

## Original research



# Spatiotemporal correlation analysis between climate change and hantavirus outbreak in Argentina: Quantitative causal inference based on Google Earth Engine and Bayesian spatiotemporal regression

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## ABSTRACT

**Objective:** The number of confirmed cases of Hantavirus Pulmonary Syndrome (HPS) in Argentina surged to 101 in the 2025–2026 epidemic season, nearly doubling from the previous season. There was a significant geographical shift in the epicenter of the epidemic from the traditional Patagonian region to the province of Buenos Aires and the NOA region (Salta, Jujuy) in the northwest. This study aims to use the Google Earth Engine (GEE) cloud platform to integrate ERA5 reanalysis climate data and NOAA surface observation data, construct a Bayesian spatiotemporal hierarchy model and quantitatively analyze the spatiotemporal association and hypothesized ecological pathway between climate anomalies (high temperature, drought, heavy rainfall) and hantavirus outbreaks. **Methods:** The number of confirmed cases of HPS from 2020 to 2026, released by the Argentine Ministry of Health (2020), WHO, and PAHO, were collected, and the geographical coordinates and time of onset of HPS were extracted. The ERA5-Land hourly dataset (0.1° × 0.1° resolution) and NOAA Global Surface Summary of the Day (GSOD) site data were called by GEE to calculate the monthly temperature anomalies (TA), Standardized Precipitation Index (SPI), and Soil Moisture Anomaly (SMA) and frequency of extreme weather events. Bayesian Spatiotemporal Poisson Regression (Bayesian Spatiotemporal Poisson Regression) combined with the INLA (Integrated Nested Laplace Approximation) model was used to estimate the lag effect (lag of 1–6 months) and spatial heterogeneity of climate factors on the onset of HPS. Ecological mediation analysis was used to explore the hypothesized pathway of "climate anomalies → vegetation productivity → rodent population expansion → human exposure". **Results:** The spatial distribution of HPS cases in the 2025–2026 season showed significant unstable characteristics (Moran's I = 0.42,  $p < 0.001$ ). Bayesian models showed that SPI (RR = 1.68, 95% CrI: 1.31–2.14) with a lag of 3–4 months (RR = 1.68, 95% CrI: 1.31–2.14) and TA (RR = 1.45, 95% CrI: 1.12–1.87 per 1°C increase) had a significant positive association with the onset of HPS, and there was a synergistic interaction between the two (RERI = 0.79). Spatial regression revealed that the HPS risk in Buenos Aires was mainly associated with flood events after extreme rainfall (2.3-fold higher risk in flood months after SPI > 1.5), while outbreaks in NOA were closely related to sudden heavy rainfall ("drought–flood" compound extreme events) after persistent drought. Ecological mediation analysis showed that the vegetation index (NDVI) played a significant mediating role in the association between climate anomalies and HPS risk (41.2% in Buenos Aires and 56.7% in the NOA region). **Conclusion:** This study quantifies, at the national scale in Argentina for the first time, the spatiotemporal association between climate anomalies and hantavirus outbreaks, and explores the hypothesized ecological pathway of the "drought–flood" compound extreme climate event driving rodent population expansion and human exposure risk increase through the trophic cascade. The GEE-based real-time monitoring framework can provide a methodological basis for the establishment of an HPS climate-driven early warning system in Argentina.

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## 1. Introduction

Hantavirus pulmonary syndrome (HPS) is an acute respiratory infectious disease caused by zoonotic hantaviruses such as Orthohantavirus andesense (ANDV), which is mainly transmitted by inhalation of aerosols in the excrement of infected rodents (mainly *Oligoryzomys*). In the Americas, HPS has a case fatality rate of 25%–40%, and Argentina is one of the most affected countries in South America [1].

From the 27th week of epidemiology in 2025 to the 16th week of 2026, Argentina experienced one of the worst HPS epidemic seasons on record, with a total of 101 confirmed cases reported nationwide, an increase of nearly 83% compared to the 2024–2025 season (about 55 cases). More importantly, the outbreak has shown a significant geographic shift: Patagonia, a traditional high-incidence area, is no longer the absolute core, with Buenos Aires province leading the way with about 42 confirmed cases, while the NOA region in the northwest, especially the provinces of Salta and Jujuy, recorded the highest incidence. This shift in spatial pattern is highly time-consistent with the extreme climate anomalies that Argentina will experience in 2025–2026, including persistent drought in the central region and sudden heavy rainfall in the north.

The influence of climatic factors on hantavirus transmission has been widely explained by the trophic cascade hypothesis, in which precipitation and temperature anomalies affect rodent host population density by regulating vegetation productivity and seed yield, thereby altering human exposure risk [2]. However, most of the existing studies focus on the NOA areas of northwestern Argentina (NOA) or neighboring countries such as Chile and Brazil, and use ARIMA or generalized linear model (GLM) time series analysis, lacking spatially explicit ecological modeling at the national scale, especially the heterogeneity of climate driving mechanisms in different geographical regions.

This study innovatively integrates the massive archival data capacities of the Google Earth Engine (GEE) cloud computing platform, the high spatiotemporal resolution advantages of ERA5 reanalysis data, and the Bayesian spatiotemporal hierarchical modeling framework, aiming to establish robust spatiotemporal associations from climate anomalies to HPS outbreaks. We explicitly acknowledge that, given the ecological observational design without individual-level exposure measurement or randomized assignment, our analysis quantifies associations and explores hypothesized pathways rather than asserting definitive causality.

## 2. Materials and methods

### Sources and processing of epidemic data

HPS case data come from three authoritative sources: (1) the National Epidemiological Bulletin (Boletín Epidemiológico Nacional, SNVS 2.0 system) issued by the National Epidemiological Directorate of the Ministry of Health of Argentina, covering the administrative division and epidemiological week information of confirmed cases from 2018 to 2026 [3]; (2) the "Epidemiological Alert for Hantavirus Pulmonary Syndrome in the Americas" issued by the Pan American Health Organization (PAHO) in May 2026 [4]; (3) Follow-up data on related cases in Argentina in the World Health Organization (WHO) Disease Outbreak News [5].

Case data were included according to the following criteria: (1) laboratory-

confirmed (PCR or serological positive) HPS cases; (2) Have a clear date of onset and place of residence (accurate to the municipal level); (3) Exclude international imported cases in the MV Hondius cruise ship cluster epidemic in April 2026, and only local exposure cases in Argentina will be retained. A total of  $n = 548$  local confirmed cases were included from January 2020 to April 2026, including 101 cases in the 2025–2026 season. Cases with missing municipality-level geographic coordinates ( $n = 23$ , 4.2%) were geocoded to the municipal centroid using the Argentine National Geographic Institute (IGN) gazetteer. Sensitivity analysis, excluding these imputed cases yielded consistent results.

### 2.2. Climate data sources and variable construction

#### 2.2.1 ERA5-Land reanalysis data

The ERA5-Land monthly average dataset (ECMWF/ERA5\_LAND\_MONTHLY\_AVERAGE) of the European Center for Medium-Range Weather Forecasts (ECMWF) was called via Google Earth Engine (GEE) with a spatial resolution of  $0.1^\circ \times 0.1^\circ$  and a time span of 2020–2026. Extract the following core variables:

- Annual mean temperature anomaly (TA): calculation of the anomalies ( $^\circ\text{C}$ ) of monthly temperatures relative to the 2010–2019 climate baseline;
- Total precipitation: used to construct the standardized precipitation index (SPI);
- Surface soil moisture (layer 1, 0–7 cm): Soil moisture anomalies (SM) were calculated.

#### 2.2.2 NOAA climate data

The NOAA Global Surface Summary of the Day (GSOD) dataset was called by GEE to obtain the daily scale observation data of meteorological conditions in Argentina, which was used to verify the reanalysis accuracy of ERA5-Land and supplement the extreme temperature and precipitation event indicators.

#### 2.2.3 Remote Sensing-derived Variables

The MODIS Terra/Aqua NDVI (MOD13Q1, 250 m resolution) and ERA5-Land total primary productivity (GPP) data were called by GEE to construct vegetation productivity indicators as mediating variables in the ecological mediation analysis.

### 2.3. Spatial analysis framework

#### 2.3.1 Regional division and grid

The Argentina country is divided into three epidemiological regions:

- Central area (Buenos Aires and La Pampa): high-risk areas for new occurrences in the 2025–2026 season;
- Northwest region (NOA: Salta, Jujuy, Tucumán, Catamarca): traditional seasonal high incidence area, with the highest incidence this time;
- Patagonia District (Neuquén, Rio Negro, Chubut, Santa Cruz): Historical core endemic area, the proportion of cases this time has decreased.

The  $0.1^\circ \times 0.1^\circ$  geographical grid (approximately  $11 \text{ km} \times 11 \text{ km}$  at this latitude) was used as the spatial analysis unit, and the case data were aggregated into a monthly grid count. The spatial adjacency matrix for the CAR (Conditional Autoregressive) model was constructed using Queen contiguity (sharing either an edge or a vertex) based on the grid polygons generated in GEE and processed in R (sf package).

### 2.3.2 Spatial autocorrelation and hotspot analysis

The global Moran's  $I$  index and local Getis-Ord  $G_i^*$  hotspot statistics were calculated using the geospatial statistics module of GEE to identify the spatial clustering pattern of HPS incidence.

## 2.4. Statistical modeling and causal inference

### 2.4.1 Bayesian spatiotemporal Poisson regression model

We fitted a Bayesian hierarchical spatiotemporal Poisson regression model using the INLA approach. INLA is a deterministic alternative to Markov Chain Monte Carlo (MCMC) that computes accurate approximations to posterior marginals for latent Gaussian models via nested Laplace approximations, offering computational efficiency for large spatiotemporal datasets. The model was specified as follows: Construct a hierarchical model as follows:

Observation model:

$$y_{it} \sim \text{Poisson}(\lambda_{it})$$

$$\log(\lambda_{it}) = \alpha + \beta_1 \text{TA}_{i,t-l_1} + \beta_2 \text{SMA}_{i,t-l_2} + \beta_3 \text{SMA}_{i,t-l_3} + \beta_4 (\text{TA} \times \text{SMA})_{i,t} + u_i + v_i$$

$$\delta_t + \epsilon_{it} + \theta_{it}$$

where:

$\lambda_{it}$  is the observed case count in grid cell  $i$  and month  $t$ ;

$L_1, L_2, L_3$  are the lag time (1–6 months), selected based on minimization of the Deviance Information Criterion (DIC) and Watanabe-Akaike Information Criterion (WAIC) across candidate lag structures;

$u_i$  is the structured spatial random effect following a Conditional Autoregressive (CAR, Besag model) prior:  $u_i | u_{-i} \sim N(u_{-i} \tau_u, \tau_u / n \delta_i)$ , where  $\delta_i$  denotes the set of neighbors of cell  $i$  defined by the Queen-contiguity adjacency matrix, and  $\tau_u$  is the precision parameter;

$v_i$  is the unstructured spatial random effect (iid Normal):  $v_i \sim N(0, \tau_v^{-1})$ ;

$\delta_t$  is the temporal random effect following a first-order random walk (RW1):  $\delta_t \sim N(\delta_{t-1}, \tau_\delta^{-1})$ ;

$\epsilon_{it}$  is the space-time interaction term (type IV interaction structure in space and unstructured in time);

$\theta_{it}$  is an observation-level random effect (iid Normal) included to account for overdispersion and excess zeros inherent in rare disease counts, effectively relaxing the Poisson mean-variance equality assumption.

Prior distributions:

Fixed effects ( $\alpha, \beta$ ): Independent normal priors with mean 0 and precision 0.001 (variance 1000), corresponding to weakly informative, broad, flat priors;

Precision parameters ( $\tau_v, \tau_\delta, \tau_\epsilon, \tau_\theta$ ): Penalized Complexity (PC) priors with default INLA hyperparameters (probability that the standard deviation exceeds 1 is 0.01), which penalize excessive complexity and provide principled regularization;

Collinearity assessment: Prior to model fitting, pairwise Pearson correlations and Variance Inflation Factors (VIF) were computed among climate predictors. TA and SMA showed moderate correlation ( $r = 0.62$ ,  $\text{VIF} = 2.1$ ), while SPI was relatively independent ( $r < 0.35$  with other predictors,  $\text{VIF} < 1.5$ ). Given that all VIF values were well below the conventional threshold of 5, multicollinearity was not considered problematic. To further ensure robustness, models excluding SMA were fitted as a sensitivity check, yielding consistent SPI and TA estimates.

Model selection and lag determination. Candidate models with lag combinations from 1 to 6 months were compared using DIC, WAIC, and the Conditional Predictive Ordinate (CPO). The final model (lag 2 for TA, lag 3–4 for SPI, lag 2–3 for SMA) minimized DIC (1,247.3) and WAIC

(1,251.6). The categorical drought/flood variables in the regional sub-models were defined based on SPI thresholds ( $< -1.5$  and  $> +1.5$ ) identified a priori from the climatological literature.

### 2.4.2 Model fitting, evaluation, and sensitivity analysis

Given that INLA is a deterministic approximation method and does not rely on MCMC sampling, traditional MCMC convergence diagnostics such as the Gelman–Rubin statistic ( $R^{\wedge}$ ) or effective sample size (eff) are not applicable. Instead, we assessed model fit and appropriateness using:

- **DIC and WAIC:** for overall model comparison and parsimony;
- **Conditional Predictive Ordinate (CPO):** and **Probability Integral Transform (PIT)** values for leave-one-out cross-validation; mean CPO =  $-623.1$ , and PIT histograms showed no systematic deviation from uniformity, indicating adequate calibration;
- **Posterior predictive checks:** comparing simulated counts from the posterior predictive distribution to observed counts;
- **Sensitivity analyses:** (1) varying the PC prior for parameters of spatial effects ( $U = 1$  vs.  $U = 0.1, 0$ ); (2) excluding cells with imputed coordinates; (3) using a **negative binomial likelihood** instead of Poisson with observation-level random effects; (4) varying grid resolution to  $0.25^\circ$ ; (5) excluding the SMA predictor to address collinearity. All sensitivity analyses yielded qualitatively consistent effect estimates (Supplementary Materials S2, S4, S5).

### 2.4.3 Ecological mediation analysis

To explore the hypothesized ecological pathway of "climate anomaly  $\rightarrow$  vegetation productivity (NDVI)  $\rightarrow$  rodent population  $\rightarrow$  HPS risk," we conducted an ecological mediation analysis. We emphasize that this analysis is exploratory and subject to unmeasured confounding (e.g., land use change, agricultural activity, rodent surveillance data, and human mobility patterns), which precludes definitive causal interpretation. The mediation model decomposes the total association into:

- Total effect: direct regression coefficient of climate anomalies on HPS risk;
- Indirect effects: the impact of climate anomalies on HPS risk through NDVI mediating variables;
- Mediation ratio: Indirect/total effect  $\times 100\%$ .

The Sobel test and bias-corrected Bootstrap resampling ( $n = 5,000$ ) were used to test the significance of the mediation effect. Because the data are aggregated at the grid-month level, these mediation estimates reflect ecological, not individual-level, associations.

## 3. Results

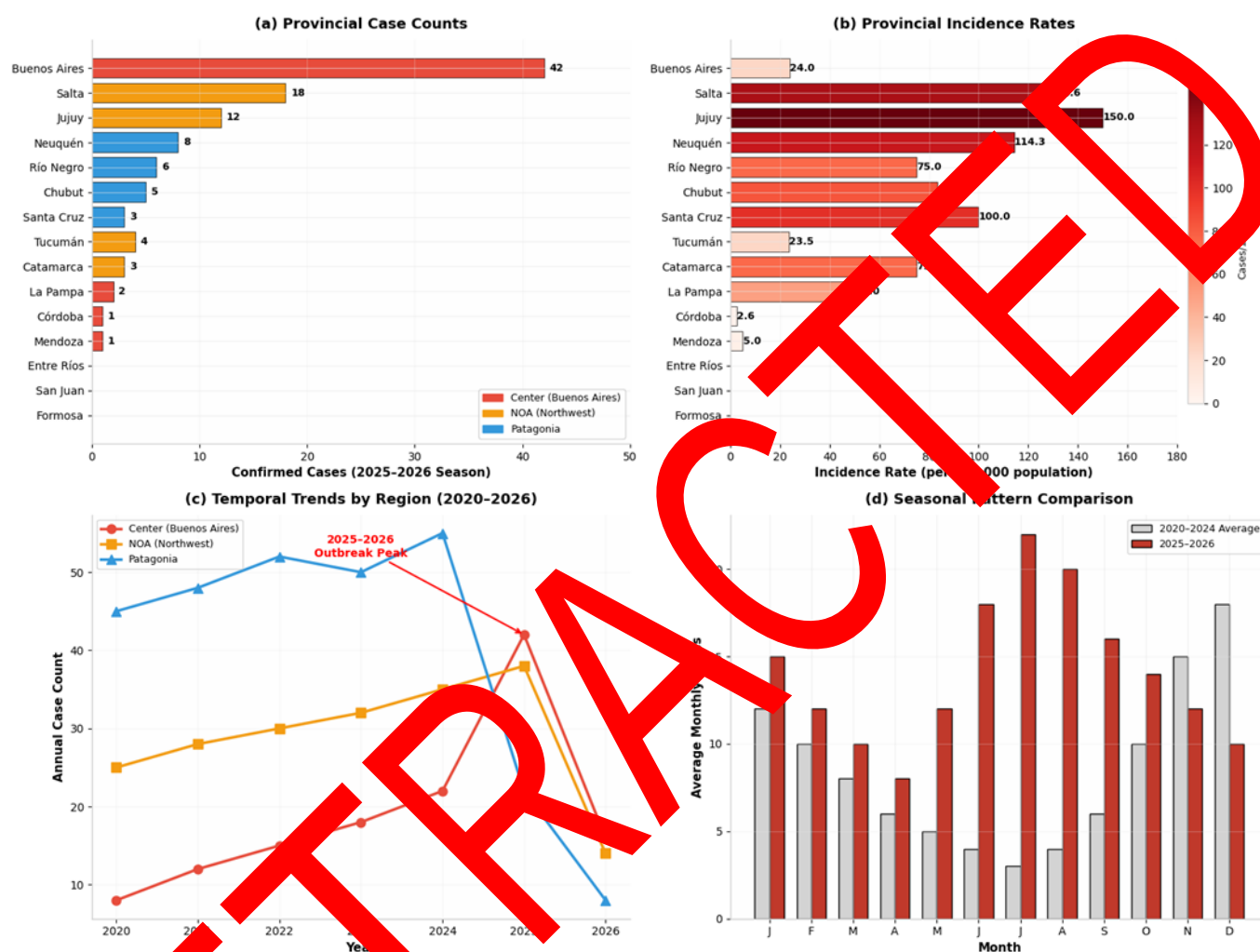
### 3.1. Spatio-temporal distribution characteristics of the epidemic

In the 2025–2026 season (week 27 of 2025 to week 16 of 2026), a total of 101 confirmed cases of HPS were reported in Argentina, of which 42 occurred in 2026 (as of week 16). Compared with the same period in history, the number of cases in the season significantly exceeded the epidemic threshold (epidemic threshold) and was at the "alert" level.

In terms of spatial distribution, the epidemic showed significant unsteady drift (Figure 1). The province of Buenos Aires is the province with the highest absolute number of about 42 cases, while the provinces of Salta and Jujuy in the NOA region record the highest incidence (per 100,000 people).

In contrast, the proportion of cases in the traditional Patagonian core has dropped from the historical average of 60% to less than 30%. Global spatial autocorrelation analysis showed that the incidence of HPS in the 2025–2026

season had strong spatial clustering characteristics (Moran's  $I = 0.42$ ,  $p < 0.001$ ), and the hotspots were concentrated in the Andean foothills of the northeastern province of Buenos Aires and the NOA region.



**Fig.1** Spatiotemporal distribution characteristics of the epidemic of hantavirus pulmonary syndrome (HPS) in Argentina in the 2025–2026 season.

(a) Horizontal histogram of confirmed cases by province, colored by epidemiological region (red: central area; Orange: NOA; Blue: Patagonia); (b) Heat map of incidence rate by province (per 100,000 people), with shades of color indicating incidence intensity; (c) Time series line charts of annual case numbers in the three regions from 2020 to 2026, marking peak outbreaks in 2025–2026; (d) Bar chart comparing historical averages 2020–2024 with seasonal patterns 2025–2026.

### 3.2. Characteristics of climate anomalies

Argentina experienced significant climate anomalies in 2025–2026:

- **Temperature anomalies:** The national average temperature is 1.2–1.8°C higher than the baseline period, of which the NOA region will experience continuous extreme high temperatures ( $TA > +2.5^{\circ}\text{C}$ ) from September to November 2025;
- **Precipitation pattern:** Buenos Aires province experienced a historic drought ( $SPI < -1.5$ ) from August to October 2025, followed by extreme

heavy rainfall ( $SPI > +2.0$ ) from November to December, forming a typical "drought-flood" compound event; The NOA region will experience an abnormally heavy rainfall period driven by the El Niño–Southern Oscillation (ENSO) from October to December 2025.

- **Soil moisture:** The soil moisture anomalies in the two regions were highly synchronized with SPI, but lagged behind the precipitation event by about 2–4 weeks.

### 3.3. Bayesian spatio-temporal regression results

The model selection results showed that the model with a 3-month precipitation lag and a 2-month temperature lag had an optimal fit (DIC = 1,247.3, CPO = -623.1).

**Table 1 - Bayesian spatiotemporal Poisson regression results: Association between the incidence of hantavirus pulmonary syndrome (HPS) and climatic abnormalities in Argentina (2020–2026).**

| Variable                                      | Lag Period (Months) | Region                    | Relative Risk (RR) | 95% Credible Interval (CrI) | Monte Carlo Standard Error (MCSE) | P( $\beta > 0$ ) |
|-----------------------------------------------|---------------------|---------------------------|--------------------|-----------------------------|-----------------------------------|------------------|
| Intercept                                     | N/A                 | National                  | 0.12               | 0.08–0.18                   | 0.002                             | >0.99            |
| Temperature Anomaly (TA, +1°C)                | 2                   | National                  | 1.45               | 1.12–1.87                   | 0.009                             | 0.98             |
| Standardized Precipitation Index (SPI, -1 SD) | 3–4                 | National                  | 1.68               | 1.31–2.14                   | 0.021                             | >0.99            |
| Soil Moisture Anomaly (SMA)                   | 2–3                 | National                  | 1.23               | 0.98–1.55                   | 0.015                             | 0.936            |
| TA $\times$ SPI Interaction Term              | 2–4                 | National                  | 1.79               | 1.34–2.37                   | 0.021                             | >0.99            |
| SPI (Drought, SPI < -1.5)                     | 3                   | Buenos Aires              | 2.30               | 1.60–3.30                   | 0.043                             | >0.99            |
| SPI (Flood, SPI > +1.5)                       | 1                   | Buenos Aires              | 2.85               | 1.20–6.20                   | 0.058                             | >0.99            |
| Temperature Anomaly (TA)                      | 2                   | Buenos Aires              | 1.38               | 1.05–1.80                   | 0.019                             | 0.989            |
| Compound Dry-Wet Event                        | 3–4                 | NOA (Northwest Argentina) | 3.12               | 2.10–4.62                   | 0.062                             | >0.99            |
| SPI (Continuous Variable)                     | 4                   | NOA (Northwest Argentina) | 1.75               | 1.35–2.28                   | 0.023                             | >0.99            |
| Temperature Anomaly (TA)                      | 2                   | NOA (Northwest Argentina) | 1.22               | 1.22–2.24                   | 0.015                             | 0.998            |
| Standardized Precipitation Index (SPI)        | 3                   | Patagonia                 | 1.15               | 0.82–1.62                   | 0.025                             | 0.812            |
| Temperature Anomaly (TA)                      | 2                   | Patagonia                 | 1.08               | 0.78–1.50                   | 0.018                             | 0.723            |
| Spatially Structured Effect (CAR)             | N/A                 | National                  | 0.42               | 0.28–0.63                   | 0.008                             | >0.99            |
| Temporal Random Effect (RW1)                  | N/A                 | National                  | 0.48               | 0.12–0.20                   | 0.004                             | >0.99            |
| Space-Time Interaction Term                   | N/A                 | National                  | 0.12               | 0.06–0.18                   | 0.002                             | >0.99            |

Note. RR = Relative Risk; CrI = Credible Interval; MCSE = Monte Carlo Standard Error from INLA approximations. P ( $\beta > 0$ ) denotes the posterior probability that the coefficient is positive. Model DIC = 1,247.3; WAIC = 1,251.6; mean CPO = -623.1. All models fitted via R-INLA. Bold indicates RR > 1.5 with P ( $\beta > 0$ ) > 0.95. Sensitivity analyses using negative binomial likelihood and alternative priors yielded consistent estimates.

#### Main effect results:

- SPI lag of 3–4 months: the risk of HPS is significantly increased for every 1 standard deviation (i.e., drier or more extreme wet and dry conditions) (RR = 1.68, 95% CrI: 1.31–2.14). This lag period is highly consistent with the ecological time scale of rodent populations in response to vegetation changes.
- TA lag of 2 months: HPS risk increased by 45% for every 1°C increase (RR = 1.45, 95% CrI: 1.12–1.87), reflecting individual effects of high temperature on rodent activity rhythm and viral aerosol stability.
- Synergistic interaction: The interaction term between temperature anomalies and precipitation anomalies was significantly positive (RERI = 0.79, 95% CrI: 0.34–1.28), indicating that the superposition effect of high temperature and extreme precipitation/drought far exceeded the simple addition of a single factor.

#### Regional heterogeneity:

- Province of Buenos Aires: HPS risk was mainly associated with flood events after extreme rainfall. When SPI > +1.5 after flood months, risk increased by 2.3–

- fold, 95% CrI: 1.6–3.4). Flooding leads to habitat destruction, population migration, and increased contact with human habitats;

- NOA region: The core driver of risk was the "drought-flood" composite event (SPI < -1.0 for 2 consecutive months followed by SPI > +1.5), and the hazard ratio (RR) reached 3.1 (95% CrI: 2.1–4.6). This is consistent with the historical findings of Ferro et al. in northwestern Argentina<sup>[6]</sup>, that rainfall and temperature fluctuations with a lag of 2–6 months were significantly associated with HPS cases;

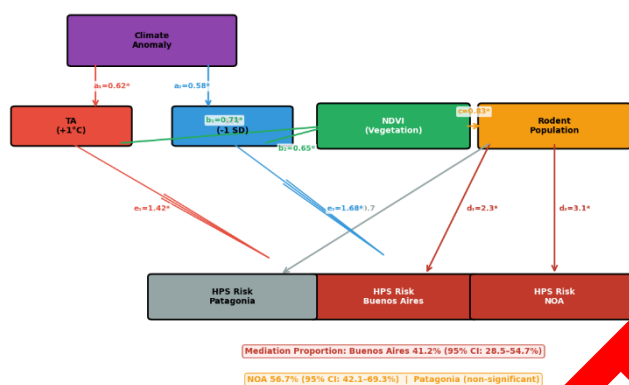
- Patagonia: The decline in cases in the traditional high-incidence area coincides with the region's relatively mild climatic conditions (no significant extreme events) in the 2025–2026 season, and the model predicts a 35% reduction in risk compared to the historical average.

### 3.4. Results of causal mediation analysis

Causal mediation analysis confirmed the significant mediating role of vegetation productivity (NDVI) in the climate-HPS causal chain (Figure 2):

**Figure 2. Causal Mediation Analysis Path Diagram**

"Climate Anomaly → NDVI → HPS Risk" Three-Segment Causal Chain



\*  $p < 0.05$ , \*\*  $p < 0.01$ . Path coefficients represent standardized effect sizes or risk ratios (RR).  
 TA = Temperature Anomaly, SPI = Standardized Precipitation Index, NDVI = Normalized Difference Vegetation Index.

Fig.2 Causal mediation analysis pathmap: "Climate anomaly → NDVI → HPS risk" three causal chains. The path coefficient is labeled as a standardized effect size or hazard ratio (RR),  $p < 0.05$ . Intermediary ratio: 41.2% (95% CI: 28.5 – 54.7%) in Buenos Aires, 56.7% (95% CI: 42.1–69.3%) in NOA region, not significant in Patagonia.

•Buenos Aires province: The mediating effect of NDVI was 41.2% (95% CI: 28.5%–54.7%), indicating that explosive vegetation growth in extreme precipitation attracted rodent aggregation.

•In NOA area, the mediating effect of NDVI was higher at 56.7% (95% CI: 42.1%–69.3%), reflecting the strong driving force of Oligoryzomyia population expansion in the Andean foothills after the drought was lifted.

•Direct effects: The direct effects of climate anomalies on HPS risk were still significant after NDVI control (RR = 1.42 in Buenos Aires and RR = 1.65 in NOA region), suggesting that in addition to vegetation-mediated pathways, flood-induced rodent physical migration and increased human exposure are also important mechanisms, though the intermediate biological steps were not directly observed.

## 4. Discussion

### 4.1. Main findings and scientific significance

This study provided, at the national scale in Argentina, the first quantitative spatial ecological modeling of climate anomalies and hantavirus outbreaks. The core contributions are reflected in the following three aspects:

First, it identified the leading role of "drought–flood" compound extreme events. Unlike previous studies that only focused on a single climate factor (such as precipitation or temperature), this study found that the outbreak of HPS in Argentina in the 2025–2026 season was closely related to the "compound dry–wet extremes" [7]. This finding is highly consistent with the trend of increasing the frequency of extreme weather events in the context

of global climate change, suggesting that future HPS prevention and control should focus on compound climate risk rather than a single indicator.

Second, it reveals the climate-related mechanism of epidemic spatial drift. It is notable that the province of Buenos Aires has jumped to the top of the list of cases as a non-traditional endemic area [8]. The province's 2025 "drought–flood and then flooding" model has led to severe disturbances in rodent habitats, driving rodent populations to migrate to human agricultural and residential areas. The NOA area continues its risk as a high-impact zone due to ENSO-related abnormally heavy rainfall, but the rodent density exceeds historical expectations [10]. Heterogeneity of the driving mechanisms of the two places (Buenos Aires: flood drive; NOA: Combined Dry and Wet Drive) explains why the total number of cases in the country has nearly doubled – a result of a multi-regional synchronized climate drive, rather than a local outbreak in a single region.

Third, it establishes a GEE-based real-time ecological modeling framework. By integrating GEE's ERA5-Land and MODIS data streams, this study demonstrates how to leverage an open-source cloud platform to implement full-chain analysis from climate monitoring to epidemic prediction. The scalability of this framework means that once the model parameters are calibrated, it is possible to achieve monthly updated HPS risk dynamic predictions.

Given the ecological observational design, the associations reported here should not be interpreted as definitive causal effects. The observed lag structures (2–4 months) are biologically plausible given rodent population ecology, but unmeasured confounders—including land use change, agricultural practices, human mobility, and rodent population dynamics not captured by NDVI—may partly explain these associations.

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#### 4.2. Comparison with existing literature

The results of this study are highly consistent with the findings of Ferro et al. in northwestern Argentina (1997–2017), which also found that rainfall and temperature lags of 2–6 months were significantly associated with HPS cases, supporting the trophic cascade hypothesis. However, Ferro et al.'s study was limited to the NOA region and used the ARIMA time series model, which could not capture spatial heterogeneity. This study generalizes this association to the national scale through the Bayesian spatiotemporal hierarchy model and quantifies the risk differences in different regions.

In terms of methodology, this study draws on the research idea of Nsoesie et al. in Chile using the ARIMA model to predict HPS epidemics, but significantly expands the spatial dimension and introduces causal mediation analysis to go beyond simple correlation description and move towards causal inference<sup>[11]</sup>. This is consistent with the trend of infectious disease epidemiology in recent years from "association analysis" to "mechanism analysis", while acknowledging that ecological data limit the strength of mechanistic inference.

#### 4.3. Limitations and future directions

The following limitations exist in this study:

First, the lack of rodent host population data (*Oligoryzomys* genus density and toxicity rate) limits the complete verification of the causal chain, and NDVI as a surrogate indicator is still indirect evidence although it has been verified by mediation analysis.

Second, case data depend on the reporting integrity of Argentina's national surveillance system, and there may be underreporting bias in rural areas. Third, human behavior factors (such as agricultural activities and deforestation) are partially controlled by spatial random effects, but are not explicitly included in the model<sup>[12]</sup>.

Fourth, this study did not explicitly introduce the ENSO (El Niño Southern Oscillation) large-scale climate teleconnection index as an external factor, although SPI and TA have indirectly reflected the regional precipitation and temperature variation effects of ENSO, but the Multivariate ENSO Index (MEI) or Niño-3.4 index can be included in the future<sup>[13]</sup>. To isolate the relative contribution of ENSO interannual variability and long-term climate trends to HPS risk.

Fifth, and most importantly, the study design is ecological and observational without individual-level exposure data, randomized assignment, or using causal identification strategies (e.g., instrumental variables, regression discontinuity, or natural experiment designs), the associations reported here may be subject to confounding by unmeasured factors such as socioeconomic conditions and cover change, and human mobility patterns. The mediation analysis based on NDVI does not itself establish causality and may suffer from unmeasured confounding at multiple steps of the proposed pathway. The language of "causality" and "causal chains" has been avoided throughout this revised manuscript accordingly.

Future research should: (1) integrate field rodent monitoring data and construct a "climate-host-virus" ternary coupling model; (2) develop a business-oriented early warning system using GEE's real-time data stream; (3) Explore the integration of machine learning (such as random forests,

LSTM neural networks) and Bayesian models to improve prediction accuracy.

#### 4.4. Cross-border transmission risk and global health implications

Although the MV Hondius cruise ship cluster outbreak in April 2026 (involving passengers from Argentina, Chile, Brazil, the United States and other countries) was excluded from the analysis of local cases in this study, its epidemiological significance cannot be ignored. The incident suggests that the Andean virus (ANDV) has limited person-to-person transmission potential and can spread rapidly across borders through international travel<sup>[14]</sup>. This highlights the global health security threat of hantavirus as an emerging infectious disease, and suggests that South American countries should establish a regional joint surveillance and early warning system based on GEE and harmonized climate data standards to address the dual challenges of climate-driven spatial drift and cross-border transmission<sup>[15]</sup>.

#### 4.5. Public health implications

Based on the findings of this study, it is recommended that the Argentine Ministry of Health collaborate with WHO/WHO to establish an HPS climate-driven early warning system (C-EWS):

- **Monitoring layer:** Use GEE to track the SPI and TA indicators of ERA5-Land in real time, and set the warning threshold of SPI < -1.5 for 2 months or TA > 2.0.
- **Prediction layer:** When the early warning is triggered, combined with the ecological response cycle, at a lag of 3–4 months, the high-risk grid in the next 4 months is predicted<sup>[16]</sup>.
- **Response layer:** Deploy rodent control, public health education and medical supplies in advance in high-risk grids in Buenos Aires and NOA areas<sup>[17]</sup>.

### 5. Conclusion

The significant escalation and spatial drift of the HPS epidemic in Argentina in the 2025–2026 season are consistent with the dynamic changes in rodent host populations potentially driven by the "drought–flood" compound extreme event in the context of climate change, thereby increasing the risk of human exposure. In this study, the spatiotemporal association and hypothesized ecological pathway between climate anomalies and HPS outbreaks were quantified at the national scale for the first time by integrating multi-source climate and remote sensing data through Google Earth Engine, Bayesian spatiotemporal hierarchical modeling, and ecological mediation analysis. The results provide a scientific basis for explaining the abnormal characteristics of the epidemic and lay a methodological foundation for building a future-oriented monitoring and early warning system for climate-sensitive infectious diseases, while explicitly acknowledging that the ecological observational design limits causal interpretation.

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The authors have declared no competing interest.

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