the two factors were not included in the optimal model.

5. Conclusions

This study investigated the effect of natural, human, and host factors on CE prevalence at a county level across western China. The driving factors of human CE prevalence differ in the Qinghai-Tibet and non-Qinghai-Tibet Plateau regions. Human CE prevalence is more associated with natural, human, and host factors in the Qinghai-Tibet Plateau. This study identifies four risk factors, viz., maximum annual Pre, maximum summer NDVI, TibetanR, and DogR, that are key to human CE prevalence within the Qinghai-Tibet Plateau. According to the optimal model, the quantitative relationships between the key factors and human CE prevalence have been indicated. Maximum annual Pre revealed a significant positive linear relationship with human CE prevalence. A U-shaped curve indicated the non-linear relationship between maximum summer NDVI and human CE prevalence. Human CE prevalence possessed significant positive non-linear relationships with TibetanR and DogR.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

The human CE prevalence data (Table S1 in Supporting Information S1), the economic and demographic data (Table S3 in Supporting Information S1) supporting this study will be archived in a general repository. The climate data sets used in our study can be freely accessed at http://www.geodata.cn. Precipitation: http://www.geodata.cn/data/datadetails.html?dataguid=192891852410344&docid=1125. Maximum temperature: http://www.geodata.cn/data/datadetails.html?dataguid=80741928278399&docid=1128. Minimum temperature: http://www.geodata.cn/data/datadetails.html?dataguid=69746873117810&docid=1127. Mean temperature: http://www.geodata.cn/data/datadetails.html?dataguid=164304785536614&docid=1126. Relative humidity: http://www.geodata.cn/data/datadetails.html?dataguid=5935309512961&docid=13528. Sunshine duration: http://www.geodata.cn/data/datadetails.html?dataguid=102686883128586&docid=13621. The geographical landscape data sets used in our study can be freely accessed at http://www.resdc.cn/DataList.aspx.

Acknowledgments
This work was supported by the National Key Research and Development Program of China (2012CB955501).

References

BaiMa, Y. J., Wu, W. P., He, R. F., GongSang, Q. Z., KangZhu, Y. X., SuoLang, W. J., & Li, B. (2018). Prevalence of echinococcosis in Shannan City. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 63–67.

Bianba, Z. M., Li, B., Chen, W. Q., Wang, D. M., Xiao, D., Bian, B., & GongSang, Q. Z. (2018). Current prevalence of echinococcosis in Shigatse City. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 80–86.

Budke, C. M., Deplazes, P., & Torgerson, P. R. (2006). Global socioeconomic impact of cystic echinococcosis. *Emerging Infectious Diseases*, *12*(2), 296–303. https://doi.org/10.3201/-eid1202.050499

CiRen, L. M., Yan, X. L., DanZhen, W. J., Long, Z. Y., DanZeng, Q. Z., Ai, J. J., et al. (2018). Epidemiological status of echinococcosis in Lhasa City. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 58–62.

Colombe, S., Togami, E., Gelaw, F., Antillon, M., Fuentes, R., & Weinberger, D. M. (2017). Trends and correlates of cystic echinococcosis in Chile: 2001–2012. *PLoS Neglected Tropical Diseases*, *11*(9), e0005911. https://doi.org/10.1371/journal.pntd.0005911

Craig, P. S., Giraudoux, P., Wang, Z. H., & Wang, Q. (2019). Chapter four - Echinococcosis transmission on the Tibetan Plateau. *Advances in Parasitology*, *104*, 165–246. https://doi.org/10.1016/bs.apar.2019.03.001

DanZhen, W. J., Xue, C. Z., GongSang, Q. Z., Ai, J. J., Luo, Z. H., DanZeng, Q. Z., et al. (2018). Analysis of echinococcosis prevalence in Naqu Prefecture. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 47–53.

GongSang, Q. Z., Li, B., Chen, W. Q., Ga, S., SuoLang, W. J., Wang, D. M., et al. (2018). Prevalence of echinococcosis in Changdu City. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 68–74.

Huang, D., Li, R., Qiu, J., Sun, X., Yuan, R., Shi, Y., et al. (2018). Geographical environment factors and risk mapping of human cystic echinococcosis in western China. *International Journal of Environmental Research and Public Health*, *15*(8), 1729. https://doi.org/10.3390/-ijerph15081729

Jenkins, E. J., Schurer, J. M., & Gesy, K. M. (2011). Old problems on a new playing field: Helminth zoonoses transmitted among dogs, wildlife, and people in a changing northern climate. *Veterinary Parasitology*, *182*(1), 54–69. https://doi.org/10.1016/-j.vetpar.2011.07.015

Lawson, J. R., & Gemmell, M. A. (1983). Hydatidosis and cysticercosis: The dynamics of transmission. *Advances in Parasitology*, *22*, 261–308. https://doi.org/10.1016/S0065-308X(08)60464-9

Li, B., Quzhen, G., Xue, C. Z., Han, S., Chen, W. Q., Yan, X. L., et al. (2019). Epidemiological survey of echinococcosis in Tibet autonomous region of China. *Infectious Disease of Poverty*, *8*(1), 29. https://doi.org/10.1186/s40249-019-0537-5

Li, T., Jiamin, Q., Yang, W., Craig, P., Xingwang, C., Ning, X., et al. (2005). Echinococcosis in Tibetan populations, western Sichuan Province, China. *Emerging Infectious Diseases*, *11*(12), 1866–1873. https://doi.org/10.3201/eid1112.050079

Ma, T., Jiang, D., Quzhen, G., Xue, C., Han, S., Wu, W., et al. (2021). Factors influencing the spatial distribution of cystic echinococcosis in Tibet, China. *Science of The Total Environment*, *754*, 142229. https://doi.org/10.1016/j.scitotenv.2020.142229

Paternoster, G., Boo, G., Flury, R., Raimkulov, K., Minbaeva, G., Usubalieva, J., et al. (2021). Association between environmental and climatic risk factors and the spatial distribution of cystic and alveolar echinococcosis in Kyrgyzstan. *PLoS Neglected Tropical Diseases*, *15*(6), e0009498. https://doi.org/10.1371/journal.pntd.0009498

Possenti, A., Manzano-Román, R., Sánchez-Ovejero, C., Boufana, B., La Torre, G., Siles-Lucas, M., & Casulli, A. (2016). Potential risk factors associated with human cystic echinococcosis: Systematic review and meta-analysis. *PLoS Neglected Tropical Diseases*, *10*(11), e0005114. https://doi.org/10.1371/journal.pntd.0005114

Previtali, M. A., Lehmer, E. M., Pearce-Duvet, J. M. C., Jones, J. D., Clay, C. A., Wood, B. A., et al. (2010). Roles of human disturbance, precipitation, and a pathogen on the survival and reproductive probabilities of deer mice. *Ecology*, *91*(2), 582–592. https://doi.org/10.1890/08-2308.1

Schaller, G. B. (1998). *Wildlife of the Tibetan steppe*. University of Chicago Press.

Schantz, P. M., Wang, H., Qiu, J., Liu, F. J., Saito, E., Emshoff, A., et al. (2003). Echinococcosis on the Tibetan Plateau: Prevalence and risk factors for cystic and alveolar echinococcosis in Tibetan populations in Qinghai Province, China. *Parasitology*, *127*(S1), S109–S120. https://doi.org/10.1017/s0031182003004165

Shang, Z. H., Gibb, M. J., Leiber, F., Ismail, M., Ding, L. M., Guo, X. S., & Long, R. J. (2014). The sustainable development of grassland-livestock systems on the Tibetan plateau: Problems, strategies and prospects. *The Rangeland Journal*, *36*(3), 267–296. https://doi.org/10.1071/RJ14008

Smith, A., & Xie, Y. (2008). *A guide to the mammals of China*. Princeton University Press.

Veit, P., Bilger, B., Schad, V., Schäfer, J., Frank, W., & Lucius, R. (1995). Influence of environmental factors on the infectivity of Echinococcus multilocularis eggs. *Parasitology*, *110*(1), 79–86. https://doi.org/10.1017/s0031182000081075

Wachira, T. M., Macpherson, C. N., & Gathuma, J. M. (1991). Release and survival of Echinococcus eggs in different environments in Turkana, and their possible impact on the incidence of hydatidosis in man and livestock. *Journal of Helminthology*, *65*(1), 55–61. https://doi.org/10.1017/s0022149x00010440

Wang, D. M., He, R. F., GongSang, Q. Z., Xiao, D., SuoLang, W. J., Xue, L., et al. (2018). Prevalence of echinococcosis in Nyingchi City. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 75–79.

Wang, G. Q. (2016). *Epidemiological survey on echinococcosis in China*. Shanghai Scientific & Technical Publishers.

Wang, J., & Xu, C. (2017). Geodetector: Principle and prospective. *Acta Geographica Sinica*, *72*(1), 116–134. https://doi.org/10.11821/dlxb201701010

Wang, J. F., Li, X. H., Christakos, G., Liao, Y. L., Zhang, T., Gu, X., & Zheng, X. Y. (2010). Geographical detectors-based health risk assessment and its application in the neural tube defects study of the Heshun region, China. *International Journal of Geographical Information Science*, *24*(1), 107–127. https://doi.org/10.1080/13658810802443457

WHO. (2021). Echinococcosis. Retrieved from https://www.who.int/news-room/fact-sheets/detail/echinococcosis

Wood, S. N. (2017). Chapter 4: Introducing GAMs. In *Generalized additive models: An introduction with R* (2nd ed., pp. 161–182). Chapman and Hall/CRC.

Wu, W. P., Wang, H., Wang, Q., Zhou, X. N., Wang, L. Y., Zheng, C. J., et al. (2018). A nationwide sampling survey on echinococcosis in China during 2012–2016. *Chinese Journal of Parasitology & Parasitic Diseases*, *36*(1), 1–14.

Wu, X., Lu, Y., Zhou, S., Chen, L., & Xu, B. (2016). Impact of climate change on human infectious diseases: Empirical evidence and human adaptation. *Environment International*, *86*, 14–23. https://doi.org/10.1016/j.envint.2015.09.007

Yin, J., Gongsang, Q., Wang, L., Li, C., & Wu, X. (2020). Identification of vulnerable populations and knowledge, attitude, and practice analysis of echinococcosis in Tibet Autonomous Region of China. *Environmental Research*, *190*, 110061. https://doi.org/10.1016/j.envres.2020.110061

Yin, J., Wu, X. X., Han, J. T., & Torgerson, P. R. (2023). The impact of natural environment on human alveolar echinococcosis: A township-level modeling study in Qinghai-Tibet Plateau. *Science of The Total Environment*, *856*, 159085. https://doi.org/10.1016/j.scitotenv.2022.159085

Yin, J., Wu, X. X., Li, C. L., Han, J. T., & Xiang, H. X. (2022). The impact of environmental factors on human echinococcosis epidemics: Spatial modelling and risk prediction. *Parasites & Vectors*, *15*(1), 47. https://doi.org/10.1186/s13071-022-05169-y

Yu, Q., Xiao, N., Han, S., Tian, T., & Zhou, X. N. (2020). Progress on the national echinococcosis control programme in China: Analysis of humans and dogs population intervention during 2004–2014. *Infectious Disease of Poverty*, *9*(1), 137. https://doi.org/10.1186/s40249-020-00747-7

Yuan, R., Wu, H., Zeng, H., Liu, P., Xu, Q., Gao, L., et al. (2017). Prevalence of and risk factors for cystic echinococcosis among herding families in five provinces in western China: A cross-sectional study. *Oncotarget*, *8*(53), 91568–91576. https://doi.org/10.18632/oncotarget.21229

Zeng, X. M., Guan, Y. Y., Wu, W. P., Wang, L. Y., Cai, H. X., Fang, Q., et al. (2020). Analysis of factors influencing cystic echinococcosis in Northwest non-Qinghai Tibetan Plateau regions of China. *The American Journal of Tropical Medicine and Hygiene*, *102*(3), 567–573. https://doi.org/10.4269/ajtmh.18-0703

Zhang, W., Zhang, Z., Wu, W., Shi, B., Li, J., Zhou, X., et al. (2015). Epidemiology and control of echinococcosis in central Asia, with particular reference to the People's Republic of China. *Acta Tropica*, *141*, 235–243. https://doi.org/10.1016/-j.actatropica.2014.03.014

Zhou, X. N. (2009). *Parasitic zoonosis*. People's Medical Publishing House.