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Modelling Malaria at the Human–Environment Interface in the Cross-Border Oiapoque Basin: A One Health ABM-GIS Approach

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Abstract

Background: Malaria persistence in the cross-border Oiapoque basin (French Guiana-Brazil) is driven by complex socio-ecological interactions, land use and land cover (LULC) changes, and extreme seasonal climate variations acting as ecological disruptors. Because traditional static epidemiological surveillance fails to capture the geographic friction and pendular movements of vulnerable populations, this study operationalises the One Health paradigm through a spatially explicit Agent-Based Model integrated with Geographic Information Systems (ABM-GIS) to assess epidemic risk and the efficacy of institutional mitigation.

Methods: Using high-resolution climatic (Copernicus ERA5-Land) and environmental (MapBiomass) data, an Elastic Net regularized Negative Binomial Generalized Linear Model extracted probabilistic weights for landscape attraction and friction, functioning as deterministic ecological proxies for vector habitat suitability. The ABM-GIS was developed in Python using a 1-km continuous hexagonal tessellation. The model simulated the pendular mobility of three occupational profiles (Miners, Farmers, and Urban dwellers) and was validated by Pattern-Oriented Modelling (POM) across seasonal extremes and empirical registries of malaria cases.

Results: The results indicate that while historical health agent deployments successfully mitigated baseline residential exposure, the current border system faces spatial saturation. POM revealed an occupational risk hierarchy, with simulated incidence rates reaching 26.82 cases per 1,000 for miners, compared to 2.13 for farmers and 0.23 for urban residents. A spatial null scenario disabling mobility flattened these rates (≤ 0.25), evidencing that extreme vulnerability emerges dynamically from deep-forest commuting. This was validated against 2025 empirical data, where miners accounted for 82.2% of real-world cases, mirroring the 84.6% simulated proportion. Finally, ABM-GIS simulations demonstrated that scaling static institutional capacity by 20% during epidemic peaks yields a mathematically conservative $\sim 4.7\%$ disease reduction (from

208.2 to 198.5 mean cases). These findings indicate that overcoming diminishing returns requires a strategic shift from static residential coverage to targeted, mobile interventions at high-risk ecotones.

Conclusions: This study demonstrates that cross-border malaria is an emergent socio-ecological property driven by pendular occupational mobility into deep-forest ecotones. ABM-GIS simulations and a static null scenario evidenced that current static health interventions have reached spatial saturation. Overcoming this bottleneck requires shifting to anticipatory One Health strategies, utilizing spatial models as early-warning tools to deploy targeted mobile teams directly at high-risk exposure sites.

Keywords: SEES; Agent-based modelling; Spatial simulation; Spatial epidemiology; One Health; Planetary Health

1. Background

Malaria is a zoonotic infectious disease that continues to affect millions of people worldwide, with a disproportionate burden in the Global South [1]. Its transmission dynamics are multifactorial, shaped mainly by interacting drivers such as climate conditions [2], land-use and land-cover (LULC) change [3], human mobility [4], and seasonality [5]. These drivers do not operate independently, and their interaction shape where, when and among whom malaria transmission occurs. This interdependence places malaria firmly within the conceptual scope of One Health, which recognises that human health is intrinsically connected to the health of animals, vectors, plants, and ecosystems [6]. To operationalise this framework, this study follows a continuous One Health pathway: anthropogenic land-use change drives local ecosystem change, which directly modifies vector ecology and habitat suitability [7,8]. In turn, these environmental shifts interact with human mobility and work-related exposure, shaping the spatial dynamics of malaria transmission and, ultimately, triggering a health-system response that feeds back into the socio-ecological system [9–11].

Within this perspective, malaria transmission emerges from complex interactions across human, vector, and environmental systems, rather than as an isolated human health outcome [10,11]. To computationally translate the One Health philosophy into a dynamic spatial model, we adopted the Socio-Ecological and Epidemiological Systems (SEES) framework [12,13]. In Amazonian pioneer frontiers, the SEES architecture captures how LULC change, driven by deforestation and agricultural expansion, reconfigures the forest landscape [14,15]. This fragmentation creates a strong edge effect, generating shaded ecotones and stagnant water collections that multiply the breeding habitats of the primary vector [14,16]. This ecological scenario interacts directly with rainfall seasonality and river flow, regulating peaks in vector abundance and human-vector contact [12,17]. Crucially, in transboundary pioneer frontiers, the One Health triad (human-vector-environment) is inherently mobile. Environmental transformations cannot be separated

from the pendular human mobility that connects remote, vector-abundant ecosystems to urban health infrastructure. Deforestation and mining not only alter the landscape but also reshape human livelihoods, triggering a continuous flow of susceptible hosts into high-risk ecotones. This mobility establishes the physical mechanism that perpetuates active transmission across administrative boundaries.

In this context, the cross-border Oiapoque basin, on the French-Brazilian border (Amapá-French Guiana), acts as a unique geographical laboratory [12]. Spanning 36,130 km² (Figure 1) - of which approximately 91% is covered by dense forest - this territory sustains a population of roughly 35,500 people [18] and an epidemiological burden that averages 1,300 malaria cases annually [19,20]. Characterised by high social vulnerability (low education levels and multidimensional poverty) and a continuous transnational flow of people across the Oiapoque River via local vessels, the region faces "imported malaria" [12]. This mobility occurs across two national health systems with distinct surveillance structures, intervention strategies, and institutional capacities, meaning that malaria control therefore depends not only on local transmission conditions but also on the spatial and institutional continuity of control measures between jurisdictions. This constant flow establishes a dynamic route that sustains continuous human exposure to endemic zones across territories [12,21].

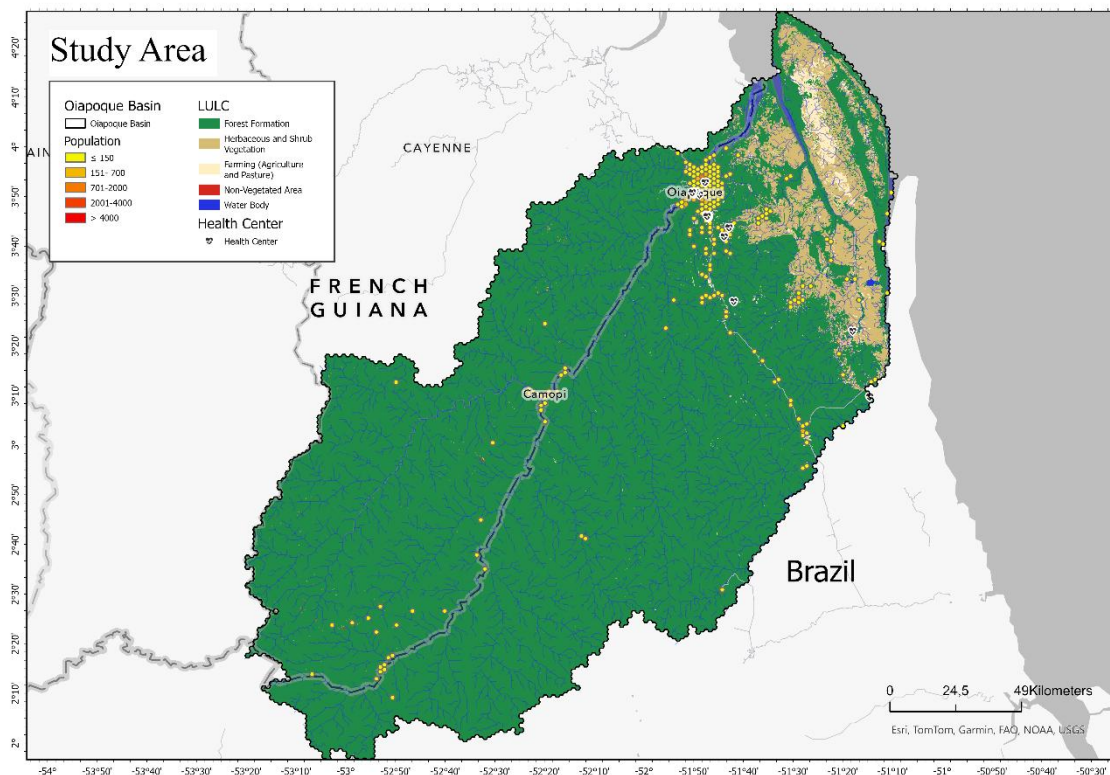


Figure 1. Study area of the cross-border Oiapoque basin (Amapá-French Guiana). The map illustrates the transnational territory, detailing the spatial distribution of the population, the local health centres, and the Land Use and Land Cover (LULC), highlighting the extensive forest formation that covers approximately 91% of the region.

Highly mobile populations, notably gold miners and agricultural workers, sustain malaria transmission in these fringe areas and protected territories. These populations operate predominantly in the informal or illegal sector, establishing themselves in clandestine camps isolated deep within the forest [12,22]. These makeshift dwellings lack adequate physical protection (such as sealed walls or mosquito nets) and are situated immediately adjacent to vector breeding sites, maximising human exposure [12]. The epidemiological risk is exacerbated by the fact that these populations maintain a recurrent pendular and circular migratory flow [12,22]. Miners relocate from urban support centres to remote dense forest areas to extract resources, periodically returning to border towns for shopping, leisure, or medical treatment [12]. This stochastic back-and-forth functions as a conveyor belt that disseminates parasites from highly endemic locations to urban peripheral areas and vice versa, creating a continuous feedback loop [22]. Given this dynamic, traditional epidemiological surveillance systems, such as SIVEP-Malária in Brazil, are insufficient. Because they operate at aggregated administrative scales, typically municipal, these systems produce a static view that conceals the micro-heterogeneity of transmission, and fails to map intermunicipal and cross-border movements [22]. Furthermore, surveillance faces under-reporting and spatial registration errors, resulting from the difficulty of accessing illegal camps, the prevalence of asymptomatic infections with low parasite loads, and patient recall biases when reporting the probable location of infection [12,22,23].

Due to these limitations, classical spatial epidemiology has been criticised for its eminently static nature. Traditional predictive models rely on environmental risk pixels, focusing almost exclusively on the presence or absence of forest cover [22,24,25]. In doing so, they ignore the complexity of physical connections and the intermodal geographic friction that mobile populations face, that is, the actual ecological and spatial transitions experienced when an individual travels across transport axes such as rivers, unpaved dirt roads, and pedestrian trails in dense forests [12,17,21]. Another factor these models have historically neglected is the temporal variable linked to mobility, especially "transit time" and individuals' accumulated exposure during journeys along these high-friction transport routes [22]. The true risk of contracting and disseminating malaria is not limited to the geographical coordinates of the patient's residence or workplace, but is strongly shaped by transit time along fluvial and terrestrial routes exposed to vectorial activity [12,22].

To fill this methodological gap, this study proposes a spatially explicit Agent-Based Model integrated with Geographic Information Systems (ABM-GIS) [26], fed by high-resolution environmental and climatic data from the Copernicus [27,28] and MapBiomass [29,30] platforms. An agent-based modelling allows one to transcend the limitations of aggregated epidemiological registries, whose purely spatial analysis frequently induces an ecological fallacy [31–33]. Only by simulating population behaviour, incorporating environmental sensing rules, behavioural adaptation, and, above all, non-Euclidean multimodal logistical friction, can one to recreate the dynamic and stochastic risk of the Amazonian terrain. By modelling the continuous and bottom-up

interaction between mobile populations, infrastructure, and a constantly mutating landscape, the ABM-GIS paradigm allows one to capture the true accumulated exposure during transit routes, overcoming the static view of the pixel [34,35].

Therefore, this research is driven by a central question: how do interactions among climate variability, land use change, human mobility patterns and health-system responses shape the spatial and temporal dynamics of malaria transmission within the cross-border Oiapoque Basin? To answer this, the central objective of this study is to translate the socio-ecological vulnerability of the transboundary basin into a spatially explicit computational model, enabling quantitative evaluation of the efficacy of territorial blockade by mobile health agents. Complementarily, the study aims to empirically parameterise the mathematical forces of spatial attraction and friction derived from climatic and land use variables; simulate pendular occupational mobility to evaluate the profound risk disparities among miners, farmers, and urban residents; and measure the impact of institutional mitigation capacity under scenarios of environmental stress. To achieve these goals, the article is organised as follows: Section 2 outlines the methodology, detailing the data lifecycle and the computational architecture of the algorithm (ODD protocol); Section 3 presents the results of the spatio-temporal simulations and the stochastic validations under seasonal extremes; Section 4 discusses the implications of these findings for optimising health governance at borders; and finally, Section 5 presents the conclusions.

2. Methods

To ensure a rigorous data lifecycle from conceptualisation to simulation, this study adopted the PACE (Plan, Analyse, Construct, Execute) methodological framework [36]. After the initial problem definition, the Analyse phase involved acquiring, harmonising across borders, and conducting exploratory spatial data analysis (ESDA) of heterogeneous datasets, cross-referencing lagged climatic time series, LULC dynamics, and healthcare registries from Brazil and French Guiana. The construct phase encompassed extracting probabilistic weights via statistical regression and subsequently engineering the Agent-Based Model (ABM-GIS) on a hexagonal grid in Python. Finally, in the Execute phase, we simulated and calibrated the model against epidemiological ground truth. The following subsections detail these operational stages.

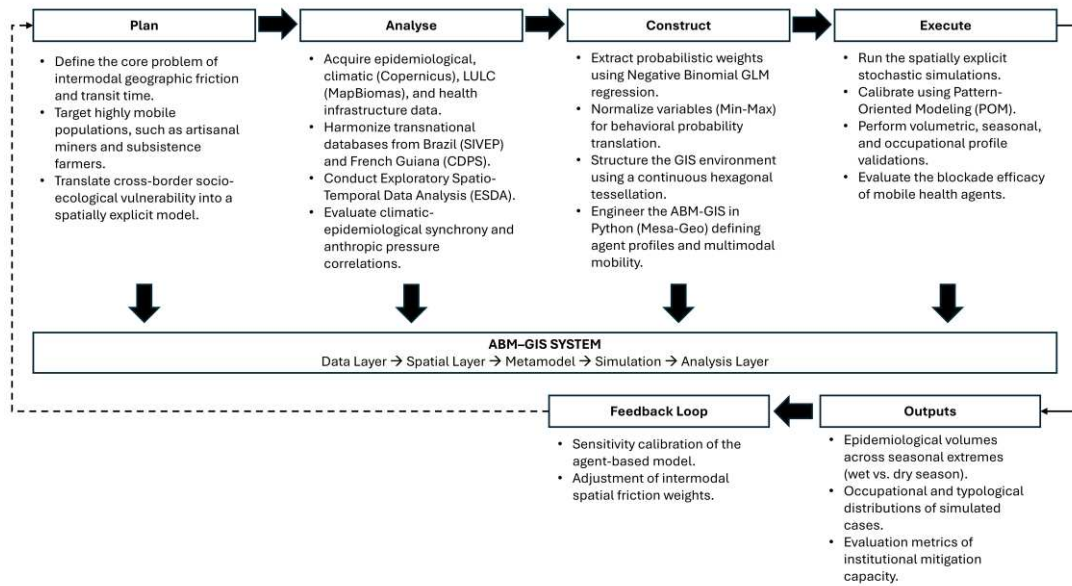


Figure 2. The PACE (Plan, Analyse, Construct, Execute) methodological framework developed for the spatially explicit Agent-Based Model (ABM-GIS). The flowchart illustrates the four sequential phases applied to structure the stochastic simulations, translate cross-border socio-ecological vulnerabilities, and evaluate institutional mitigation capacities.

As summarised in Figure 2, the flowchart outlines the full data lifecycle, from the cross-border harmonisation of epidemiological and LULC datasets to the extraction of empirical weights via Negative Binomial regression. The foundational system layer dynamically integrates macro-environmental risks with intermodal geographic friction, while the feedback loop illustrates the iterative sensitivity calibration using Pattern-Oriented Modelling (POM).

2.1. Data Acquisition and Harmonisation.

To establish the spatial and temporal baseline for the ABM-GIS, heterogeneous datasets covering the cross-border Oiapoque basin were acquired and harmonised into a continuous 262-month matrix (March 2003 to December 2024). Supplementary File 1 provides detailed data processing, cleaning protocols, and variable normalisation procedures.

Data Availability

We consolidated all harmonised epidemiological, climatic, landscape, and institutional variables into a unified temporal matrix, which served as the core data infrastructure for subsequent statistical parameterisation. A comprehensive inventory of these variables - explicitly detailing their temporal coverage, original data sources, and units of measurement - is provided in the metadata of the dataset, which is openly available in the Zenodo repository (<https://doi.org/10.5281/zenodo.22663582>)[37].

2.1.1. Epidemiological and Institutional Data

Epidemiological ground truth was extracted from the Malaria Lite 1.2 platform [19,20], which consolidates registries from both the Brazilian surveillance system (SIVEP-Malária) and the French Guianese health centres (CDPS). The critical variable for spatial anchoring in the GIS environment was the Probable Place of Infection (LPI), yielding a spatially filtered dataset of 81,808 notifications. To quantify institutional mitigation capacity, geographic coordinates of healthcare facilities and the active volume of mobile health agents were extracted from the National Registry of Healthcare Establishments (CNES/DataSUS) [38].

2.1.2. Environmental and Landscape Dynamics

Continuous meteorological variables were obtained from the Copernicus ERA5-Land reanalysis dataset [27,28] (approx. 9 km resolution). To capture the biological dynamics of the *Anopheles* vector and the extrinsic incubation period of *Plasmodium*, temporal lags were applied: a one-month lag (Lag 1) for mean temperature and a two-month lag (Lag 2) for accumulated precipitation, reflecting vector maturation and the ecological recession of water bodies. Concurrently, landscape evolution was characterised using 30-metre spatial resolution data from MapBiomas Amazonia (Collection 10) [29,30]. The spatio-temporal matrix isolated variables representing strong anthropic pressure and environmental risk, specifically Agriculture, Water Bodies, and Urban Areas.

2.2. Statistical Parameterisation and Territorial Risk Modelling

Prior to advanced statistical parameterisation, an Exploratory Spatio-Temporal Data Analysis (ESDA) was conducted on the consolidated 262-month matrix to identify historical seasonality patterns and preliminary socio-environmental correlations. As part of this exploratory phase, independent pairwise Negative Binomial regressions were run to evaluate the individual epidemiological significance of each variable and select robust predictors. Following this exploratory phase, a two-step statistical framework was developed to independently evaluate historical determinants and derived unbiased probabilistic weights for the spatial simulation.

To quantify the retrospective efficacy of institutional mitigation, an initial baseline Negative Binomial Generalised Linear Model (GLM) was fitted, including active mobile health agents alongside environmental predictors. Preliminary analysis of the dependent variable (monthly counts of total infections) revealed strong overdispersion, a common phenomenon in vector-borne epidemiological data driven by clustered outbreaks [39,40]. The Negative Binomial distribution effectively overcomes the restrictive assumptions of

traditional Poisson regression [39,41]. This first model served exclusively to establish the historical context of the transboundary healthcare system's performance.

Although evaluating historical health agent deployments is critical for context, retaining institutional variables in the final spatial-risk equation of the ABM-GIS introduces a methodological flaw. Embedding institutional mitigation within the baseline environmental GLM while simultaneously applying a clinical blocking function to the simulated agents creates an artificial double-counting effect. To strictly avoid this compounded statistical bias, all institutional variables were deliberately stripped from the spatial parameterisation.

The baseline environmental risk was modelled as a unified function of the socio-ecological triad (Agriculture, Water bodies, Urbanisation) and lagged climatic triggers. To overcome the severe seasonal multicollinearity between temperature and precipitation - which frequently distorts coefficients in standard models - a Regularized Negative Binomial GLM equipped with an Elastic Net penalty (L1/L2) was applied [42,43]. This penalized regression technique shrinks overestimated coefficients and handles collinear confounders, extracting mutually adjusted topological weights while preserving the biological cycle.

To ensure interoperability between the statistical model and the subsequent computational algorithm, all independent variables were Min-Max normalised to a continuous range between 0 and 1 [44,45]. This step ensures the resulting regression coefficients (beta) are dimensionless and directly comparable, allowing them to be translated into behavioural probability weights. The analysis was implemented in a Python environment using the Statsmodels library. Rather than using traditional p-value significance filtering, the Elastic Net penalty performed feature selection by shrinking redundant coefficients, producing mathematically robust friction and attraction surfaces that govern agent mobility across the territory.

2.3. Spatially Explicit Agent-Based Model (ABM-GIS)

2.3.1. A One Health conceptualisation of the system

Before detailing the computational architecture of the spatial environment and the agent behaviours, it is necessary to establish how the theoretical dimensions of One Health are operationalised within the simulation framework [10,11]. The ABM-GIS translates complex, real-world socio-ecological interactions into programmable variables [7,46,47]. Table 1 outlines this conceptual mapping, demonstrating how climatic drivers and landscape transformations act as explicit ecological proxies for *Anopheles* habitat suitability, and how they interact with human mobility and cross-border governance to represent the malaria system holistically.

Table 1. Operationalisation of the One Health framework dimensions into the ABM-GIS variables and indicators for the Oiapoque basin.

One Health Dimension	Operationalisation in the ABM-GIS (Oiapoque Basin)	Model Variables & Indicators
Environmental Health	Continuous macro-climatic variables (temperature, precipitation) and structural landscape elements (LULC, agriculture, deforestation, water bodies).	temp_C_lag1 (T_{normL1}); prcp_mm_lag2 (P_{normL2}); LULC_Farming; LULC_Water; LULC_Urban
Vector Ecology	Indirectly modelled through ecological proxies; environmental and climatic variables determine spatial habitat suitability and the temporal conditions for vector abundance and breeding.	Macro-environmental risk burden (λ_{macro}); Dynamic spatial risk exponent ($S_{dynamic}$); Temporal development lags (Lag 1 and Lag 2)
Human Health & Vulnerability	Stochastic probability of malaria infection, cumulative spatial exposure during transit, and occupational susceptibility.	Daily baseline probability (P_{base}); Final probability of infection (P_{final}); Physiological carrier period (14 days)
Human Behaviour & Socioeconomic System	Pendular multimodal mobility networks, occupational profiles (artisanal gold miners, subsistence farmers, urban dwellers), and transit times across geographical frictions.	Occupational ratios (pct_mine, pct_farm); Distance-to-speed ratios (30-400 km/day); Occupational exposure periods (18-26 days); Spatial jitter effect
Health System & Governance	Spatial deployment of mobile health agents, governance friction exerted by permanent health facilities, and the systemic challenge of cross-border coordination between Brazil and French Guiana.	Field health workers (TT_AGENTS); Blocking factor (Fblocking); Permanent facility indicator function (I_{ubs})

Note: ABM-GIS: Agent-Based Model integrated with Geographic Information Systems; LULC: Land Use and Land Cover. Variables such as T_{normL1} (temperature), P_{normL2} (precipitation), λ_{macro} (environmental risk burden), P_{base} (baseline probability), and I_{ubs} (permanent facility indicator) represent the mathematical parameters and functions coded into the stochastic spatial simulations.

To visually synthesise this operationalisation, Figure 3 illustrates the coupled socio-ecological dynamics that govern the simulation. The flowchart maps the continuous feedback loop in which climatic triggers and landscape alterations cascade into vector habitat suitability, which in turn dictates the stochastic exposure of mobile human populations and is ultimately intercepted by the institutional friction of the health system. The entire system is enveloped by the overarching challenge of cross-border governance.

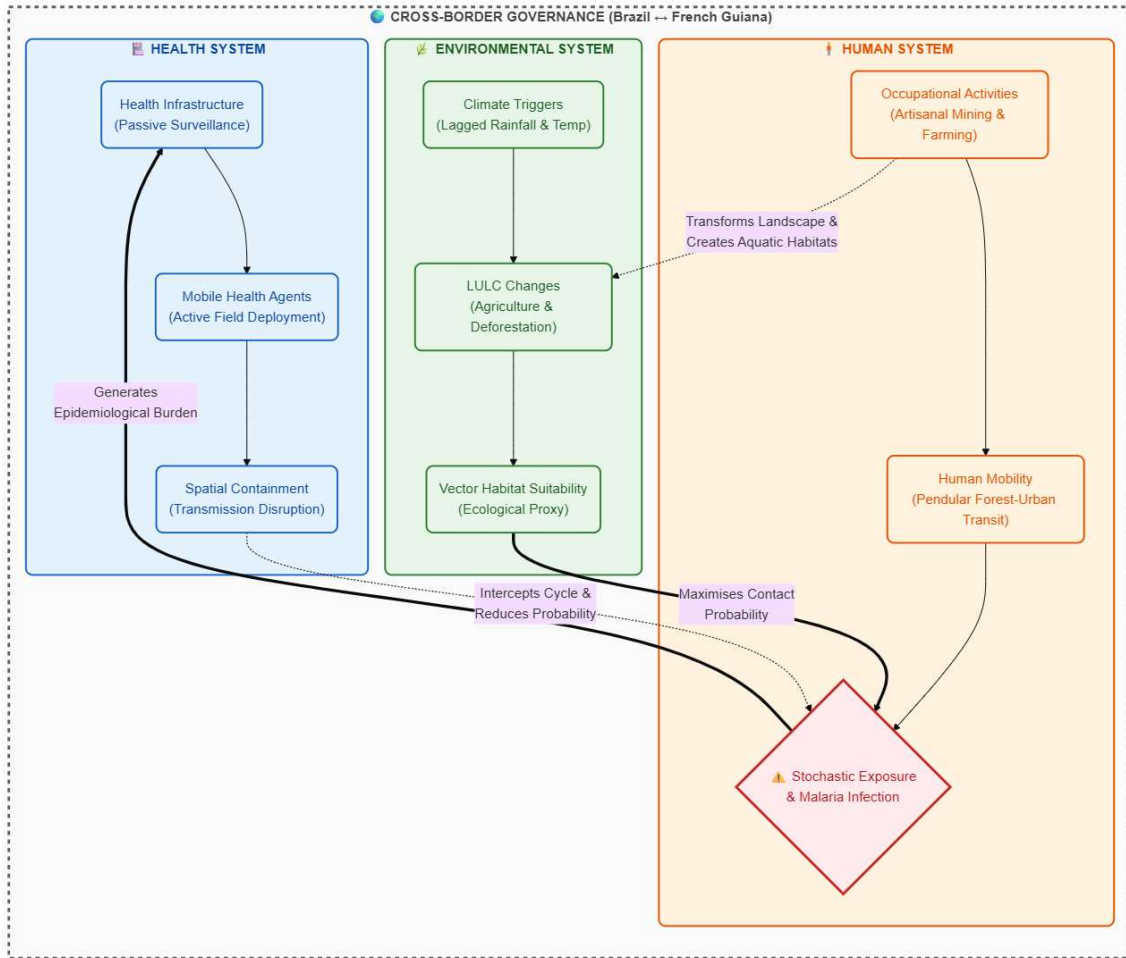


Figure 3. Conceptual One Health framework of the ABM-GIS. The framework illustrates dynamic interactions among the environmental, human, and health systems within a transboundary governance context. Environmental triggers and occupational activities drive human mobility and vector habitat suitability, maximizing contact probability. Simultaneously, the health system intercepts this cycle through passive surveillance and active spatial containment by mobile health agents, ultimately modulating the stochastic probability of infection.

2.3.2. Spatial Environment Architecture and Topological Integration

The simulation environment was built on a high-resolution spatial data infrastructure in vector GeoJSON format, designed for direct integration into a Python environment [26]. The cross-border Oiapoque basin was discretised using a continuous hexagonal tessellation with an approximate cell radius of 1 km [48–50], establishing the year 2023 as the baseline environmental and demographic cross-section.

To endow each hexagonal cell with the necessary simulation attributes, multiple independent data sources were integrated in the GIS environment via spatial intersection and topological containment, transforming heterogeneous raster and vector data into continuous variables per cell. This topological aggregation incorporated land use classes from MapBiomas [30] and residential population counts from WorldPop [18]. Crucially, each hexagon was topologically flagged for the presence or absence of terrestrial roads (OpenStreetMap [51]) and waterways (HydroRIVERS [52]), creating the navigable routing graph and intermodal friction paths needed to calculate agent displacements across the territory [53–55].

Finally, the institutional healthcare infrastructure (CNESST) was integrated by mapping Basic Health Units and equivalent posts using their geographic coordinates and aggregating the number of facilities and available health agents within each cell through spatial overlay [31,56]. This procedure successfully condensed environmental, demographic, and institutional heterogeneity into a unified topological grid, where each hexagon serves as a landscape agent holding dynamic variables that interact in real-time with populations and mobile health agents [32,33].

2.3.3. Agent Model Specification and Computational Dynamics (ODD Protocol)

The spatially explicit agent-based modelling was fully developed in Python using the *Mesa* framework and its geospatial extension, *Mesa-Geo* [26]. The methodological architecture follows the ODD (*Overview, Design concepts, and Details*) protocol and operates on a discrete temporal scale in which each iteration (tick) corresponds to one day. The model's backbone integrates macro-climatic risk factors with micro-spatial frictions extracted from statistical modelling, establishing a dynamic vector field that governs population mobility and stochastic contagion rates.

From a One Health perspective, the ABM-GIS provides a computational representation of the interactions between environmental conditions, vector-mediated transmission, human behaviour and mobility, and institutional health responses [7,46,47]. Rather than modelling malaria transmission strictly as an isolated epidemiological process, the model represents transmission risk as an emergent property of a coupled socio-ecological system [10,11,57]. Environmental conditions shape landscape suitability for vector transmission [7,8,47]; land-use change and occupational activities influence human exposure [7,58]; mobility connects otherwise spatially separated transmission environments [57,58]; and health interventions modify infection probability through targeted territorial action [9,46,47].

In compliance with the ODD protocol architecture, the model's design concepts are operationalised through core behavioural mechanisms: *Sensing* is driven by the agents' continuous reading of the hexagonal cell's dynamic environmental and institutional variables ($S_{dynamic}$); *Adaptation* and movement are governed by pendular responses to intermodal spatial friction and distance-to-speed ratios; *Stochasticity* is

explicitly embedded in the daily probabilistic draw of infection (P_{final}) and spatial jitter effects around occupational destinations; and macro-level epidemiological patterns emerge bottom-up from the daily interactions between individual human agents and their dynamic spatial environment (hexagonal cells), rather than through direct human-to-human contact.

Crucially, at the human-vector-environment interface, although the mosquito vector is not explicitly represented as an autonomous moving agent in the current model, vector ecology is incorporated directly through these dynamic environmental variables [46,47]. Temperature, lagged precipitation, proximity to water bodies, and land-use patterns function mathematically as deterministic ecological proxies for the processes governing vector abundance, habitat suitability, and the probability of vector-human contact [7,8,58]. This proxy-based representation constitutes the core operationalisation of the One Health perspective within the spatial grid, ensuring that the epidemiological risk emerges from the physical landscape rather than spontaneous contagion [7,10,11].

To ensure full methodological transparency and reproducibility, the complete Python script - alongside the detailed parameters for non-Euclidean mobility routing, spatial jitter effects, and occupational exposure periods - is openly available in the Zenodo repository [37].

The mathematical backbone of the model integrates macro-climatic risk factors with micro-spatial frictions to govern population mobility and stochastic contagion rates, as defined by the following core formulations:

A. Macro-Environmental Risk Formulation

The baseline monthly infection burden within the cross-border basin is estimated using a log-linear equation that mathematically translates the coefficients obtained from the Regularized Negative Binomial Generalized Linear Model (Elastic Net). The specific numerical values in the equation come from empirical coefficients estimated from the 262-month historical series, providing an unbiased ecological baseline rather than heuristic approximations. The aggregated magnitude of expected cases (λ_{macro}) is defined by:

$$\lambda_{macro} = e^{5.9018 + 0.6094T_{normL1} - 0.441P_{normL2}}$$

In this mathematical formulation, the model intercept ($\beta_0 = 5.9018$) a critical epidemiological meaning. Because all predictors were Min-Max normalized, it represents the logarithm of the expected number of malaria cases within the basin under baseline environmental conditions - specifically, when the climatic triggers are at their absolute historical minimums. Ecologically, this intercept quantifies the irreducible endemic floor

of the transboundary frontier: the continuous baseline transmission sustained by perennial habitats and persistent human mobility, independent of acute seasonal weather peaks.

The coefficients multiplying the climatic predictors act as temporal elasticity weights that exponentially amplify or suppress this endemic baseline. By using Elastic Net regularization, the severe seasonal collinearity between temperature and rainfall was resolved, allowing both variables to be retained with their correct biological signs. The positive weight of +0.6094 assigned to the one-month lagged temperature (T_{normL1}) preserves the fundamental mechanism of the Plasmodium Extrinsic Incubation Period (EIP), quantifying the exponential increase in vector reproduction gradients triggered by air warming. Conversely, the negative coefficient of -0.441 assigned to the two-month lagged accumulated precipitation (P_{normL2}) reflects the flushing effect of breeding sites during severe rainfall peaks, reducing larval density past the water saturation threshold—a dynamic thoroughly documented in Amazonian health geography [59–61].

Crucially, to prevent the methodological flaw of double-counting institutional efficacy, health agent deployments were deliberately excluded from this macro-environmental equation, ensuring that the simulation's baseline volume is dictated strictly by unchecked climatic drivers before any spatial blocking functions are applied.

B. Landscape Parameterisation and Justification of Attraction Weights

To execute the spatial downscaling of the macro-environmental risk (λ_{macro}) into the micro-geographic scale of the hexagonal grid, each hexagonal cell dynamically calculates a local spatial risk exponent ($S_{dynamic}$). This equation translates empirical regression coefficients into epidemiological friction, incorporating the active presence of healthcare professionals:

$$S_{dynamic} = 1.11 \cdot LULC_FARM - 0.13 \cdot LULC_WATER - 2.33 \cdot LULC_URBAN$$

The magnitude and sign of each numerical weight in this equation are justified by the ecological and socioeconomic nature of the pioneer fronts within the Oiapoque basin. The regularized weight of +1.11 assigned to agricultural zones (LULC_Farm) confirms these surfaces as the primary hubs of occupational vulnerability, where fragmented deforestation and farming maximise the edge effect and human-vector contact [62,63]. Inversely, the strong negative weight of -2.33 associated with the urban footprint (LULC_Urban) serves as an epidemiological protective factor, mimicking the effect of vegetation clearing and housing improvements that mitigate indoor transmission in towns. Notably, under Elastic Net regularization, water bodies (LULC_Water) were retained with a mild repulsive weight (-0.13). This indicates that when adjusted for the high-risk agricultural edge - which captures the true micro-habitats of the vector - the

mere presence of bulk water surfaces at a 1-km resolution operates spatially as an uninhabitable barrier to human settlement rather than a direct occupational hotspot.

To simulate the spatial diffusion of environmental risk beyond artificial geometric boundaries, the model applies a low-pass spatial smoothing filter. The final probabilistic weight of a cell (W_{t+1}) is a composite of its internal risk and the mean risk of all immediately adjacent intersecting cells, weighted at an 80/20 ratio [64,65]:

$$W_{t+1} = 0.8 \cdot e^{(S_{dynamic})} + 0.2W_{neighbors}$$

C. Agent Profiles, Multimodal Mobility, and Spatial Jitter

At the initialization phase ($t = 0$), the instantiated human population is anchored to residential baseline geometries that strictly follow the WorldPop demographic density [18]. This baseline population is subsequently categorized into three occupational profiles: Miners, Farmers, and Urban dwellers, distributed according to regional probability parameters (pct_mine and pct_farm). Given the systematic structural underreporting of informal artisanal mining and temporary agricultural labour in official demographic censuses, these proportions were established as a representative heuristic baseline for an Amazonian pioneer frontier [22,23,66]. Crucially, the model's objective is not to assert an exact demographic census, but to simulate the relative epidemiological vulnerability. The disproportionate infection burden subsequently observed among simulated miners emerges from the algorithmic rules of their pendular mobility into high-friction remote zones, rather than their absolute initial population size.

Agent mobility is governed by pendular economic attraction and multimodal spatial friction. Transit times are non-Euclidean and explicitly calculate the distance-to-speed ratio across topological networks. Movement speeds are parameterised as 400 km/day on terrestrial roads, 200 km/day on navigable rivers, and 30 km/day for off-road/walking trajectories [67]. Upon arriving at a high-risk occupational destination (such as a mining site), the algorithm applies a spatial jitter effect, a random uniform geometric deviation, to scatter workers around the centroid, mimicking the diffuse spatial footprint of artisanal camps. Occupational exposure periods are strictly parameterised, retaining agents at their work destinations for continuous intervals of 18 to 26 days before returning home [68,69].

D. Infection Stochasticity and Institutional Mitigation

The translation of environmental risk into actual disease occurrence is a daily stochastic process at the individual level. The daily baseline probability (P_{base}) of a susceptible agent contracting malaria is derived from the cell's spatial attractiveness ratio relative to the entire basin ($\frac{W_{local}}{W_{total}}$), divided by the local population density, and multiplied by an empirical field calibration factor of 1.4:

$$P_{base} = \left(\frac{\lambda_{macro} \times \left(\frac{W_{local}}{W_{total}} \right)}{30 \times Pop_{local}} \right) \times 1.4$$

If an agent is in transit between cells, the risk is averaged between the origin and destination, and an attenuation modifier of 0.85 is applied to P_{base} to reflect continuous movement. The expected monthly infection burden dictated by macro-climatic risk (λ_{macro}) is computationally disaggregated into an averaged uniform daily pressure ($\frac{\lambda_{macro}}{30}$). While this abstraction assumes an evenly distributed incubation pressure across the 30-day simulation window—rather than a continuous daily interpolation of weather variables—it isolates the contagion process stochasticity to the agent's spatial routing and intermodal friction, which is the core focus of this study.

This baseline probability is subjected to a dual-layered institutional mitigation mechanism. Mobile Health Agents originate from existing healthcare facilities and execute field missions in remote, densely populated areas lasting 20 to 25 days. The final probability of infection (P_{final}) evaluated against the daily stochastic draw, is calculated as:

$$P_{final} = \max(0.0, \min(1.0, P_{base} \times F_{blocking}))$$

Where the blocking factor ($F_{blocking}$) has a hard minimum cap of 0.08 (representing an absolute maximum mitigation efficacy of 92%) and is calculated dynamically:

$$F_{blocking} = 1.0 \times 0.45^{I(ubs)} \times 0.42^{HealthAgents}$$

These specific institutional multipliers are heuristic. In line with established practices for agent-based modelling in spatial epidemiology [70], when precise empirical clinical coefficients are absent, the adoption of fixed baseline values is methodologically sound provided they are subjected to rigorous sensitivity testing. Until explicitly calibrated we conducted a comprehensive clinical sensitivity analysis (Scenarios 6–9) to verify that conclusions regarding spatial saturation hold across both highly optimistic and pessimistic clinical profiles. To ensure model robustness, we conducted a comprehensive clinical sensitivity analysis (Scenarios 6–9) to verify that conclusions about spatial saturation hold across both highly optimistic and pessimistic clinical profiles.

To prevent double counting the protective effect of health workers, their institutional friction was isolated entirely within this stochastic mitigation layer $F_{blocking}$, rather than modifying the underlying environmental spatial risk ($S_{dynamic}$). The operational framework governing these mobile health agents follows strict algorithmic rules: **(1) Capacity and Deployment:** In scenarios projecting institutional reinforcement (e.g., a 20% increase), the fractional increment is converted into whole integer agents. These additional agents are instantiated at randomly selected existing permanent health

facilities (UBS). **(2) Destination and Constraints:** Their field destinations are stochastically chosen from populated cells across the basin. Crucially, their operational capacity is constrained by the exact same multimodal geographical friction defined for human populations. Transit times across these networks are mathematically subtracted from their 20 to 25-day field missions. **(3) Intervention Mechanics:** The mitigation multipliers (0.42 per mobile agent, 0.45 for permanent facilities) and the hard cap of 0.08 simulate the combined clinical impact of rapid diagnostics, bed net distribution, and timely antimalarial treatment that mitigates the probability of infection in high-risk zones [71]. Once infected, an agent remains an active carrier for a strict physiological period of 14 days before returning to a susceptible state [72,73]. Finally, these specific institutional multipliers are heuristic. Until explicitly calibrated by external clinical field trials, they serve to establish an exploratory scenario evaluating assumed institutional efficacy thresholds, rather than providing an exact predictive clinical measure.

2.4. Seasonal Calibration and Pattern-Oriented Validation (POM)

Because official epidemiological data often aggregate the Probable Location of Infection (LPI) to the notifying health facility without exact coordinates [12,22,23], classical point-to-point precision validation is impractical and prone to the ecological fallacy. Alternatively, the computational performance of the ABM-GIS was evaluated using the POM methodology [74,75].

This approach aims to evaluate whether the model can adequately approximate the macroscopic epidemiological and demographic signatures of the real system under contrasting environmental stress scenarios. Two temporal cross-sections were selected to represent Amazonian seasonality: a high-transmission peak (characterised by elevated temperatures and low precipitation) and a low-transmission trough (characterised by heavy rainfall and lower temperatures).

The validation operated across two macroscopic dimensions:

1. **Volumetric and Seasonal Validation:** The model's capacity to replicate the overall epidemiological curve was evaluated by measuring the fit between simulated and actual cases across seasonal extremes, testing the accuracy of the macro-environmental risk equation (λ_{macro}).
2. **Occupational and Typological Profile Validation:** The simulated incidence rates (cases per 1,000 agents) generated across LULC-classified zones (Mining, Agriculture, and Urban) were cross-referenced with the official socio-demographic profile of notified cases. This validates the ABM-GIS pendular mobility architecture and intermodal friction while explicitly preventing circular reasoning.

To account for stochasticity and establish strict methodological controls, the simulation used a Monte Carlo approach across a core set of five distinct scenarios. These

combined seasonal extremes with institutional variations (baseline versus a 20% increase in mobile health agents), alongside a static Null Scenario (Scenario 5) where all intermodal occupational mobility was disabled to isolate the mechanical effect of spatial friction. Additionally, to ensure robustness against parameter uncertainty, four supplementary scenarios (Scenarios 6–9) were executed as a clinical sensitivity analysis to test optimistic and pessimistic intervention profiles. For each scenario, the model ran 30 independent iterations (totalling 270 simulation runs across the validation and sensitivity phases), systematically aggregating macroscopic outputs to calculate robust descriptive statistics for comparison against official notification records.

3. Results

This section presents the quantitative findings and empirical validations from spatial modelling (ABM-GIS) for malaria propagation within the cross-border Oiapoque basin. The results are organised into four central dimensions, grounded in the conceptual framework of Socio-Ecological and Epidemiological Systems (SEES).

3.1. Spatio-Temporal Dynamics and Baseline Exposure.

The longitudinal analysis over the last two decades reveals a continuous and linear growth trajectory of the population residing in the cross-border basin (Figure 4). Between 2003 and 2024, the population size nearly doubled, creating a constant demographic pressure on the area. Historically, it would be expected that this population densification would be accompanied by a proportional increase in exposure and in the number of cases. However, the total infections curve shows marked, non-linear fluctuations, contrasting sharply with the stable demographic growth observed over the same period.

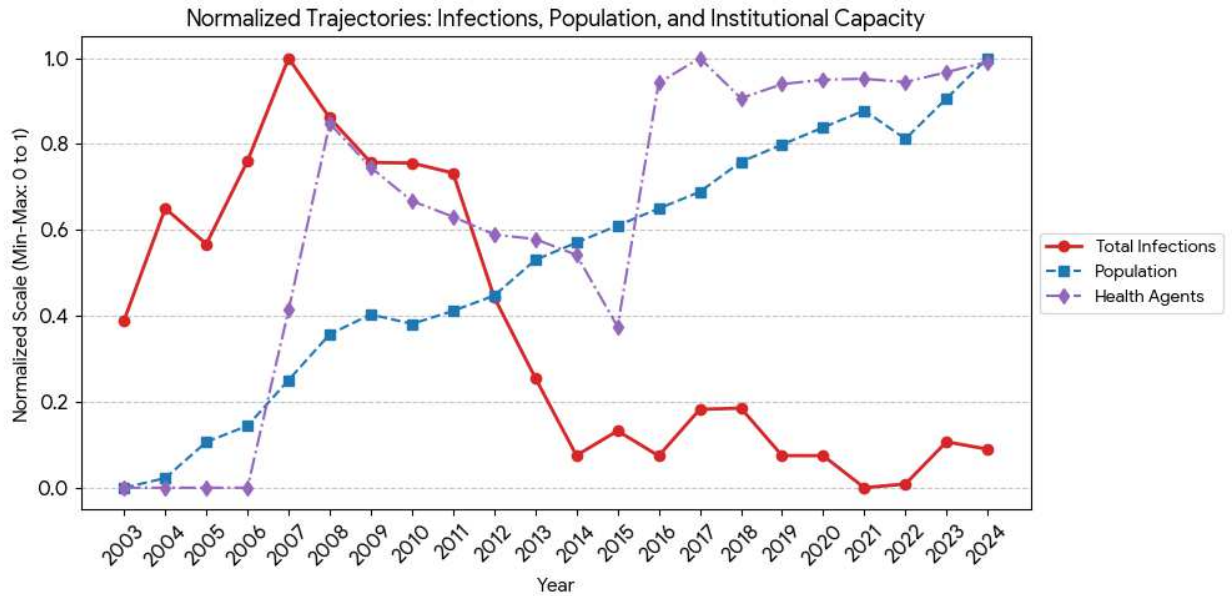


Figure 4. Min-Max normalized trends (0 to 1) comparing total malaria infections, population size, and the number of active health agents between 2003 and 2024.

A notable phenomenon in the historical series is what we define as epidemiological decoupling, or the "Scissor Effect", which becomes evident from the year 2013 (Figure 4). From this milestone onward, a sustained reduction in overall infection volume is observed, diverging from the historical trajectory alongside population growth. This inversion of the case curve coincides with the consolidation and escalation of the number of Health Agents allocated to the territory. This temporal alignment suggests that increased on-the-ground human resources contributed to practical institutional friction, effectively mitigating residential and community-level exposure before the disease reached new fronts of population expansion. Although this ecological correlation precludes definitive causal claims—given that macro-level socio-economic drivers, such as commodity market fluctuations governing artisanal mining intensity, introduce significant external variance—the robust temporal alignment strongly supports the hypothesis that active health governance acts as a key mitigator of baseline environmental pressure, even if its macroscopic impact eventually faces saturation limits against highly mobile occupational groups.

Beyond annual variation, malaria dynamics in the cross-border basin show a markedly seasonal pattern. Infections are not distributed linearly throughout the year, concentrating significantly in the last quarter (Figure 5). Analysis of monthly average cases indicates a consolidated epidemic peak that reaches its absolute apex between October and November. This temporal concentration shows that transmission does not act chaotically but follows a climatic clock that prepares the environment for disease proliferation at specific times of the year.

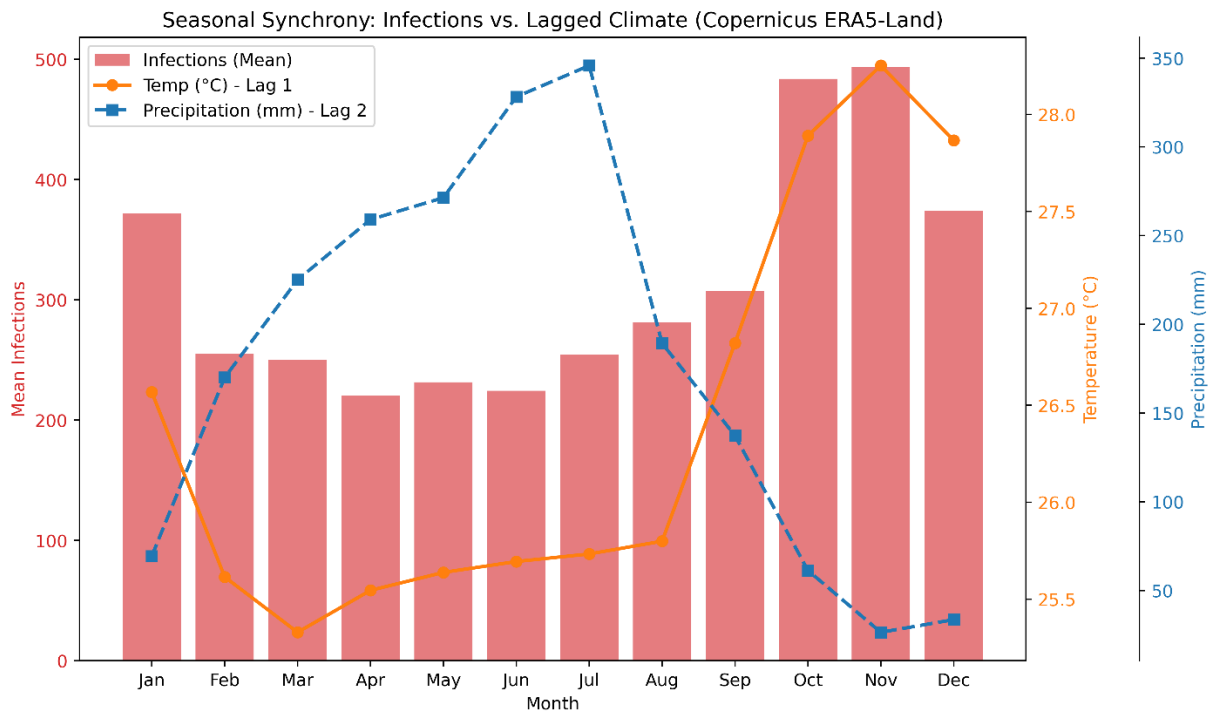


Figure 5. Monthly average of malaria infections plotted against lagged temperature (1-month lag) and precipitation (2-month lag) data derived from Copernicus ERA5-Land.

The epidemic peak is driven by fundamental climatic triggers that act with time lags (Figure 5). The first is the Thermal Trigger (Temperature - Lag 1), which demonstrates a direct alignment between thermal elevation and the surge in malaria cases in the immediately following month. This exact one-month interval reflects the time of accelerated extrinsic incubation of *Plasmodium* under conditions of increased heat.

Complementarily, the Hydrological Preparation (Precipitation - Lag 2) acts as the ecological precursor of the outbreak (Figure 5). These lag structures are biologically plausible and consistent with delayed effects of climatic conditions on vector development and habitat suitability. Nevertheless, interpret them as selected temporal associations rather than exact estimates of the biological delay between climate exposure and infection.

3.2. Variable Selection and Regularized Spatial Parameterisation

Selecting variables for the spatial model required a rigorous two-step evaluation of socio-environmental determinants. First, independent pairwise Negative Binomial regressions were conducted to screen candidate parameters (Table 2). Six variables showed statistically significant bivariate associations with monthly malaria counts, confirming the individual epidemiological relevance of macro-climatic drivers, land-use categories, and institutional presence. The complete table detailing these initial bivariate associations is provided in Supplementary Material 2.

Table 2. Pairwise Negative Binomial Generalized Linear Model (GLM) coefficients and statistical significance used for exploratory variable screening.

Variable	ABM Weight (Coefficient)	Value	Standard Error
LULC_Urban	-2.6298	< 0.001	0.2207
TT_AGENTS	-1.0813	< 0.001	0.1966
prcp_mm_lag2	-1.0352	< 0.001	0.228
temp_C_lag1	0.7027	0.0043	0.246
LULC_Water	1.1993	< 0.001	0.1829
LULC_Farming	2.0413	< 0.001	0.2073

Note: LULC: Land Use and Land Cover; TT_AGENTS: Active field health agents. The climatic variables incorporate temporal development delays, where temp_C_lag1 represents temperature with a one-month lag, and prcp_mm_lag2 represents precipitation with a two-month lag.

Quantifying these initial unadjusted associations reveals the primary vectors historically driving epidemic risk. Agricultural areas (LULC_Farming) exhibited the largest positive coefficient, while consolidated urbanisation (LULC_Urban) and the allocation of human resources (TT_AGENTS) provided substantial spatial and institutional friction forces. However, relying solely on these bivariate associations for the spatial simulation risks overestimating baseline effects due to unadjusted confounding factors and seasonal multicollinearity. Furthermore, as established in the methodological framework, embedding the institutional variable (TT_AGENTS) directly into the environmental risk equation would artificially double-count its mitigation capacity within the subsequent ABM-GIS logic.

Therefore, to extract unbiased probabilistic weights, a Regularized Negative Binomial GLM equipped with an Elastic Net penalty was implemented, deliberately excluding TT_AGENTS. The presented analysis (Figure 6) details the mutually adjusted regression coefficients derived from this regularized model, which serve as the definitive spatial weights for the simulation.

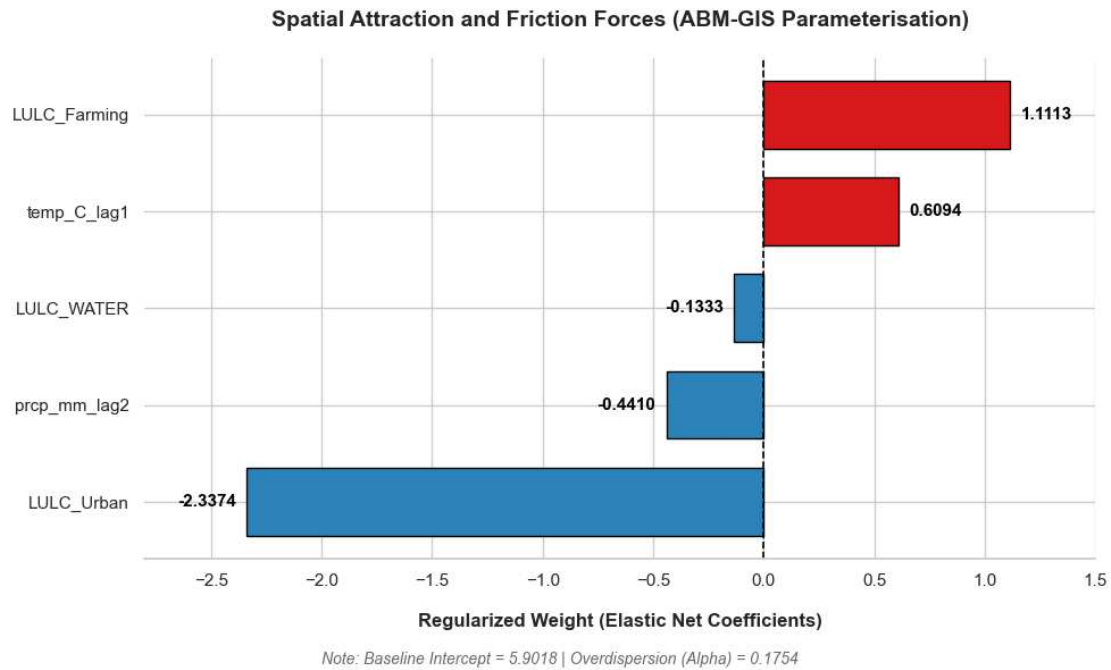


Figure 6. Horizontal bar chart displaying the final mutually adjusted weights (Elastic Net Regularized Negative Binomial GLM coefficients) used to parameterize attraction surfaces (positive values) and friction forces (negative values) within the ABM-GIS simulation. The dispersion parameter (Alpha) for the baseline macro-environmental equation is 0.1754 (95% CI: 0.1448 – 0.2059), confirming overdispersion and validating the Negative Binomial specification.

Under the multivariate regularized adjustment (Figure 6), agricultural areas (LULC_Farming) retained a strong positive coefficient (+1.11), confirming fragmented farming zones as the primary risk-related landscape component. Consolidated urbanisation (LULC_Urban) maintained its role as the main containment barrier (-2.34). Notably, when adjusted for the high-risk agricultural edge, bulk water surfaces (LULC_Water) assumed a mildly negative weight (-0.13), indicating that at a 1-km resolution, they operate spatially as uninhabitable barriers to human settlement rather than direct occupational hotspots.

Finally, the climatic triggers preserved their biological integrity despite their inherent collinearity. Temperature (temp_C_lag1) maintained a positive driver effect (+0.61) on vector reproduction, while precipitation lagged by two months (prcp_mm_lag2) demonstrated an adjusted negative association (-0.44). This confirms the hypothesis that periods of intense, accumulated rainfall temporarily flush breeding habitats, a seasonal fluctuation now mathematically captured as an unbiased baseline parameter within the simulation.

3.3. Spatial Simulation (ABM-GIS) and POM Validation

The spatial simulation stage, developed within the ABM-GIS environment, aimed to test the region's epidemiological behaviour under different environmental pressures, establishing baseline climatic scenarios for evaluation. The analysis initially focused on the contrast between two seasonal extremes while maintaining the current institutional capacity: Scenario 1, characterised by high temperatures and low rainfall, and Scenario 2, defined by low temperatures and high rainfall.

The cartographic projection capability constitutes a primary analytical product of the ABM-GIS, allowing the visualisation of the tangible spatial dispersion of the disease along the French-Brazilian border. To assist in visualising these dynamics, specific output maps were generated (Figures 7a and 7b) that illustrate the spatial distribution of risk under each projected environmental configuration. Visual analysis of these simulated surfaces allows precise identification of geographical *hotspots*, where environmental exposure effectively penetrates and sustains the endemic baseline within the territory.

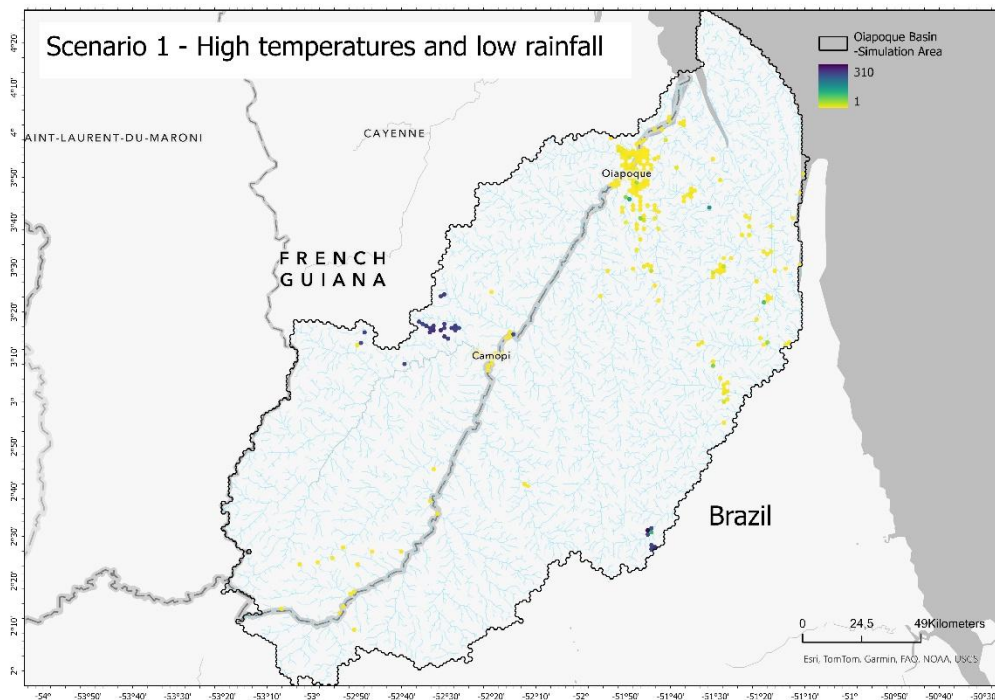


Figure 7a. Spatial distribution of simulated malaria cases across the Oiapoque basin under Scenario 1 (high temperatures and low rainfall). Colour gradients represent the concentration of simulated cases per spatial unit, peaking at 310 cases. The dispersion highlights heightened spatial risk driven by favourable thermal conditions, predominantly clustering in transboundary and mining areas.

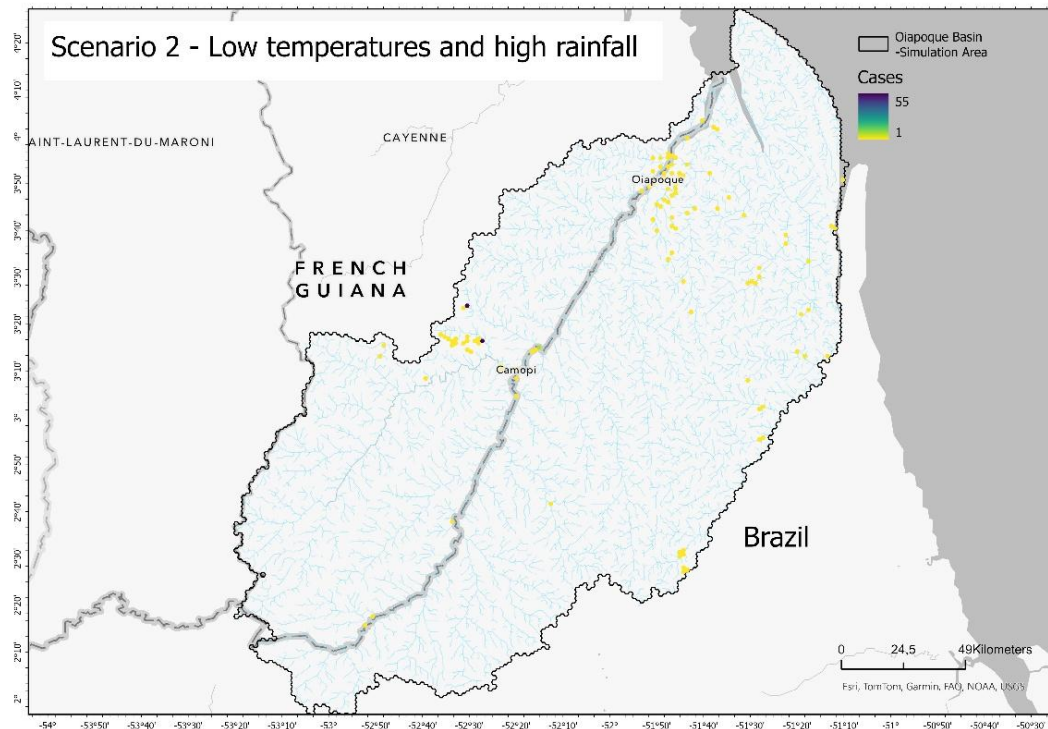


Figure 7b. Spatial distribution of simulated malaria cases across the Oiapoque basin under Scenario 2 (low temperatures and high rainfall). Colour gradients display the contraction of transmission intensity, with a maximum peak of 55 cases. This pattern demonstrates the environmental constraints imposed by unfavourable climatic parameters on the simulated epidemiological dynamics.

The model results show a disparity in disease burden that depends heavily on the established climatic context (Table 3). In Scenario 1, which simulates the seasonal peak of thermal vulnerability, the model generated a significant average of 208.2 total malaria cases. In contrast, Scenario 2 resulted in an average of only 73.7 simulated cases, reflecting a period of low transmission driven by environmental conditions. As demonstrated, the model captures the signature of the seasonal trigger, indicating that elevated thermal conditions combined with retained rainfall provide favourable ecological conditions for amplified transmission in the basin.

Furthermore, the simulation evaluated the impact of institutional reinforcement across these seasonal extremes. Increasing the active contingent of mobile health agents by 20% resulted in a consistent, albeit modest, reduction in disease burden. During the seasonal peak (Scenario 3), average cases decreased from 208.2 to 198.5, while during the seasonal trough (Scenario 4), cases fell from 73.7 to 69.0. This dynamic indicates that while targeted institutional mitigation provides a crucial protective layer, the absolute volume of transmission in the cross-border basin remains overwhelmingly constrained by the underlying socio-ecological and climatic baseline.

Crucially, the internal validity of the spatial mobility architecture is demonstrated by the Null Model (Scenario 5). By explicitly disabling intermodal occupational mobility

and restricting agents strictly to their residential baseline exposure, the average number of simulated cases plummeted to an irreducible floor of 14.7. This dramatic reduction effectively isolates the mechanical role of spatial friction, mathematically confirming that pendular mobility towards high-risk, fragmented landscapes - rather than static residential exposure - is the primary engine driving the epidemiological burden in this pioneer frontier.

Table 3. Simulated epidemiological outcomes across seasonal climatic extremes under current institutional capacity.

Scenario	Climate & Institutional Description	Mean Total Cases	Standard Deviation	Minimum	Maximum
1	High Temp, Low Precip (Current HA)	208.2	16.4	180	247
2	Low Temp, High Precip (Current HA)	73.7	10.4	55	99
3	High Temp, Low Precip (+20% HA)	198.5	14.5	155	221
4	Low Temp, High Precip (+20% HA)	69.0	7.9	52	83
5	Null Model (No Occupational Mobility)	14.7	3.3	8	21

Note: HA: Health Agents. The descriptive statistics (mean, standard deviation, minimum, and maximum) represent the distribution of total stochastic malaria cases generated by the ABM-GIS iterations under varying combinations of temperature and precipitation. Scenario 5 serves as a static methodological control, explicitly removing intermodal occupational mobility to isolate base residential exposure.

To ensure the simulation's internal robustness and explicitly rule out circular reasoning (tautology) regarding occupational vulnerability, the POM technique was applied using true incidence rates (cases per 1,000 agents). This validation contrasted the dynamic epidemic peak (Scenario 1) against a static Null Scenario (Scenario 5) where all intermodal occupational mobility was disabled. The incidence rate distribution of revealed a profound asymmetry in vulnerability driven entirely by spatial friction (Figure 8). Under normal mobility, the Miners group showed an overwhelming predominance of infections, registering 26.82 cases per 1,000 agents (an average of 94.7 absolute simulated cases). Crucially, when occupational mobility was disabled in the Null Scenario, this severe disparity vanished entirely, resulting in mathematically indistinguishable baseline residential rates across all profiles (Miners: 0.25; Farmers: 0.24; Urban: 0.16). This confirms that the model's epidemiological hierarchy emerges dynamically from pendular

exposure to high-risk environmental ecotones, rather than from hard-coded occupational probabilities.

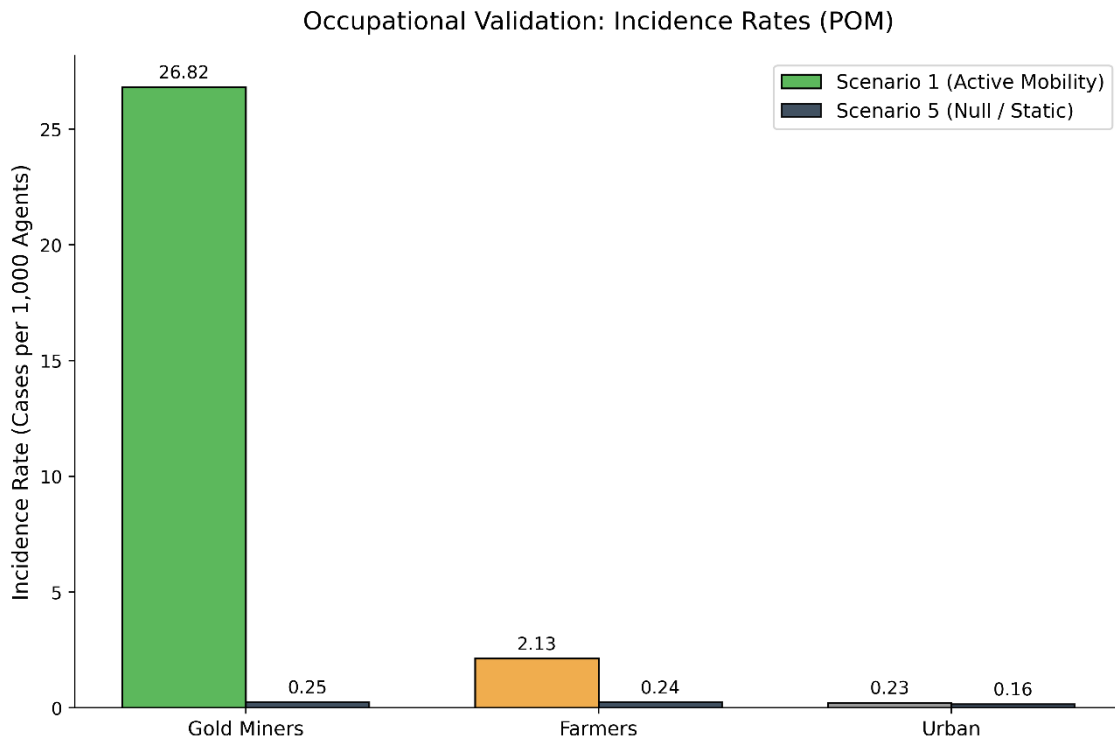


Figure 8. Occupational validation comparing simulated malaria incidence rates (cases per 1,000 agents) between the epidemic peak with normal pendular mobility (Scenario 1) and the static Null Scenario (Scenario 5). This stark contrast shows that miners' heightened vulnerability is mechanically driven by their spatial mobility toward hazardous environmental ecotones, and that the occupational hierarchy emerges from the interaction between the specified mobility rules and the environmental-risk surface, rather than from occupation-specific infection probabilities.

With significantly lower representation during active mobility, Farmers presented an incidence rate of 2.13 cases per 1,000 agents (an average of 11.3 absolute cases), whilst agents classified as Urban recorded only 0.23 cases per 1,000 agents (6.0 absolute cases) during the same peak period. This pronounced risk hierarchy reproduced by the ABM-GIS reflects the varying degrees of environmental exposure inherent in each spatial footprint. As the flattened incidence rates in the Null Scenario visually confirm, miners' severe vulnerability is not a tautological artifact but a mechanical consequence of their intense mobility and deep insertion into remote forest ecotones. By parameterising these distinct pendular trajectories, the exploratory spatial model effectively isolates intermodal spatial friction as the primary driver of occupational risk.

The next step involved externally validating of the model by comparing the internal simulation outputs with real epidemiological data. For this purpose, the official registry of malaria cases notified in the municipality of Oiapoque throughout the year 2025 (Figure 9) was used, categorised according to the activities undertaken by the patients in the 15 days prior to diagnosis. The qualitative comparison between the

behaviour of the simulated agents and the empirical occupational records served to assess the model's capacity to reproduce macroscopic risk distribution.

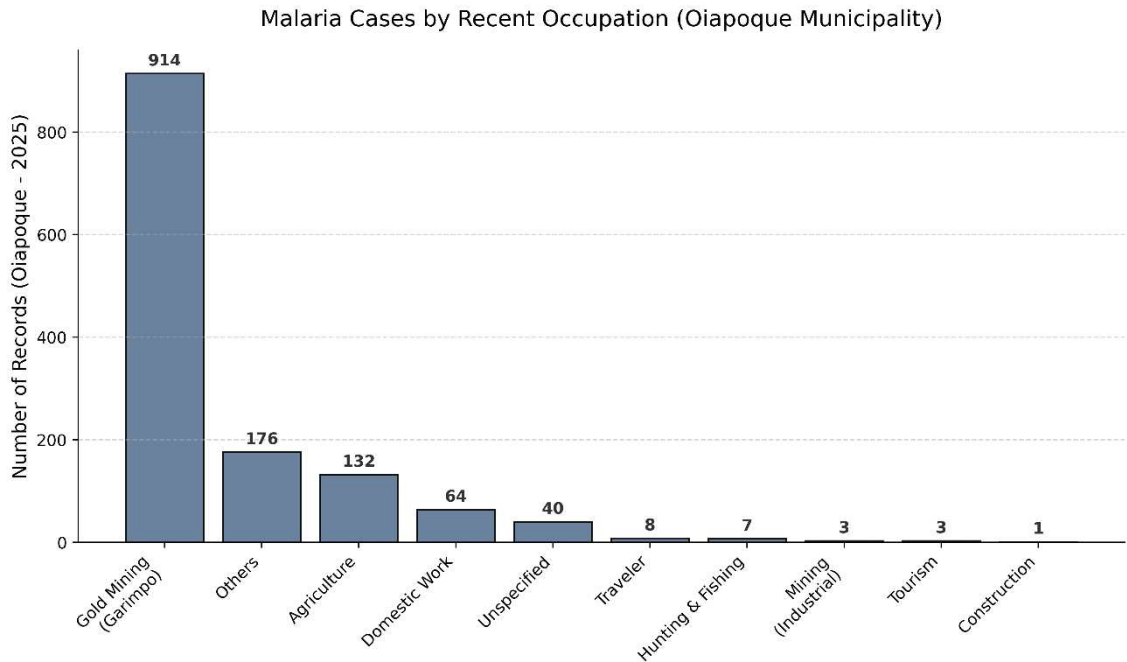


Figure 9. Number of malaria cases notified in the municipality of Oiapoque during 2025, categorised by the patient's reported occupation in the 15 days prior to diagnosis. Data source: Brazilian Ministry of Health (2026).

The bar chart of real cases from 2025 (Figure 9) validated the model's alignment with the epidemiological reality at the border [76]. In the official registries, mining activities (garimpo) alone led the statistics with a massive volume of 914 records, followed by Agriculture (132 records). Crucially, when isolating the empirical dataset strictly to the three socio-occupational profiles represented within the ABM-GIS framework - excluding unclassified administrative noise such as 'Others' or 'Unspecified' - the empirical distribution mirrors the internal infection hierarchy generated by the simulation. Within this matched comparative universe, real miners accounted for 82.2% of cases, farmers 11.8%, and urban residents 5.8%. The spatial model (Scenario 1) reproduced this systemic behaviour, simulating a proportional split of ~84.6% for Miners, ~10.1% for Farmers, and ~5.4% for Urban agents.

3.4. Evaluation of Institutional Mitigation.

The final stage of the spatial simulations focused on evaluating institutional mitigation, exploring the marginal utility of expanding human resources within the territory. To this end, the ABM-GIS model contrasted the baseline response capacity against an exploratory scenario projecting a 20% increase in allocated mobile health

agents. Crucially, to address earlier methodological constraints and eliminate spatial double-counting, the mitigative action of these agents was strictly limited to the clinical blocking layer (reducing susceptibility), without artificially altering the terrain’s underlying environmental friction.

The corresponding chart (Figure 10) details the quantitative analysis of these projections. As demonstrated, the 20% institutional reinforcement yielded a mathematically conservative reduction in cases during the epidemic peak (falling from a mean of 208.2 to 198.5 cases, within the bounds of the ± 16.4 stochastic variance). Furthermore, during the seasonal trough (Scenario 2 vs. 4), adding health agents produced only a marginal macroscopic impact (73.7 vs. 69.0 mean cases), as environmental constraints had already severely restricted the baseline spatial risk. This lack of significant statistical variance illustrates the saturation limits of institutional intervention: simply scaling static institutional capacity offers diminishing returns against an epidemiological profile driven by the intense pendular mobility of vulnerable groups embedded in remote, inaccessible ecotones.

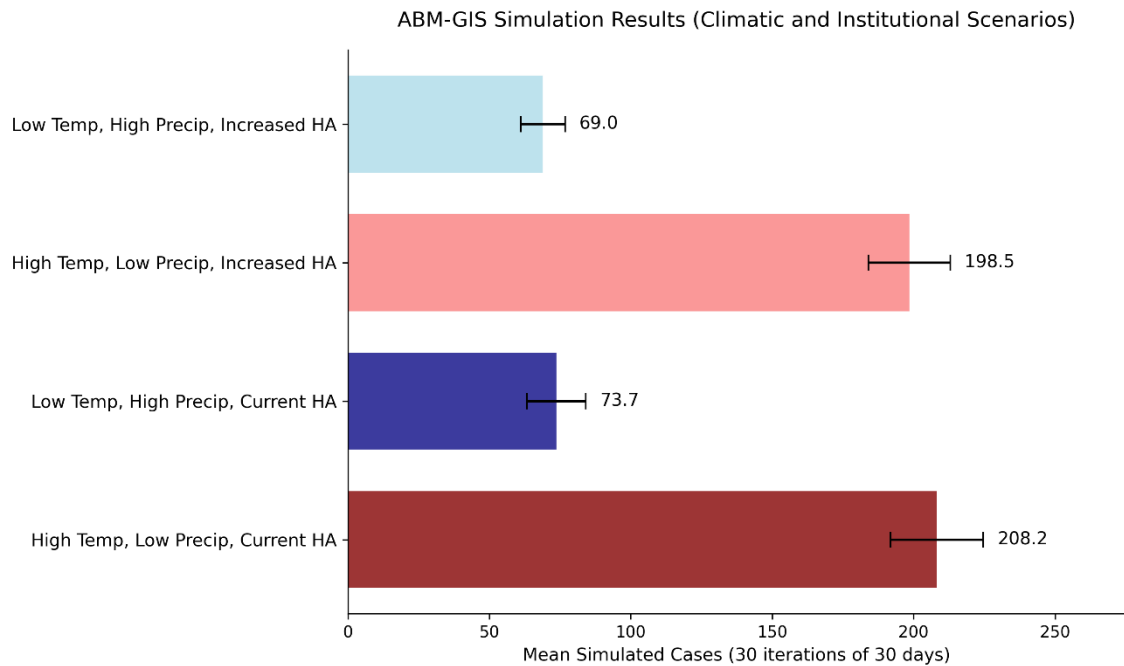


Figure 10. Horizontal bar chart presenting the mean simulated malaria cases from the ABM-GIS under four distinct climatic and institutional scenarios. Error bars indicate the standard deviation across 30 iterations, showing that the marginal reduction from a 20% increase in Health Agents (HA) falls within the model's stochastic variance.

In the high-transmission scenario (High Temperature and Low Precipitation – Figure 10), characterised by elevated temperatures and low rainfall, environmental pressure on the basin reaches its ecological limit. With the current institutional capacity, the model projected an average of 208.2 simulated cases. With a 20% increase in the

number of agents, the simulation recorded an average of 198.5 cases. This difference yields a nominal reduction of approximately 4.7% of the total infections. This reduction remains heavily constrained by the model's stochastic variance (standard deviations of ± 16.4 and ± 14.5 , respectively). This limited proportional impact indicates that the modest variation reflects mechanical saturation rather than effective macroscopic containment.

Although this marginal impact contrasts with historical baseline improvements, it reflects current spatial and epidemiological saturation. The model shows that when climatic risk reaches its absolute peak in remote ecotones, simply expanding the health workforce at static residential or urban nodes fails to intercept the outbreak's primary drivers. The intense pendular mobility of highly vulnerable groups (such as miners) continuously exposes them to environmental hazards far beyond the operational reach of community-based health agents, effectively neutralizing the systemic benefits of institutional reinforcements.

The evaluation of institutional mitigation reveals a similarly saturated behaviour when applied in a low context of environmental endemicity, albeit driven by distinct ecological mechanisms. The low-transmission scenario (Low Temperature and High Precipitation – Figure 10) establishes a baseline in which the environment itself is the primary limiting factor for vector proliferation. The simulation data clearly reflect this abrupt drop in baseline ecological pressure.

Under these restrictive climatic conditions, baseline institutional capacity operates in an environment already suppressed by nature, resulting in an average of 73.7 simulated cases. With the 20% increase in health agents, the model recorded 69.0 cases. This minor fluctuation (falling well within the ± 10.4 case baseline standard deviation) reflects a residual epidemiological impact, confirming that when environmental constraints severely restrict spatial risk, intervention capacity reaches absolute redundancy.

The outcomes across these scenarios highlight the spatial limitations of public health interventions in Amazonian frontiers. The diminishing returns observed under both environmental extremes indicate that the healthcare system has reached a structural threshold. Additional static resources do not yield proportional epidemiological gains because they cannot overcome the spatial friction inherent to deep-forest occupational mobility. This finding reinforces that the true value of spatial modelling is not to justify continuous blanket hiring, but to identify systemic bottlenecks, proving that future mitigation strategies must shift from scaling static personnel towards developing occupationally targeted interventions in high-risk ecotones.

To ensure the robustness of these findings against parameter uncertainty, a clinical sensitivity analysis was conducted (Scenarios 6 through 9). By modifying the mitigative multipliers of health facilities and agents to represent pessimistic and optimistic clinical profiles, the model evaluated whether improved intervention efficacy could overcome spatial barriers. Strikingly, under the epidemic peak, the simulated outcomes remained statically anchored: pessimistic baseline efficacy yielded an average of 202.7 cases (Scenario 6), while optimistic efficacy produced 199.2 cases (Scenario 8). Even with a

20% institutional increase (Scenarios 7 and 9), the variations remained entirely within the stochastic noise margin (see Supplementary file 2). This sensitivity analysis solidifies the premise that the barrier to malaria containment in the Oiapoque basin is not the clinical quality of the intervention, but the geographical impossibility of systematically intercepting highly mobile populations in remote ecotones.

4. Discussion

4.1. The Validation and Predictability of the Ecological Subsystem

Malaria dynamics in the cross-border basin followed macro-environmental fluctuations. The literature widely supports the premise that climatic and hydrological cycles (such as the flood pulse) act as primary regulators of vector abundance and disease exposure risk [24,59–61,77]. Furthermore, the synchrony between the infections simulated by the ABM-GIS and the Copernicus ERA5-Land historical series supports the model structural alignment of the spatial model, given that these climate reanalyses show a highly validated correlation with data from physical stations [78]. The fact that the simulated epidemic peak invariably occurs in the last quarter of the year reinforces that the ecological subsystem acts as a rigid climate clock, a pattern of seasonal concentration that finds empirical parallels in other municipalities of the Amazon basin [79]. Together, these factors support the hypothesis that regional epidemiological risk is an ecologically orchestrated process.

This predictability operates through a climate cascade marked by highly specific time lags that drive ecological interactions. The results showed that the precipitation peak occurs with a two-month lag (Lag 2) relative to the disease outbreak [60,79]. Physically, initial intense rains exert a flushing effect, destroying incipient aquatic habitats and dispersing larvae [59,61,78,80]. It is only after the decline of this water volume that the waters stabilise on the riverbanks, forming the perennial pools that serve as an ideal nursery for the *Anopheles* vector [59,60].

Concomitantly, the thermal rise acts as the final trigger with a one-month lag (Lag 1) [61,81]. This thirty-day window accurately reflects the time required for the acceleration of the Extrinsic Incubation Period (EIP). As widely established in vector biology, high temperatures accelerate metabolic development and shorten *Plasmodium*'s maturation cycle in the mosquito [78,82]. In vitro assays with local species (such as *An. aquasalis* infected with *P. vivax*) also corroborated this heat-exacerbated vector efficiency: temperatures around 28°C produced markedly higher sporogonic maturation than lower temperatures [83], culminating in the subsequent regional epidemiological explosion.

Notwithstanding the biological clarity of these triggers, the supremacy of the climate clock requires interpretative caution in certain Amazonian contexts. Despite its

undeniable mechanistic role in vector development (EIP), longitudinal epidemiological studies indicate that, due to the low annual thermal amplitude typical of the equatorial zone, heat variation tends to act as a statistically secondary factor [84]. In these environments, rainfall volumes and abrupt variations in river levels usually dominate seasonal malaria fluctuations [84].

Beyond this purely meteorological caveat, it is fundamental to recognise that climate predictability is not universal and encounters critical exceptions driven by anthropogenic action. The literature demonstrates that the "rigid climate clock" model is frequently refuted in mining areas [85]. In these environments, cyclicity tests point to the absence of statistical seasonality [85]. The continuous creation of artificial breeding sites stemming from excavations subverts the natural hydrological cycle, maintaining heightened exposure perennially and stochastically year-round [85]. Additionally, social dynamics such as disorderly migrations and governmental vector control interventions introduce additional "noise" that alters epidemiological behaviour. This consensus aligns with our spatial simulation findings (Section 3.3), showing that cross-border malaria cannot be predicted solely from baseline climate variables without accounting for the friction of human pendular mobility [79,80,85].

4.2. The Human-Environment Interface: Land Use and Socio-Ecological Vulnerabilities

Although climate dictates the rhythm of transmission, model evidence indicates that landscape alteration drives epidemic severity [24,25]. Agricultural expansion emerged as the strongest positive spatial predictor (+1.11), illustrating the practical value of a One Health interpretation: land-use changes simultaneously alter ecological conditions, reshape human mobility, and increase opportunities for vector-human contact [7,8,57,58]. Conversely, the strong negative friction of consolidated urbanisation (-2.34) and the mildly protective spatial effect of bulk water bodies (-0.13) highlight how landscape and hydrological transformations govern environments favourable - or hostile - to vector development [7,8,47]. These findings indicate that malaria risk emerges not from a single environmental or epidemiological determinant, but from the interaction between ecosystem transformation and human activity [11,57,58]. For instance, the clear-cutting of primary forest and forest fragmentation generate vast ecotone zones (abrupt ecological transition edges) [14,15]. These fragmented fringes bring together residual moisture and ideal breeding sites (partially shaded pools and streams) [14,16,63] with vulnerable human settlements [14,63]. This spatial overlap creates ideal conditions for continuous exposure and epidemiological spread, precisely characterising the "frontier malaria" scenario, where severity peaks in deforested areas and young settlements [15].

In this context, a profound complementarity between the variables becomes evident: climate acts primarily as a timer (dictating the "when", through intra-annual seasonality and time lags) [62], whilst anthropogenic action, manifested by the loss of forest cover that regulates the abundance of the main vector, determines the severity and

the "where" (the spatial distribution of risk) [63]. Without human intrusion into the ecotones, the favourable environment would not result in an outbreak.

However, biome-scale models highlight a critical nuance: risk does not reside in isolated agricultural use. Areas with consolidated anthropogenic use (extensive plantations or cleared pastures) can actually reduce risk through habitat loss and landscape homogenisation [62]. The higher risk of dissemination lies not in agriculture itself, but in contact zones (spatial mosaics) where preserved forest or water-border areas interface with areas recently transformed by human land-use activities [62].

Another challenge in land-use-based analyses is artisanal mining (garimpo). The literature recognises illegal mining as a highly severe driver of outbreaks, propelled by the high mobility of workers who commute between urban areas and isolated forest mines, dispersing parasite strains [22,23,66,86]. The strong concentration of simulated infections among artisanal miners in our model - registering a staggering incidence rate of 26.82 cases per 1,000 agents during peak exposure, compared to just 2.13 for farmers and 0.23 for urban dwellers - further demonstrates the interconnected nature of the coupled socio-ecological system [10,11]. Mining is not simply an isolated occupational risk: it represents a coupled process in which illicit economic activity transforms the environment, creates artificial aquatic habitats in excavated pits [7,11,57], concentrates vulnerable populations in remote areas [9], and generates recurrent pendular mobility between forest sites and urban settlements [57,58]. Together, these processes modify ecological conditions and patterns of human exposure, ultimately sustaining malaria transmission across the border [9,57,58]. However, capturing this dynamic is complex, as official notification systems, such as SIVEP-Malaria, suffer from severe geographical inaccuracies, under-reporting due to self-medication, and static omissions in these areas [22,23,66].

Although high-resolution remote sensing (such as Landsat and Sentinel) is actively used to monitor fine forest alterations [87], demystifying the idea of an absolute "blind spot" under the tree canopy, purely conventional spatial mapping of land cover faces limits in translating the clandestinity and inaccuracy of local data [22,23].

To overcome the limitations of static notification flows and to explore dynamics that empirical mobility networks [22] have been adopted. Within the scope of this work, the ABM-GIS approach demonstrates its methodological advantage by moving beyond the map pixel to computationally incorporate artisanal miners' commutes and risk behaviour. Although empirical field data [22,23,66] already confirm the high prevalence in miners, the internal POM validation of the model - specifically the stark contrast in incidence rates between active commuting scenarios and the static Null Scenario - provides robust evidence that this extreme vulnerability is an emergent property of spatial friction rather than a hard-coded assumption. By dynamically parameterising these trajectories, the model adequately captures the mechanical exposure dynamics that are partially invisible or under-reported in conventional spatial analyses.

4.3. Cross-border Governance Dynamics and Institutional Mitigation

The historical results (2003–2024) provide robust empirical validation of the SEES framework, demonstrating that the disease trajectory results from the direct clash between environmental pressures and the social response. The "Scissor Effect" observed from 2013 onwards shows that socio-ecological vulnerability in border zones is not purely a geographical or climatic fatality. The sustained drop in cases, coinciding with the reinforcement of health workers, evidences the mechanism of "institutional friction". Global literature corroborates that active governance and the mobilisation of human resources mitigate spatial risk and reduce disease burden, as observed through interventions on the China-Myanmar border [88], the Elimination 8 initiative in Southern Africa [89], and the Malakit project in the Guiana Shield [21]. Studies conclude that border malaria persists mostly because of systemic operational challenges, rather than local community failures [90]. However, the geographical environment and climate impose real physical limits on this response. Mountainous and forested topographies harbour highly efficient wild vectors that often escape traditional control [21,91,92], while severe rainy-season weather renders roads impassable and a lack of technological infrastructure delays timely notifications and focused investigations [90,91].

The spatial simulations, however, reveal a critical spatial mismatch, showing that this governance model currently operates under non-linear epidemiological saturation. From a One Health perspective, the divergence between the historical success of health agents (capturing urban mitigation) and their marginal impact in the ABM-GIS scenarios illustrates the limitations of static institutional capacity [10,11]. The simulation demonstrated that a 20% increase in staff during the high-exposure peak yielded a statistically insignificant reduction in cases (~4.7%), falling entirely within the model's stochastic variance. This lack of macroscopic impact exposes the health system's physical and spatial ceiling [9]. This mechanical limit was further corroborated by the clinical sensitivity analysis (Supplementary Material 2), which demonstrated that even assuming highly optimistic clinical efficacy, the spatial barrier of the remote forest effectively neutralizes the intervention. While baseline governance successfully protects consolidated settlements, simply scaling static health posts offers diminishing returns against an epidemiological profile overwhelmingly driven by highly mobile groups (such as miners) commuting into deep-forest ecotones far beyond the operational reach of conventional agents. Under extreme climatic pressures and continuous migratory flows, border systems reach a chronic operational bottleneck [21,90]. Conversely, the lack of statistical variation observed when adding personnel in the low-exposure scenario confirms that when the environment itself severely restricts vector proliferation, additional static interventions become entirely redundant. Nevertheless, the literature introduces a critical systemic nuance: in low endemicity settings, the real limit is often not ecological, but stems from political and financial deprioritisation [89,90]. As cases fall, funding is cut and surveillance teams are reduced under the false premise that the problem is resolved [90]. This institutional weakening leaves the region systematically

exposed to catastrophic resurgences, showing that the ceiling imposed by low transmission is also political [90].

This state of saturation points to an urgent need to transition the health management model. The practical application of this research argues against purely reactive or spatially static strategies. The true value of the ABM-GIS, combined with the identification of 1- and 2-month climate lags, lies in its capacity to function as a spatial "early warning system". Climatic predictability allows health planning to move beyond *a posteriori* response and enable surgical, anticipatory allocation. Because adding resources to static community posts offers negligible gains against frontier dynamics, the literature supports positioning mobile teams at critical logistical nodes, intercepting isolated high-mobility miners (*garimpeiros*) [21,86] and seasonal agricultural workers [91] before they penetrate deep-forest ecotones. Proactive, localised interventions at these transit points have shown strong mitigating efficacy [21,86]. Implementing these targeted actions, however, runs into the structural rigidity of public health systems [89,90,93]. Bureaucratic barriers, centralised delays in the procurement of supplies [90], and the frequent misalignment between the governmental fiscal year and the epidemiological year hinder the agile transfer of funds [89,93]. Ultimately, the cross-border nature of the Oiapoque basin further reinforces the need for a One Health perspective to overcome these barriers [9–11]. Ecological processes, vector habitats, and human mobility extend seamlessly beyond administrative boundaries, whereas surveillance and health interventions remain rigidly organised according to national jurisdictions [7,57,58]. Consequently, malaria control cannot be understood solely as a function of individual national health systems [9,11]. Effective control requires robust cross-border coordination that integrates the human, environmental, and institutional dimensions of the shared socio-ecological system [10,11,57].

4.4. Methodological Limitations and Future Work

Despite the robustness achieved through the analytical integration of Geographic Information Systems and the Agent-Based Model (ABM-GIS), this research design has intrinsic limitations that must be duly contextualised.

Firstly, the spatial discretisation of the environment through a hexagonal tessellation with an approximate 1 km radius introduces a necessary spatial generalisation but remains susceptible to the Modifiable Areal Unit Problem (MAUP). In tropical health geography, human-vector friction and ecotone ecology frequently operate at a micro-local scale. However, adopting this resolution was an unavoidable methodological compromise to ensure the computational viability of stochastic simulations across the entire extent of the cross-border Oiapoque basin, enabling seamless topological reconciliation between global databases (such as WorldPop and ERA5) and the multimodal network.

Furthermore, although the ABM-GIS generates high-resolution continuous risk surfaces, classical point-to-point quantitative spatial validation against official

notification data (SIVEP-Malária/CDPS) was deliberately eschewed. In Amazonian cross-border contexts, the Probable Location of Infection (LPI) is structurally hindered by severe spatial uncertainty, as cases are frequently aggregated to the geographic coordinates of the notifying healthcare facility rather than the exact environmental locus of contagion (such as clandestine mining camps). Attempting a quantitative spatial goodness-of-fit against such artificially clustered data would inevitably introduce an ecological fallacy. Therefore, adopting Pattern-Oriented Modelling (POM) is not merely a pragmatic fallback, but a rigorous methodological necessity. POM allows extraction of macroscopic volumetric and occupational signatures from stochastic noise, validating emergent spatial dynamics without overfitting the algorithm to the structural spatial errors inherent to border surveillance systems.

Second, regarding the algorithm's temporal architecture, the simulations were deliberately parameterized for 30-iteration windows (30 days) without a prior stabilization or burn-in period. This design choice aims to isolate and measure the system's stochastic stress during specific seasonal epidemic peaks (a temporal "snapshot"), rather than model the disease's continuous longitudinal cycle. Consequently, while this restriction precludes long-term interannual forecasting, it maximizes computational efficiency and analytical focus when evaluating acute institutional responses at critical environmental thresholds.

A third methodological limitation lies in the purely heuristic formulation of institutional friction. While this study successfully addressed previous spatial double-counting by strictly isolating mitigation to the clinical susceptibility layer - thereby successfully revealing the spatial saturation limits of static interventions - the mathematical decay function utilised to quantify the blocking factor of Health Agents still represents an idealized clinical scenario. It assumes theoretically perfect spatial overlap and uninterrupted operational capacity. Mitigating interventions in cross-border pioneer frontiers face severe logistical friction, such as flooded terrestrial routes during the wet season, exhaustion of rapid diagnostic tests (RDTs), and physical barriers to remote ecotones. This algorithmic abstraction overestimates on-the-ground operational efficiency. Future iterations of this spatial framework should replace the exponential function with a logistic saturation curve, parameterized through empirical surveys of local clinical response capacities to better reflect real-world operational bottlenecks.

Fourth, the relatively high intercept represents the estimated baseline log count when all Min-Max-normalised predictors included in the model are at their observed minimum values. Interpret this baseline cautiously, as the simultaneous minimum of all predictors may not correspond to an observed or epidemiologically meaningful state. The intercept may also capture variation associated with factors not explicitly included in the model, but it cannot be attributed to unobserved processes. Overdispersion is represented separately by the dispersion parameter of the Negative Binomial specification (Dispersion parameter: 0.1754, 95% CI: 0.1448 – 0.2059).

Finally, from an epidemiological perspective, the mosquito vector is not explicitly simulated as an autonomous agent, nor does the model employ a compartmental framework (e.g., SEIR) to calculate the force of infection arising from human-to-vector-to-human interactions. Consequently, the current framework is strictly an exposure-risk ABM, rather than a full mechanistic transmission model. Continuous climatic variations and land-use transformations function as deterministic spatial proxies for vector habitat suitability, dictating an environmental probability draw for infection. While this abstraction limits micro-level entomological analysis, it aligns with the computational scope of this research: by prioritizing the evaluation of human intermodal friction, occupational mobility, and spatial exposure over biological vector mechanics.

Future research should explore directly integrating ABM-GIS outputs with local ecological calendars. Aligning computational early warning systems with the traditional knowledge of seasonal mobility and land-use cycles can provide a more culturally and ecologically resonant framework for anticipatory malaria control.

5. Conclusions

We assessed malaria infection dynamics in the cross-border Oiapoque basin by integrating climate, LULC, and human mobility data within a spatially explicit computational model (ABM-GIS). The approach enabled quantitative evaluation of the spatial limitations of institutional mitigation, empirical parameterisation of socio-environmental forces of attraction and friction, and simulation of risks associated with pendular occupational mobility along the French-Brazilian border.

The model application and POM validation showed that malaria dynamics result from a complex intersection of the ecological clock, landscape alteration, and human geographic friction. Statistical parameterisation confirmed the presence of thermal and hydrological lags. Furthermore, agricultural land emerged as the strongest positive spatial predictor within the regularised Elastic Net model and was therefore incorporated as an attraction component in the spatial-risk surface. Concurrently, the stochastic mobility simulation mirrored the epidemiological reality by identifying artisanal miners as the highest-risk population. Crucially, by contrasting active commuting with a static Null Scenario, the model proved that intermodal transit routes and deep-forest insertion mechanically perpetuate human exposure to high-risk environments. Finally, the evaluation of institutional mitigation revealed the non-linear nature of epidemiological control: while baseline governance successfully mitigates residential risk, scaling static health agents during seasonal peaks reaches a spatial saturation point (yielding mathematically conservative marginal reductions that persist regardless of assumed clinical efficacy). This demonstrates that static institutional reinforcements offer diminishing returns against highly mobile populations, while during periods of low environmental stress, interventions reach absolute redundancy.

In summary, mitigating border malaria requires anticipatory strategic policy actions that transcend static territorial presence. More broadly, this study demonstrates how the One Health paradigm can be operationalised through spatially explicit agent-based modelling. By connecting environmental transformations, vector-related ecological proxies, human mobility, occupational exposure, and institutional health responses within a unified spatial framework, the ABM-GIS captures malaria vulnerability as a true emergent property of a coupled socio-ecological system. This systemic perspective reinforces the urgent need for cross-border strategies that integrate continuous environmental monitoring, mobility-informed surveillance, and health-system preparedness, rather than addressing the disease solely as a reactive clinical or epidemiological problem. Ultimately, health planning in the Amazon can use these models as early warning tools, anticipating seasonal and spatial shifts in risk to deploy mobile health teams when and where they are most likely to disrupt occupational exposure. The model should presently be understood as an exploratory scenario framework rather than an operational forecasting system.

List of abbreviations

ABM-GIS: Agent-Based Model integrated with Geographic Information Systems

CDPS: *Centres Délocalisés de Prévention et de Soins* (French Guianese health centres)

CNES: *Cadastro Nacional de Estabelecimentos de Saúde* (National Registry of Healthcare Establishments)

DataSUS: *Departamento de Informática do Sistema Único de Saúde*

EIP: Extrinsic Incubation Period

ESDA: Exploratory Spatio-Temporal Data Analysis

GLM: Generalised Linear Model

HA: Health Agent

LPI: Probable Location of Infection (ou *Local Provável de Infecção*)

LULC: Land Use and Land Cover

MAUP: Modifiable Areal Unit Problem

ODD: Overview, Design concepts, and Details

POM: Pattern-Oriented Modelling

SEES: Socio-Ecological and Epidemiological Systems

SIVEP: *Sistema de Informação de Vigilância Epidemiológica da Malária* (Brazilian surveillance system)

Declarations

Ethics approval and consent to participate.

The epidemiological data used in this study (SIVEP-Malária and CDPS) were obtained from secondary, anonymized, and aggregated public health surveillance registries. Therefore, formal ethics approval and consent to participate were not required.

Availability of data and materials

The datasets generated and analysed during the current study, including the spatially explicit Python scripts for the ABM-GIS framework, are available in the Zenodo repository, <https://doi.org/10.5281/zenodo.22663582> [37].

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors actively participated in the conceptualization of the study. ALR acquired and harmonized the datasets, developed the ABM-GIS framework in Python, conducted the spatial data analysis, and drafted the primary manuscript. PM, PA and AA contributed to the methodological design and provided substantial critical revisions to the text. EMC, as the group coordinator, secured the research funding, guided the integration of the One Health paradigm into the manuscript, indicators selection and provided a critical review. PM, PA, AA, AL, provided critical reviews of the manuscript and contributed substantial

suggestions for its improvement. All authors read and approved the final manuscript and agreed to be personally accountable for their own contributions, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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