

Biotic factors limit the invasion of the plague pathogen (*Yersinia pestis*) in novel geographical settings

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Abstract

Aim: The distribution of *Yersinia pestis*, the pathogen that causes plague in humans, is reliant upon transmission between host species; however, the degree to which host species distributions dictate the distribution of *Y. pestis*, compared with limitations imposed by the environmental niche of *Y. pestis* per se, is debated. We test whether the present-day environmental niche of *Y. pestis* differs between its native range and an invaded range and whether biotic factors (host distributions) can explain observed discrepancies.

Location: North America and Central Asia.

Major taxa studied: *Yersinia pestis*.

Methods: We use environmental niche models to determine whether the current climatic niche of *Y. pestis* differs between its native range in Asia and its invaded range in North America. We then test whether the inclusion of information on the distribution of host species improves the ability of models to capture the North American niche. We use geographical null models to guard against spurious correlations arising from spatially autocorrelated occurrence points.

Results: The current climatic niche of *Y. pestis* differs between its native and invaded regions. The Asian niche overpredicted the distribution of *Y. pestis* across North America. Including biotic factors along with the native climatic niche increased niche overlap between the native and invaded models, and models containing only biotic factors performed better than the native climatic niche alone. Geographical null models confirmed that the increased niche overlap through inclusion of biotic factors did not, with a couple of exceptions, arise solely from spatially autocorrelated occurrences.

Main conclusions: The current climatic niche in Central Asia differs from the current climatic niche in North America. Inclusion of biotic factors improved the fit of models to the *Y. pestis* distribution data in its invaded region better than climate variables alone. This highlights the importance of host species when investigating zoonotic disease introductions and suggests that climatic variables alone are insufficient to predict disease distribution in novel environments.

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KEYWORDS

biotic interactions, ecological niche model, invasion ecology, niche shift, null modelling, plague, *Yersinia pestis*, zoonotic disease

1 | INTRODUCTION

Yersinia pestis, the bacterial agent of plague, has caused three trans-continental pandemics, led to millions of human fatalities and repeatedly catalysed societal re-organization (Stenseth et al., 2008). However, its importance for human health is not only historical; a large epidemic occurred in Madagascar in late 2017, leading to nearly 2500 reported cases (Majumder et al., 2018). Given that all of the World Health Organization's top emergent disease are, like plague, zoonotic, or caused by spillover from animals (World Health Organization, 2015), it is important to understand what limits the geographical spread of pathogens, reservoirs and hosts outside periods of human epidemics. Ongoing climate change has led to multiple vector-borne diseases expanding their ranges or intensifying within their current distributions, with further changes expected. For example, malaria has moved into the East African highlands (Caminade et al., 2014), *Borrelia burgdorferi*, the bacterial agent of Lyme disease, is expanding northwards through Canada (Eisen et al., 2016), and plague is predicted to intensify in the Balkhash region of Kazakhstan (Kausrud et al., 2010).

Although the spread of plague and other zoonotic diseases through human populations depends on a range of epidemiological factors, predicting the likelihood or risk of these outbreaks requires an understanding of the geographical distribution of the pathogen. The presence of a pathogen does not guarantee that animal-to-human transmission will occur, whereas absence of the pathogen ensures that it will not (Messina et al., 2015). Like other zoonotic diseases, non-human plague maintenance is affected by climate across a range of spatial and temporal scales (Ben-Ari et al., 2011). However, its dynamics are not determined solely by direct effects of climate, but also depend on the dynamics of the pathogen, vectors and hosts, all of which might be affected by changing climate (Ben-Ari et al., 2011; Kausrud et al., 2007). The geographical distribution of *Y. pestis* might reflect both abiotic (e.g., climate) and biotic (e.g., host and vector species) interactions. Disentangling these pathogen–host–vector–climate relationships should improve predictions of the geographical spread of plague under future environmental change and shed light on the role of abiotic and biotic factors in determining species distributions, a long-standing and fundamental goal of biogeography (Blois et al., 2013; Hutchinson, 1957; Soberón, 2007).

The fact that *Y. pestis* relies on both enzootic (maintenance) and epizootic (amplifying) hosts for transmission and expansion has led to two competing hypotheses to describe the distribution of *Y. pestis* (Maher et al., 2010). The host niche hypothesis (HNH) suggests that the distribution of *Y. pestis* is determined by the combined niches of host species, which define the limits of the host range. In contrast,

the plague niche hypothesis (PNH), proposes that the niche is independent of host niches. According to this hypothesis, the distribution of *Y. pestis* will be limited by environmental conditions (e.g., climate) and will fill only a subset of host ranges. By comparing the total range of host species with the plague-infected range of host species across North America, Maher et al. (2010) found evidence for the PNH over the HNH. However, recent work using environmental niche modelling has contradicted this finding, suggesting that the strongest predictor of *Y. pestis* distribution across North America is the distribution of *Peromyscus maniculatus* (the deer mouse), consistent with the HNH (Walsh & Haseeb, 2015). Further recent work suggests that *P. maniculatus* is not even a maintenance species and might be infected with *Y. pestis* only as a result of an endemic period within other hosts (Danforth et al., 2018). Thus, there is no consensus on whether the current distribution of *Y. pestis* is determined primarily by hosts or by its own environmental niche. An unexplored possibility is that the hypotheses are not mutually exclusive and that both contribute to the distributional limits of *Y. pestis*. Given the large range of hosts and vectors that are susceptible to *Y. pestis* (Gage & Kosoy, 2005) and its near-global distribution (Stenseth et al., 2008), it is also plausible that the relative importance of different factors might vary geographically and with spatial and temporal scales (Ben-Ari et al., 2011).

Yersinia pestis evolved in Asia from *Yersinia pseudotuberculosis* c. 6000 yr BP (Rascovan et al., 2019). It is enzootic within several host populations across Asia and has caused plague epidemics in humans since ≥ 5000 yr BP (Spyrou et al., 2018). *Yersinia pestis* was introduced to the west coast of the USA at the beginning of the 20th century and rapidly spread eastwards (Adjemian et al., 2007). Several human epidemics were recorded before 1925 CE, and, simultaneously, *Y. pestis* established itself as a permanent presence within rodent host species (Gage & Kosoy, 2005). Plague initially spread at rates of ≤ 87 km/year, but expansion halted at the 103rd Meridian in the 1950s and has remained static since (Adjemian et al., 2007).

In this paper, we test whether the climatic niche of *Y. pestis* differs between its native and invaded regions and, if so, whether this difference can be explained by biotic factors. We use information on the current climatic niche of *Y. pestis* in its native (Asia) and invaded (North America) ranges to test whether the native and invaded niches differ, which is common in non-disease cross-continental invasions (Early & Sax, 2014), and to evaluate whether incorporating information on putative host distributions can improve predictions of the American range. We find evidence that host distributions limit the North American distribution of plague and that biotic factors are key, both independently and with abiotic factors, to explain the distributional limits of *Y. pestis* in North America.

2 | MATERIALS AND METHODS

2.1 | Data

2.1.1 | *Yersinia pestis* localities

Yersinia pestis occurrence records were extracted from two sources: Walsh and Haseeb (2015) for the North America data, and Cui et al. (2013) for the Asian data. The sample sizes of the *Y. pestis* occurrence data across Asia and North America were 68 and 62, respectively. The American data include all cases of *Y. pestis* infection in animals across the USA from 2000 to 2015, reported through the Program for Monitoring Emerging Diseases (ProMED), to a spatial resolution of 1 km². It is unlikely that all plague surveillance data for this period will have been reported through ProMed; hence, our data can represent only a subset of *Y. pestis* occurrences for this time. Further to this, the North American data also include occurrences from domestic animals which, although not responsible for plague maintenance in the wild, function as a proxy for local plague infection owing to the much higher sampling effort expended upon domesticated animals. Most of the Central Asian data were from China between 1952 and 2006. Once again, these data represent only a subset of plague occurrences during this time and were selected initially to represent genetic diversity of *Y. pestis* (Cui et al., 2013). All data were from hosts or vectors, with human cases removed. These datasets represent all the *Y. pestis* occurrences that we could access, and we make the assumption that they are representative of the *Y. pestis* niche. We consider the potential for bias in these data to affect our conclusions in the Discussion.

2.1.2 | Host species localities

We selected 15 North America rodent species based on previous evidence suggesting that they might influence the North American distribution of *Y. pestis* (Walsh & Haseeb, 2015) or co-occur commonly with *Y. pestis* as a reservoir species (Maher et al., 2010; Mahmoudi et al., 2021). Six of the species (*P. maniculatus*, *Otospermophilus beecheyi*, *Cynomys gunnisoni*, *Neotamias townsendii*, *Otospermophilus variegatus* and *Cynomys ludovicianus*) were the most commonly sampled rodent species co-occurring with *Y. pestis* (Maher et al., 2010) and have each been hypothesized as species regionally or continentally important to *Y. pestis* distribution (Hubbart et al., 2011; Mahmoudi et al., 2021; Pauli et al., 2006). The nine further species (*Cynomys leucurus*, *Cynomys parvidens*, *Sciurus aberti*, *Sciurus griseus*, *Sciurus niger*, *Neotamias amoenus*, *Neotamias dorsalis*, *Neotamias minimus* and *Neotamias umbrinus*) are all known reservoir species (Lowell et al., 2009; Mahmoudi et al., 2021). Modelled distributions of these species are shown in the Supporting Information (Appendix S1, Figure S1.1). These are all either enzootic (maintenance), epizootic (amplifying) or resistant (*P. maniculatus* only) hosts (Gage & Kosoy, 2005). We do not

consider predators and scavengers because they are not considered a primary driver or maintainer of *Y. pestis* (Savage et al., 2011), although more research in this area is required (Salkeld & Stapp, 2006).

Species occurrence data for the 15 host species were obtained from the Global Biodiversity Information Facility (GBIF; GBIF, 2019) and initially cleaned by removal of not applicable values and duplicates. Probable erroneous localities were identified and removed through visual examination and comparison with previous literature for the species *N. amoenus*, *S. griseus*, *O. beecheyi*, *N. umbrinus*, *C. gunnisoni*, *C. ludovicianus*, *C. leucurus*, *N. townsendii* and *N. minimus* (Braun et al., 2011; Carraway & Verts, 1994; Miller & Cully Jr, 2001; Pizzimenti & Hoffmann, 1973; Smith et al., 2016; Sutton, 1992; Verts & Carraway, 2001; Supporting Information Appendix S1, Figure S1.2). Owing to computational constraints, we limited the number of occurrences of each individual species to 1500. Following Boria and Blois (2018), we randomly selected 1500 occurrences from across its range without replacement for subsequent modelling. Treating each species separately, we thinned occurrence data such that occurrences were separated by ≥ 10 km using the “*spThin*” package (Aiello-Lammens et al., 2015) to increase computation speed while also addressing potential spatial sampling biases.

2.1.3 | Climate data

We used the 30 arc-sec WorldClim dataset aggregated to 10 km resolution (Hijmans et al., 2005) to quantify climatic variation across North America (longitude -134.5 to -4.0° , latitude 26.4 – 52.5°) and Asia (longitude 60.0 – 144.3° , latitude 7.1 – 54.3°). This resource was constructed from data from the period 1950–2000 and therefore represents a time-averaged estimate of climate variables. We selected eight WorldClim climate variables to use by identifying uncorrelated climatic variables across the research areas (Asia and North America). To avoid the inclusion of overly correlated variables, we ran pairwise correlation analysis on all climate variables across both regions. Variables were retained if all pairwise correlation values were $< .8$ in both the North American and Asian regions. We also included precipitation of the driest quarter because previous research has suggested a strong link between this variable and *Y. pestis* maintenance in host species from varying localities (Ben-Ari et al., 2010; Holt et al., 2009; Kausrud et al., 2010; Neerincx et al., 2008). We validated our variable selection through a literature review of biologically significant variables in previous studies of climatic influence on *Y. pestis* (Ben-Ari et al., 2010; Holt et al., 2009; Kausrud et al., 2010; Neerincx et al., 2008; Walsh & Haseeb, 2015). The selected variables were as follows: mean diurnal range (BIO2), isothermality (BIO3), mean temperature of wettest quarter (BIO8), mean temperature of driest quarter (BIO9), precipitation seasonality (BIO15), precipitation of driest quarter (BIO17), precipitation of warmest quarter (BIO18) and precipitation of coldest quarter (BIO19). All data cleaning and analysis were completed in the R statistical programming environment (R Core Team, 2013).

2.2 | Niche modelling

To quantify the climatic niche of *Y. pestis* in its native (Asia) and invaded (North America) ranges, we fitted environmental niche models (ENMs) in each region using the MAXENT algorithm (Phillips et al., 2006). For each model, we used ENMEVAL (Muscarella et al., 2014) to tune the regularization multiplier and feature classes, with the linear, quadratic, hinge, threshold and product feature classes included and the regularization multiplier ranging from .5 to 4 in increments of .5. We selected the “best” model for each region by sorting on lowest omission rate, then selecting the model with the lowest Akaike information criterion corrected for small sample size (AICc) (Galante et al., 2018). We used the spatially structured partitioning method “checkerboard2” from the “ENMeval” package, which splits the data into four bins based on a nested checkerboard structure; models are then run iteratively using $k - 1$ bins for training (where k is the total number of bins), with the remaining one for testing. We found that the “best” model varied when the optimization was repeated, owing to variation in the random selection and subsequent partitioning of the background data; therefore, this process was repeated 50 times, and the most commonly selected “best” model was used subsequently. This method enabled us to ensure that the regularization multiplier and feature class selected were suited to the occurrence data for each species and were not products of background data selection and partitioning. We used the same approach as that described above to model the potential distributions in the USA of the 15 putative hosts of *Y. pestis* for subsequent hypothesis testing (model projections and settings are shown in Supporting Information Appendix S1, Table S1.1; Figure S1.1).

2.3 | Hypothesis testing

2.3.1 | Native and invaded niche similarity

We projected the Asian model (Table 1) into North America and calculated the niche overlap between the projected Asian model (Asian-proj; Table 1) and the North American model (N.am-obs; Table 1) using Schoener's D . We used the “identity test” and “background test” through “ENMtools” (Warren et al., 2008, 2010) to test the null hypotheses that the Asian and North American climatic niches were identical (identity test) and that niches do not differ more than expected by chance given environmental differences between regions (background test). We also completed multivariate environmental similarity surfaces (MESS) analysis to identify areas of non-analogous climate in North America in comparison to the Asian occurrences.

2.3.2 | Biotic influences on the invaded niche

We tested the extent to which potential host species distributions might be responsible for differences in the climatic niche of *Y. pestis*

in North America (see Results) by comparing the overlap between the N.am-obs model (Table 1) and a series of ENMs of *Y. pestis* in North America that used the modelled distributions of putative hosts and the projected Asian climatic niche as predictors (Table 1). If host distributions are responsible for the observed differing niche in *Y. pestis*, we expect higher overlap between the N.am-obs model and models using hosts as predictors than between the N.am-obs model and an ENM that includes only the Asian-proj model as a predictor. Projecting the Asian niche into North America and using this as a predictor in an ENM of North American *Y. pestis* allowed us to evaluate the overlap between the North American and Asian niches in a manner that is consistent with how we measured overlap from models using host species distributions; this also allowed us to include both the Asian niche and host distributions within the same model. If host distributions are not responsible for the climatic niche difference in North America, we would not expect greater overlap between the N.am-obs and models using host distributions than with models using only the Asian niche projection. We fitted models including all host species, in addition to models including only the distribution of *P. maniculatus* based on findings by Maher et al. (2010). We also fitted models including 14 hosts and excluding *P. maniculatus*. Details on the predictors included in each model are given in Table 1.

We fitted ENMs of *Y. pestis* in North America using the projected Asian niche and host distributions as predictors, following the approach outlined above to select the regularization multiplier and feature classes. We also repeated our analysis using the most commonly selected regularization multiplier and feature class across all models (linear and quadratic and a regularization multiplier of .5) to determine to what degree our results are a product of varying model settings. To train each model, we used spatially structured partitioning methods (checkerboard2) to split the occurrence and background data into training and test sets. This partitioning resulted in very slightly different model parameters (see Table 1) in each run, owing to the variation in background localities and partitioning. To ensure that this did not influence our subsequent analyses, we re-selected and partitioned the background data 100 times and carried out all downstream analyses on these 100 model sets. After model fitting, we computed the overlap of each Asian niche and/or host distribution model (Table 1) with the N.am-obs model using Schoener's D . We also computed the niche overlap of Asian niche and/or host distribution models using thresholded projections, using the specificity–sensitivity threshold (the threshold at which model sensitivity and specificity are highest) applied to confirm that our results were not an artefact of the continuous MAXENT projections (Supporting Information Appendix S1, Figure S1.3).

2.3.3 | Geographical null modelling

Spatial autocorrelation of species' occurrences and environmental variables can create spurious associations in ENMs (Dormann et al., 2007). Thus, relationships between *Y. pestis* occurrences and

TABLE 1 Naming protocol and performance for models used to predict the North American niche of *Yersinia pestis*

Model name	Predictors	Mean AUC	SD
Asian model	Asian WorldClim variables at 10 km resolution (BIO2, BIO3, BIO8, BIO9, BIO15, BIO17, BIO18 and BIO19)	.709	-
N.am-obs	North American WorldClim variables at 10 km resolution (BIO2, BIO3, BIO8, BIO9, BIO15, BIO17, BIO18 and BIO19)	.914	.00276
Asian-proj	Model fit in Asia projected into North America	.798	.00334
<i>P.man</i> -only	<i>Peromyscus maniculatus</i> suitability in North America	.831	.00277
Multi-host	<i>Peromyscus maniculatus</i> , <i>Otospermophilus beecheyi</i> , <i>Cynomys gunnisoni</i> , <i>Neotamias townsendii</i> , <i>Otospermophilus variegatus</i> , <i>Cynomys ludovicianus</i> , <i>Cynomys leucurus</i> , <i>Cynomys parvidens</i> , <i>Sciurus aberti</i> , <i>Sciurus griseus</i> , <i>Sciurus niger</i> , <i>Neotamias amoenus</i> , <i>Neotamias dorsalis</i> , <i>Neotamias minimus</i> and <i>Neotamias umbrinus</i> distributions	.937	.00220
Multi-host (limited selection)	<i>Peromyscus maniculatus</i> , <i>O. beecheyi</i> , <i>C. gunnisoni</i> , <i>C. ludovicianus</i> , <i>N. townsendii</i> and <i>O. variegatus</i> distributions	.931	.00162
Asia+ <i>P.man</i>	Projected Asian model and the projected <i>P. maniculatus</i> distribution	.897	.00223
Asia+Multi-host	Projected Asian model and the projected <i>P. maniculatus</i> , <i>O. beecheyi</i> , <i>C. gunnisoni</i> , <i>N. townsendii</i> , <i>O. variegatus</i> , <i>C. ludovicianus</i> , <i>C. leucurus</i> , <i>C. parvidens</i> , <i>S. aberti</i> , <i>S. griseus</i> , <i>S. niger</i> , <i>N. amoenus</i> , <i>N. dorsalis</i> , <i>N. minimus</i> and <i>N. umbrinus</i> distributions	.941	.00307
Multi-host, no <i>P.man</i>	<i>O. beecheyi</i> , <i>C. gunnisoni</i> , <i>N. townsendii</i> , <i>O. variegatus</i> , <i>C. ludovicianus</i> , <i>C. leucurus</i> , <i>C. parvidens</i> , <i>S. aberti</i> , <i>S. griseus</i> , <i>S. niger</i> , <i>N. amoenus</i> , <i>N. dorsalis</i> , <i>N. minimus</i> and <i>N. umbrinus</i> distributions	.939	.00192
Asia+Multi-host, no <i>P.man</i>	Projected Asian model and the projected <i>O. beecheyi</i> , <i>C. gunnisoni</i> , <i>N. townsendii</i> , <i>O. variegatus</i> , <i>C. ludovicianus</i> , <i>C. leucurus</i> , <i>C. parvidens</i> , <i>S. aberti</i> , <i>S. griseus</i> , <i>S. niger</i> , <i>N. amoenus</i> , <i>N. dorsalis</i> , <i>N. minimus</i> and <i>N. umbrinus</i> distributions	.943	.00280

Note: Predictors included in each model are shown, along with the accuracy of each model, calculated as the area under the curve (AUC) of the receiver operating characteristic, using known occurrences of *Y. pestis* in North America. The mean AUC and SD are calculated from 100 replicates of each model.

host species' suitability maps could arise solely because both are spatially structured. It could be that any spatially structured predictor would have a significant effect on *Y. pestis* distribution and thus overlap, even in the absence of a functional relationship (e.g., Fourcade et al., 2018). To guard against this, we used a null modelling procedure. Following Beale et al. (2008), Algar et al. (2013) and Nunes and Pearson (2017), we generated a set of null occurrences for each host species with the same number of points and the same degree of spatial clustering as the observed species, using the "fauxcurrence" package (v.1.1.0) in R (Osborne et al., 2021; for details on the null modelling algorithm, see Supporting Information Appendix S1). Our algorithm also preserved spatial clustering of interspecies centroid

distances to account for the fact that host species might be found in similar environments (see Supporting Information Appendix S1). We then modelled the null distribution of each host using MAXENT as described for real species and used these modelled distributions as predictors in models of *Y. pestis* occurrence. We then measured overlap with N.am-obs. This null overlap value describes the expected overlap if a series of spatially structured predictors, from anywhere in the study area, were used to predict the distribution of *Y. pestis*. We repeated this process 1000 times to obtain a null distribution of Schoener's *D* values for each model and compared the observed Schoener's *D* with this null distribution, computing two-tailed *p*-values.

3 | RESULTS

3.1 | Native and invaded niche similarity

The identity test (Supporting Information Appendix S1, Figure S1.4) found that there was significantly less overlap between the native and invaded niches of *Y. pestis* than expected under the null hypothesis of identical niches ($p = .01$). We also used the background test (Supporting Information Appendix S1, Figure S1.5), which suggested that the native and invaded niches were significantly less similar than expected given the geographical regions in which they reside ($p = .01$). In combination, these results suggest that the current native and invaded niches are non-identical and that the difference is not attributable purely to their differing geographical regions. We constructed and projected models in both regions to identify factors that contributed to this dissimilarity. Within Asia, the best-fitting MAXENT niche model for *Y. pestis* had an area under the curve (AUC) of the receiver operating characteristic of .709, whereas in North America (N.am-obs; Table 1) the equivalent model had a mean AUC of .914 (individual species models and North American settings are given in Supporting Information Appendix S1, Tables S1.1 and S1.2, respectively). The overlap between the native and invaded niches of *Y. pestis* had a Schoener's D value of .497. The Asian model AUC was close to the AUC value of .7 above which models are considered fair, and the model was also relatively simple owing to the singular linear feature. Our Asian data did not include any occurrences in south-eastern coastal China, and this area was thus poorly represented in the projected species distribution. Despite no occurrences in Kyrgyzstan and Kazakhstan, regions of permanent plague reservoirs (Kausrud et al., 2007), our model predicted the presence of plague in Kyrgyzstan and moderately in Kazakhstan, but did not include the Balkhash reservoir region (Kausrud et al., 2007).

The N.am-obs model showed the niche of *Y. pestis* generally falling into two regions: California, where *Y. pestis* was introduced, and the eastern Rocky Mountains up the length of the USA, through New Mexico, Colorado, Wyoming and Montana. Our model matched previous modelled distributions of plague in California in addition to records of *Y. pestis* within human populations across a similar period of sampling (Holt et al., 2009; Kugeler et al., 2015). The differences between the native and invaded niches were highlighted through projection of both niches into the alternative region (Figure 1a–d). The North American model represented the Asian distribution poorly, primarily predicting presence of *Y. pestis* adjacent to the Quighai–Tibet Plateaux, which was probably attributable to the elevation of North American occurrence points within the Rockies. Meanwhile, the Asian model substantially overpredicted the distribution of *Y. pestis* in North America, with the largest overprediction into midwestern grasslands (Figure 1c,e). The Asian model performed better when predicting the distribution in California, but consistently overpredicted elsewhere. MESS analysis suggested that non-analogous climate in North America (with regard to Asian occurrences) was

focused on the north western coast, whereas California and the central belt of North America where the Asian model predicted distribution (Figure 1c) was an area of more analogous climate (Supporting Information Appendix S1, Figure S1.6).

3.2 | Biotic influences on the invaded niche

To determine whether host distributions can explain difference in niches of *Y. pestis* in North America, we first projected the Asian-fitted model into North American climate space and used the resulting suitability map as the only predictor to fit a MAXENT model to North American *Y. pestis* occurrences. This model (Asian-proj; Table 1) had an AUC of .798, which is above the .7 threshold that indicates a “good” model. This model (Asian-proj) and the North American model (N.am-obs; Table 1) showed a low niche overlap (Figure 1e) in geographical space (Schoener's $D = .497$). Next, to test whether putative host species can explain the North American distribution of *Y. pestis*, we used the suitability maps of rodent species as predictors in a series of MAXENT models fitted to North American occurrences of *Y. pestis* (Figures 2 and 3; Table 1; Supporting Information Appendix S1, Tables S1.2 and S1.3). All models including hosts achieved a greater niche overlap than the Asian projection alone (Figures 1e and 2). The model containing only *P. maniculatus* performed moderately better (Schoener's $D = .592$) than the Asian projection alone (Figure 2a), and the model containing all putative host species performed better again and produced the greatest niche overlap of any of the models (Schoener's $D = .722$; Figure 2b). The second highest niche overlap was achieved by the model containing the Asian projection and the *P. maniculatus* model (Figure 2c); however, we urge caution in interpreting these results by suggesting that *P. maniculatus* is a key host species because it is possible that its higher modelled suitability in the western USA, where the model tends to overpredict (Figure 2a), reflects sampling density, given that *P. maniculatus* has a broad North American range. In contrast, all other models achieved greater niche overlap and showed less overprediction to the west (Figure 2b–f). The model containing all host species, which showed the greatest niche overlap values (Figure 2b), performed well in the Californian region and the southern Rockies, with the largest area of underprediction in the northern Rockies (Montana and Wyoming). The models that contained both the Asian projection and one or more hosts performed marginally worse than the equivalent models with only hosts included. When we held model settings consistent across all models (Supporting Information Appendix S1, Figures S1.7 and S1.8), we found that our key result, that including host distributions improved niche overlap, remained. However, there were minor differences in terms of which host model performed best. The Asia + *P. maniculatus* model showed the greatest niche overlap, followed by the multi-host model with a limited selection of host species. Although we think that the optimized models are most likely to show the most reliable results, our major findings are robust to details in model selection.

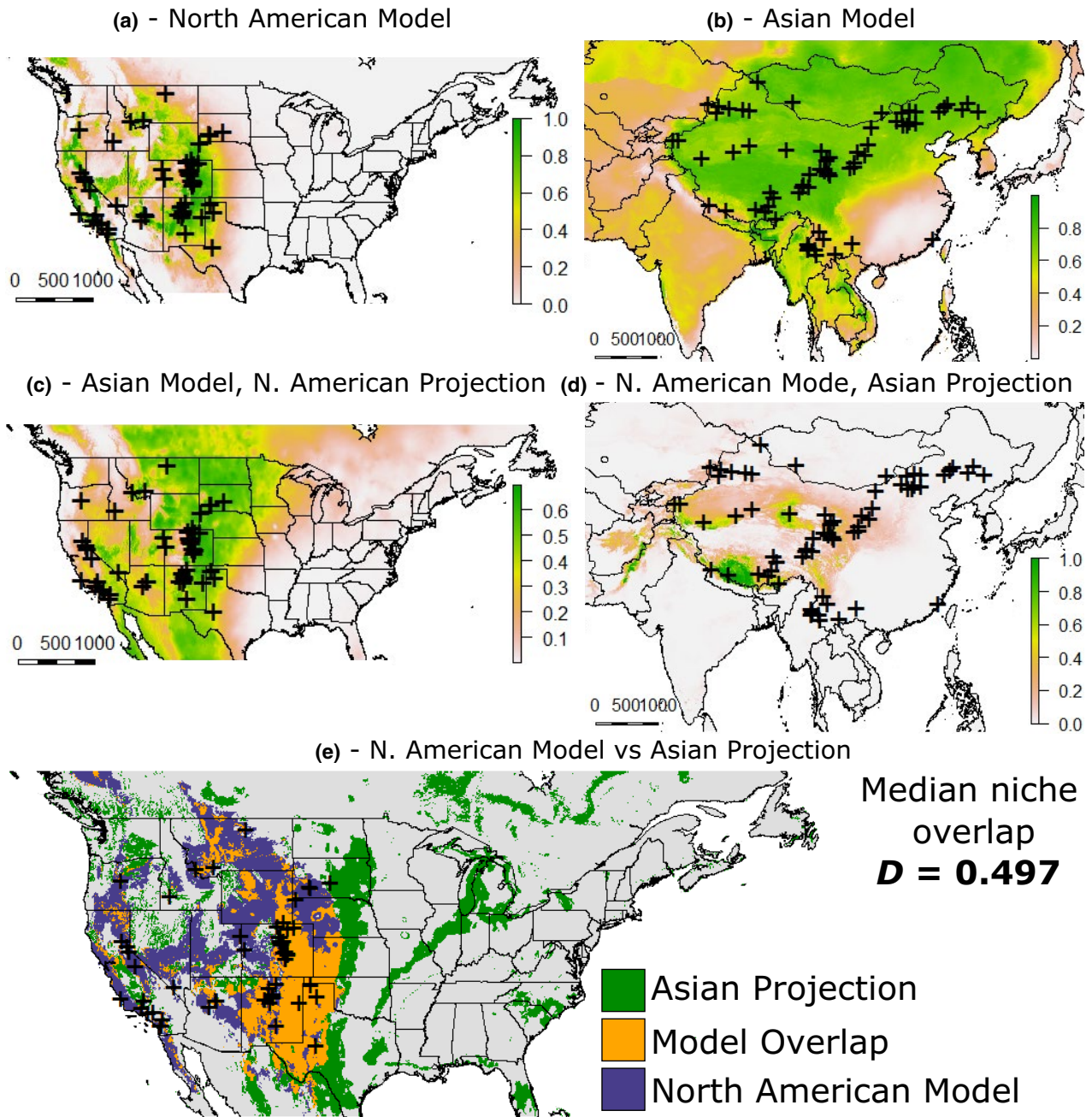


FIGURE 1 Comparison of *Yersinia pestis* native and invaded niches. (a–d) *Yersinia pestis* distribution models built within: (a) the invaded North American region, (b) the native Asian region and (c, d) both models projected into the alternative region. (e) Differing projected distribution of *Y. pestis* across North America using a model fitted in North America and a model fitted in Asia and projected to North America. The Asian projection (Asia-proj in Table 1) overpredicts *Y. pestis* to the east of the North American model. For visualization purposes, the figure uses the spec_sens threshold, which is the threshold at which sensitivity and specificity are highest. The same pattern was observed using other threshold methods; however, spec_sens is one of the more conservative visualizations (Supporting Information Appendix S1, Figure S1.14). Mean niche overlap values calculated using Schoener's D (Schoener, 1968) were derived from 100 replicates of the models with a random selection of background points leading to slight variation in predicted distribution. A scale bar (in kilometres) is provided (a–d)

3.3 | Geographical null modelling

Niche models based on null occurrences had lower AUC values than models based on real data (Supporting Information Appendix S1, Figure S1.9), suggesting that our model fits are not solely an artefact of spatially clustered occurrence data. Moreover, most of

our models had significantly greater overlap with the N.am-obs model than expected from the null expectation (Figure 4). The two exceptions were the Asia+Multi-host model ($p = .993$; Figure 4c) and the Asia+Multi-host model excluding *P. maniculatus* ($p = .683$; Figure 4f). These results suggest that even randomly placed sets of occurrence points can interact with the Asian-proj to produce

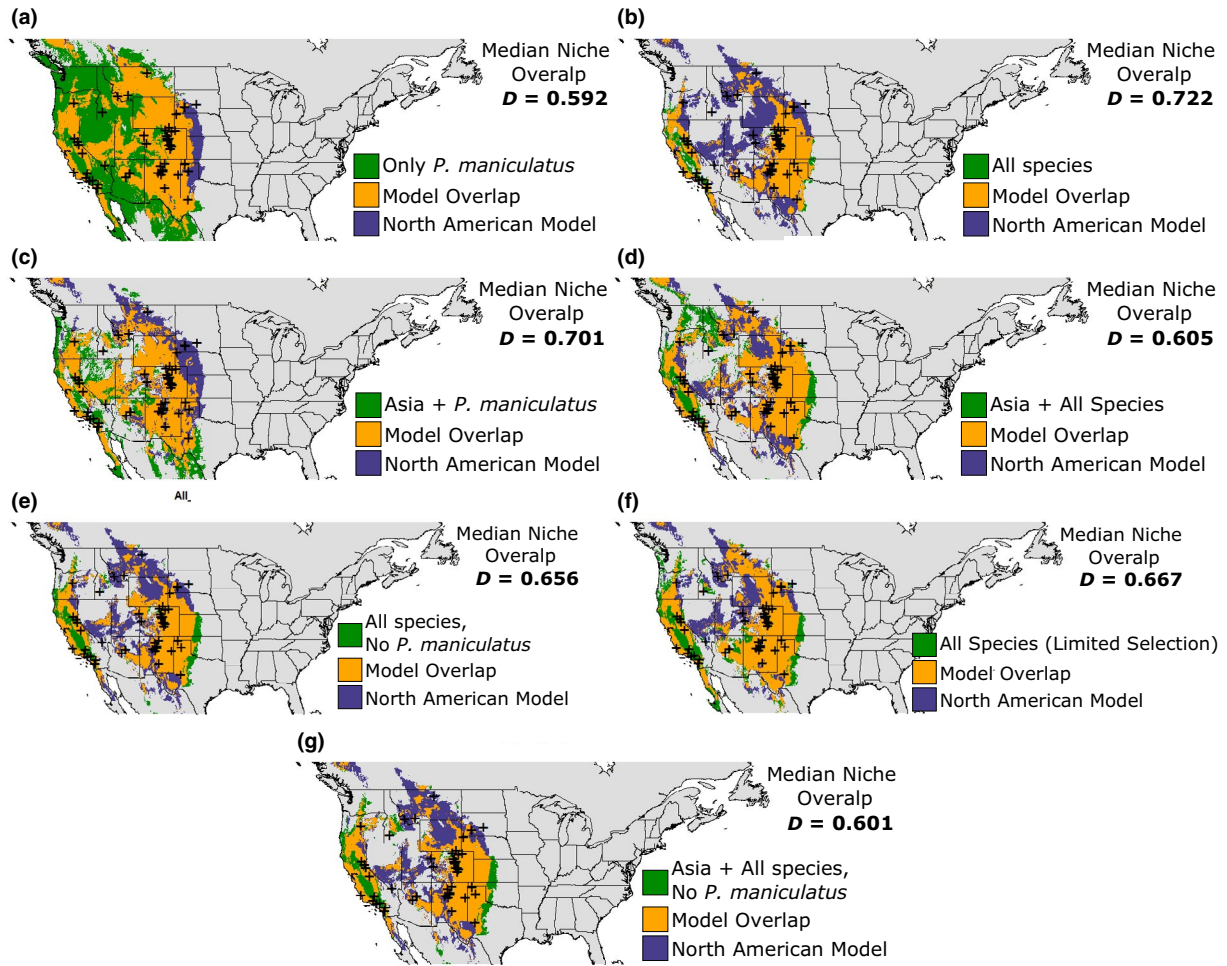


FIGURE 2 Differing projected distribution of *Yersinia pestis* across North America using a model fitted in North America and: (a) a model with only *Peromyscus maniculatus* distribution included (*P.man* only in Table 1); (b) a model with 15 rodent species (Multi-host in Table 1); (c) a model fitted in Asia and projected to North America with *P. maniculatus* distribution included (Asia+*P.man* in Table 1); (d) a model fitted in Asia and projected to North America with 15 rodent species (Asia+Multi-host in Table 1); (e) a model built with a limited selection of only six species based on co-occurrences with *Y. pestis*; (f) a model without *P. maniculatus* but including the 14 further selected host rodent species (Multi-host, no *P.man* in Table 1); and (g) a model fitted in Asia and projected to North America without *P. maniculatus* but including the 14 further host rodent species (Asia+Multi-host, no *P.man* in Table 1)

relatively high apparent overlap. However, the overlap (Schoener's D) of these models was lower than that when the multi-hosts model was used alone, a result which was significantly different from the null expectation, indicating that the increase in overlap attributable to host distributions (from either the complete set or the limited set) is not an artefact of spatially autocorrelated occurrences. Using consistent model settings, we saw fewer results retain significance (Supporting Information Appendix S1, Figure S1.8), which is likely to reflect the poorer performance of these sub-optimized models but highlights the importance of considering how model selection and parameterization influence the outcome of ENMs.

4 | DISCUSSION

We found that the current climate niche of *Y. pestis* in Central Asia differs from the climate niche in North America. Despite the

presence of suitable climate space, *Y. pestis* has failed to fill its potential range in central North America. Incorporating information on mammalian host distributions greatly improved concordance between the observed and predicted range edge in North America. This indicates a role for biotic factors in limiting the North American distribution of *Y. pestis*, at least at broad continental scales, although the same might not be true at more regional scales (Ben-Ari et al., 2011; Danforth et al., 2018). Including information on the native climatic niche of plague had mixed impacts on our models, improving niche overlap in one of the models but reducing the rest, suggesting that although both climatic and biotic factors might interact to limit the spread of the plague pathogen in North America, biotic factors appear to have the larger impact. Further effects of host distributions might be revealed by conducting targeted regional studies. Consideration of vectors and their distributional limits in addition to the impact of further biotic factors, such as soil and vegetation variables, will provide

Niche Overlap, Schoener's D

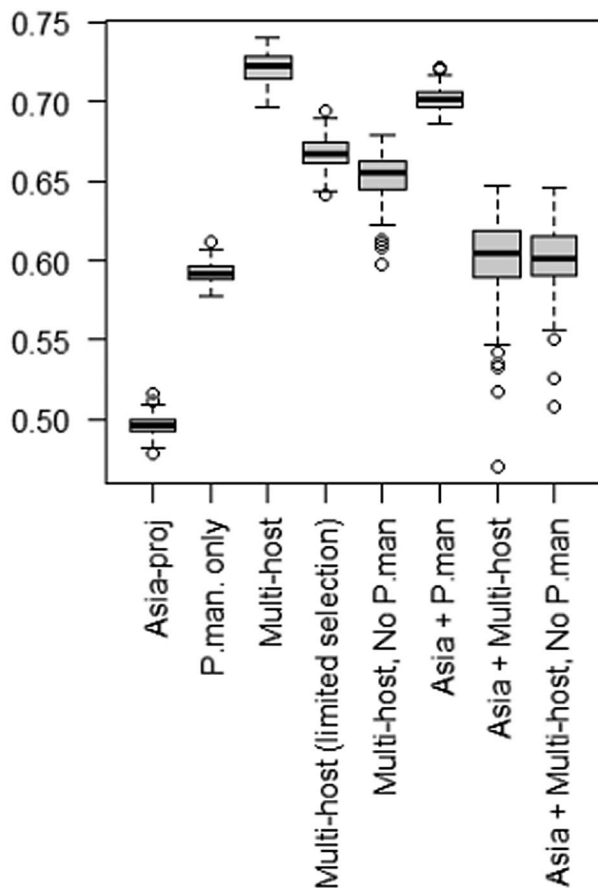


FIGURE 3 Niche overlap values of the observed distribution models. Boxplots of the niche overlap values (Schoener's D) produced through the 100 replicates of each niche model. Model descriptions are provided in Table 1. Higher values of Schoener's D indicate greater niche overlap

a more complete picture of the North American *Y. pestis* invasion (Adjemian et al., 2006).

Our models allowed us to determine the impact of a subset of putative host distributions on *Y. pestis* distribution and evaluate competing hypotheses [plague niche (PNH) and host niche (HNN)] for the dominant factors limiting the niche of *Y. pestis* in North America. Models using only host distributions (Figure 2a,b) outperformed models based on the Asian climatic niche, suggesting that biotic factors are responsible for the discrepancy between the Asian and North American niches, as proposed by the HNN. Response curves from MAXENT models showed positive relationships linking host and *Y. pestis* occurrences for 12 of the 15 selected species (Supporting Information Appendix S1, Figure S1.10). This suggests that the three species that showed negative response curves, *N. townsendii*, *C. parvidens* and *S. niger*, might not represent host species that drive *Y. pestis* infection at a continental scale. A further species, *S. griseus*, had a permutation importance of zero in the Asia+Multi-host model. Each of these species might still be important regionally or across a subset of their range. Removal of these species had mixed impact on

empirical and null models, suggesting that further work is required to determine their impact on *Y. pestis* distribution at a continental scale (Supporting Information Appendix S1, Figures S1.11–S1.13; Table S1.3). Overall, we found that the combination of host species that best explained *Y. pestis* distribution was sensitive to the model settings used (compare Figure 3 and Supporting Information Appendix S1, Figure S1.7), highlighting the importance of careful calibration of environmental niche models.

The role of *P. maniculatus* as a host species of *Y. pestis* is debated, with recent work suggesting that it might represent a spillover host and not drive transmission, at least within California (Danforth et al., 2018). Our null modelling results (Figure 4) showed that models with *P. maniculatus* as the only variable or as one of two variables showed significantly greater niche overlap than our spatial nulls. Thus, our results, like those of Walsh and Haseeb (2015), cannot eliminate *P. maniculatus* as an important North American host species, nor can they confirm that it drives transmission. Given regional evidence suggesting that *P. maniculatus* might represent only an overflow host in some regions (Danforth et al., 2018), we urge caution in the use of *P. maniculatus* as a driver of *Y. pestis* distribution, especially given that with our optimized models, including information on additional hosts provided an improvement in overlap with the North American distribution of *Y. pestis*.

The constraining effects of host distributions on the niche of *Y. pestis* in North America mean that it is in disequilibrium with climate (*sensu* Araújo et al., 2005) in its invaded range. Given that host species limit the niche of *Y. pestis* in North America, it seems likely that hosts also constrain the climatic niche of *Y. pestis* within Asia, meaning that it is probably in disequilibrium with climate in both its invaded and native ranges, a situation that might be common for invasive species more broadly (Early & Sax, 2014; Guisan et al., 2014). Conceptually, the difference in the current climatic niches of *Y. pestis* in Asia and North America, therefore, reflects the relaxation of biotic constraints as the pathogen is transmitted from its native region, only to be replaced by novel biotic constraints in its invaded range. However, the constraints on the native range have occurred in a different part of climate space from those in the invaded range, leading to an alteration in realized niche, driven by the change in host species from its native to invaded region. Another possibility is that the Asian climatic niche has expanded, owing to either evolutionary change or relaxation of biotic constraints, since the introduction of *Y. pestis* to the Americas, creating the appearance of a reduction in niche width in the Americas. Although we cannot discount this possibility, to explain our results it would have had to occur in such a way as to align coincidentally with the distributions of known host species; hence, we think limitation by biotic factors in North America is a more likely explanation. Given that both the native and invaded niches incorporate biotic factors, the degree of niche underfilling (Guisan et al., 2014; Strubbe et al., 2013) in North America is likely to be greater than we detected here, because the native niche model is likely to have failed to capture fundamental niche limits.

Could differences observed between the current native and invaded niches reflect limiting factors other than host distributions

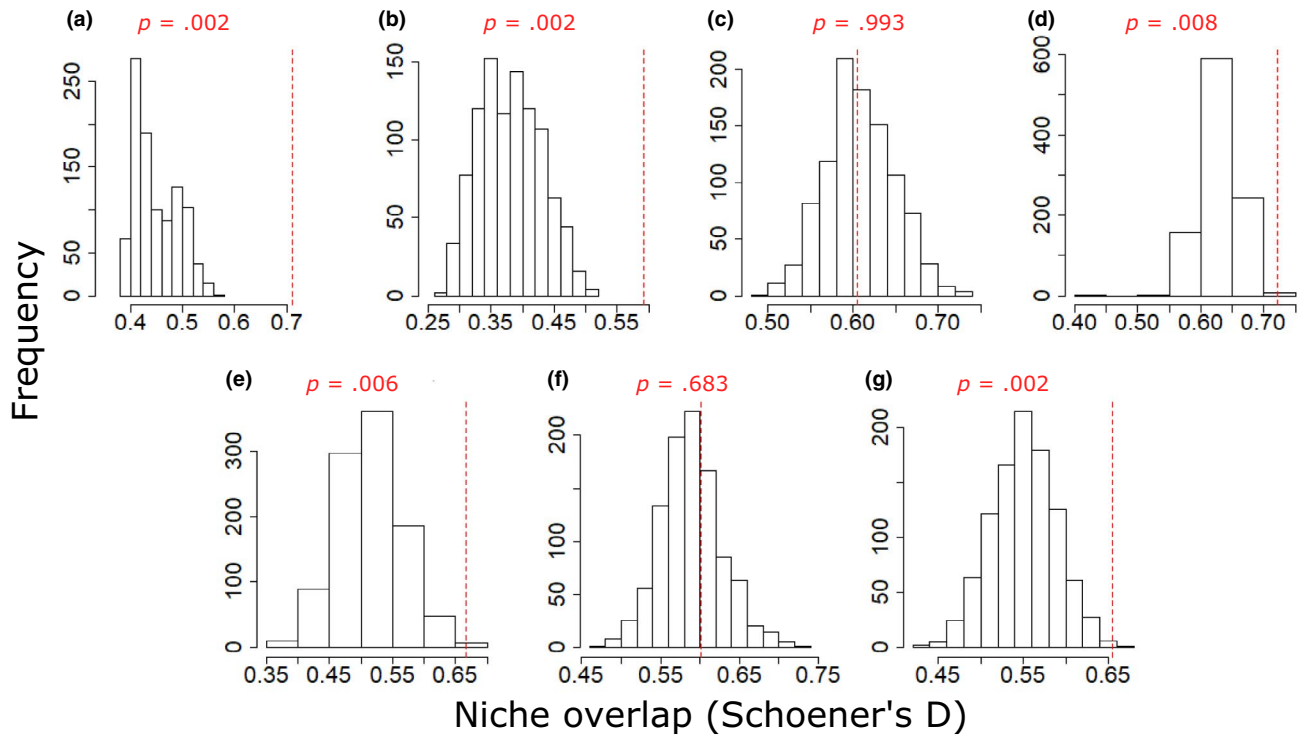


FIGURE 4 Null and observed overlap (Schoener's *D*) between the North American niche of *Yersinia pestis* and the predicted niche based on: (a) *Peromyscus maniculatus* and the Asian niche (Asia+*P.man*); (b) a single host species distribution (*P.man*-only); (c) multiple hosts and the Asian niche (Asia+Multi-host); (d) only multiple host species (Multi-host); (e) limited selection of multiple hosts (Multi-host limited); (f) multiple hosts with the Asian niche but without *P. maniculatus* (Asia+Multi-host, no *P.man*); and (g) multiple host species without *P. maniculatus* (Multi-host, no *P.man*). Histograms show the distribution from 500 null simulations, and red lines show observed values

and climate? Two alternative possibilities are a limited time for dispersal and founder effects. Given that recent invaders often fail to fill their potential niche simply because they have had insufficient time to do so (Strubbe et al., 2013), *Y. pestis* could thus be limited to its current range in North America owing to a lack of time to expand into viable climatic niche space further east of its current extent. However, this explanation is unlikely, because *Y. pestis* reached its maximum eastern extent c. 70 years ago and has remained static since (Adjemian et al., 2007), suggesting that something else, such as biotic factors, has halted its eastward expansion.

Founder effects can induce changes in the fundamental niche because only a limited proportion of genetic variation is retained in the invaded population (Pearman et al., 2008), which can lead to invaders filling only a subset of the native niche of the species (dos Santos Ribas et al., 2018). Given that only one strain of *Y. pestis* (1.ORI1) was introduced into North America (Morelli et al., 2010), we cannot discount this possibility, because we lack sufficient data to quantify the climatic niche of the 1.ORI1 strain in its native range. Although we cannot discount founder effects, we think it unlikely that they would manifest in such a way that they produce spurious correlations with host distributions. Additionally, although we have focused on the pathogen and its hosts here, the distribution of the former will also reflect influences of the vector; hence, a fuller understanding of the effect of biotic factors on the distribution of the

pathogen will require data not only on hosts, but also on the niche and distribution of the vector.

Our results suggest a role for host distributions in limiting the expansion of *Y. pestis* in North America, but these findings must be interpreted cautiously owing to the limited data available for modelling. The predicted distributions are based on Asian and North American occurrence data that overlap only in time only in part (2000–2006), with the Asian data collected over a longer time period. We therefore assume that the Asian climatic niche has not undergone substantial change during this period. Given that we also used time-averaged climatic data (Hijmans et al., 2005), we also assume that recent climate changes have not drastically altered the measurement of the climatic niche.

The North American data represent only a subset of plague cases recorded in animals because these data were originally sourced through ProMED, which might not represent all plague surveillance data and might represent cases only investigated after human infection (Cowen et al., 2006). Previous studies have used alternative data sources, but these were inaccessible to us. There are also limitations of the Asian data, which are biased toward China and were originally selected to represent the genetic diversity of *Y. pestis* in China (Cui et al., 2013). Although more complete data would provide more certainty in our estimates of *Y. pestis* niche, there are two reasons why a more extensive dataset is unlikely to

change our major conclusion. Firstly, additional data on the occurrence of *Y. pestis* throughout Asia would expand, not contract, the breadth of the Asian niche and increase the range of environment in which *Y. pestis* could occur in North America, further reducing niche overlap. Second, including data on the distribution of *Y. pestis* in other regions of the world, outside of China, in our estimate of the non-American climatic niche would only expand the measured breadth of the climatic niche and expand the potential distribution in the Americas. Underestimation of the North American distribution of *Y. pestis*, possibly from a reduced range of sampling years relative to the Asian data, could result in reductions in observed overlap; therefore, it is possible that we have overestimated the niche difference in North America. However, the major area of underfilling is at the eastern edge of the distribution of *Y. pestis*, and the expansion and recent stasis of this eastern edge of the distribution are well described (Adjemian et al., 2007), suggesting that the observed niche contraction is unlikely to be attributable solely to a sampling artefact. Nonetheless, improved accessibility of existing *Y. pestis* distribution data, increased surveillance of non-human-associated cases and, as importantly, increased information on vector distribution and niches will all contribute to improved understanding of the dynamics of *Y. pestis* invasions.

Prediction of the geography of zoonotic diseases in the past, present and future depends on an understanding of the factors limiting the geographical distribution of the pathogen. Here, we have shown that, as for many ecological invasions (Early & Sax, 2014; Guisan et al., 2014; Strubbe et al., 2013), the climatic niche of *Y. pestis* has shifted after introduction to a novel region, suggesting that environmental niche models based solely on climate might not provide reliable predictions of zoonotic disease distributions under rapid environmental change, particularly as they invade new regions. Our work suggests that reliable information on host distributions is more important in predicting pathogen distributions than information on the climatic niche of the pathogen itself. Thus, identification of potential hosts and what influences their distributions is key to understanding the future geography of emerging and established zoonotic pathogens.

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AUTHOR CONTRIBUTIONS

Henry G. Fell, Adam C. Algar, Matthew D. Jones and Steve Atkinson designed the research and drafted the manuscript. Henry G. Fell collected the data. Henry G. Fell and Owen G. Osborne performed the analysis. Henry G. Fell, Adam C. Algar, Matthew D. Jones, Steve Atkinson, Owen G. Osborne, Simon Tarr and Suzanne H. Keddie contributed to the discussion and initial manuscript revisions.

DATA AVAILABILITY STATEMENT

The raw data for this analysis are all freely available. WorldClim global climate data were used throughout (www.worldclim.org). Host species (*Peromyscus maniculatus*, *Otospermophilus beecheyi*, *Neotamias townsendii*, *Otospermophilus variegatus*, *Cynomys gunnisoni*, *Cynomys ludovicianus*, *Cynomys leucurus*, *Cynomys parvidens*, *Sciurus aberti*, *Sciurus griseus*, *Sciurus niger*, *Neotamias amoenus*, *Neotamias dorsalis*, *Neotamias minimus* and *Neotamias umbrinus*) occurrences were obtained from GBIF (www.gbif.org). The *Yersinia pestis* occurrences were extracted from the papers by Walsh and Haseeb (2015) and Cui et al. (2013) for the North American and Asian data, respectively. Although the above data are openly available, all cleaned species occurrence data, climatic variables and examples of the R script used throughout have been uploaded to Figshare (10.6084/m9.figshare.17025230).

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BIOSKETCH

Henry G. Fell's research is focused upon the evolution and ecology of zoonotic diseases, particularly *Yersinia pestis*, and understanding how abiotic and biotic variables impact disease transmission and distribution.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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