Spatio-temporal modelling of *Leishmania infantum* infection among domestic dogs in rural Brazil

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1. Motivation & aims

The **parasite *Leishmania infantum*** causes zoonotic **visceral leishmaniasis (VL)**, a potentially fatal vector-borne disease of canids and humans. *Leishmania infantum* parasites are transmitted between hosts during blood-feeding by infected female phlebotomine sand flies. With a **principal reservoir host** of *L. infantum* being **domestic dogs**, limiting prevalence in this reservoir may result in a reduced risk of infection for the human population.

One country severely afflicted by zoonotic VL is **Brazil**:

- Serological studies have estimated **prevalence in dogs** to range from 25% to more than 70% in endemic northern regions [1,2].
- A reported 3500 **human VL cases** occur in the country per year, 90% of all VL cases reported in the Americas [3].

Through sand fly abundance and seasonality, *L. infantum* infection, and thus VL cases, has both spatial and temporal dependencies. There is, however, a surprising **scarcity of mathematical models capable of capturing these spatio-temporal characteristics** [4].

Study objectives:

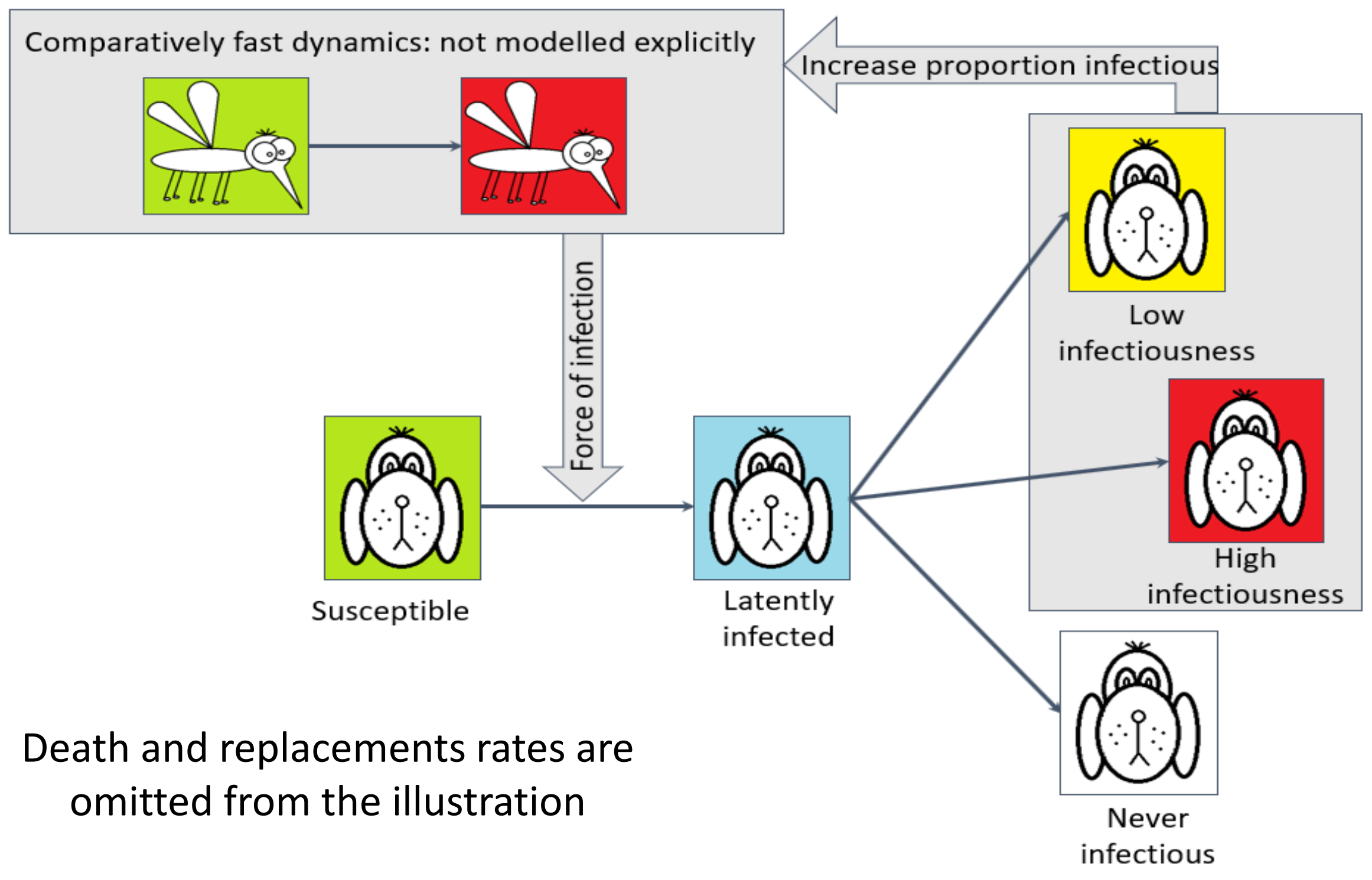
i. Develop a **stochastic, spatial, individual-based mechanistic model** of *L. infantum* transmission in domestic dogs;

ii. For a **rural Brazilian village setting**, identify the model parameters with the **greatest sensitivity** of average *L. infantum* infection prevalence to their variation.

2. Model overview: Infection progression

- Sand fly dynamics operate on a faster time-scale compared to the other host species. Therefore, we did not explicitly track disease state transitions in sand flies.

Fig. 1: **Model of *L. infantum* infection status.**



Death and replacements rates are omitted from the illustration

- Prior work has established heterogeneities in the infectiousness of dogs [5].
- We therefore stratified infected dogs into four states (Fig. 1):
  (i) latently infected;
  (ii) never infectious;
  (iii) low infectiousness;
  (iv) high infectiousness.

3. Model overview: Spatio-temporal framework

- Spatial variation of both hosts (adults and adolescents, children, dogs and chickens) and vectors (sand flies) at the household level.
- Infectious dogs increase the force of infection within a radius of the household (Fig. 2).
- Sand flies exert a force of infection λ on dogs at household *h* at time *t:*

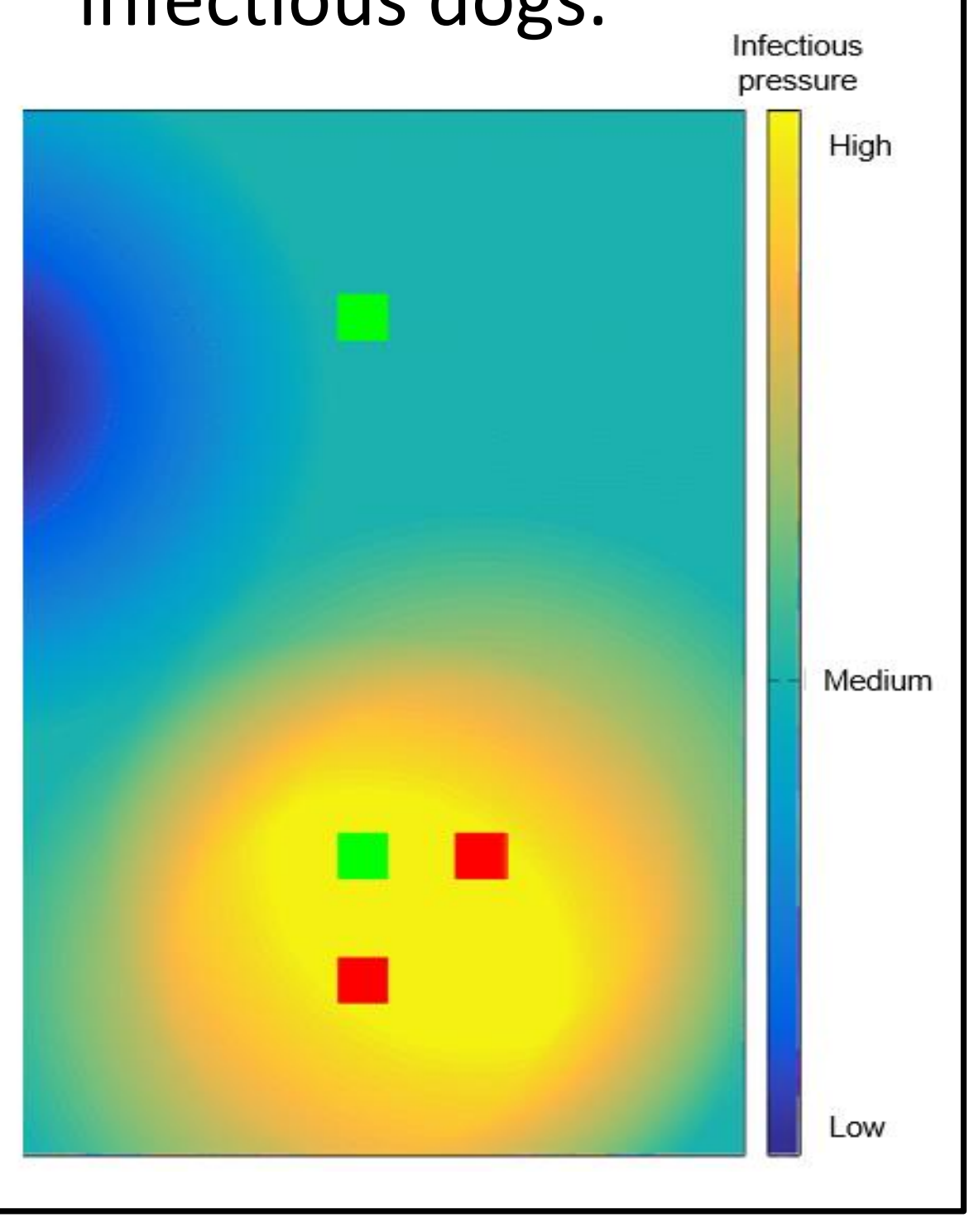
$$\lambda_h(t) = \alpha \times \delta \times L_h(t) \times \eta_{h,\mathrm{dog}}(t) \times \phi_h(t)$$

- α: biting rate of sand flies;
- δ: probability of *L. infantum* transmission to dogs as a result of a single bite from an infectious sand fly;
- L_h: abundance of sand flies at household *h;*
- $\eta_{h,\mathrm{dog}}$: probability of sand flies biting dogs at household *h* as opposed to any other host (linked to host biomass);
- ϕ_h : proportion of sand flies that are infectious at household h.

- Probability for a susceptible dog at household *h* becoming infected on day *t* obeys:

$$p_h(t) = 1 - e^{-\lambda_h(t)}$$

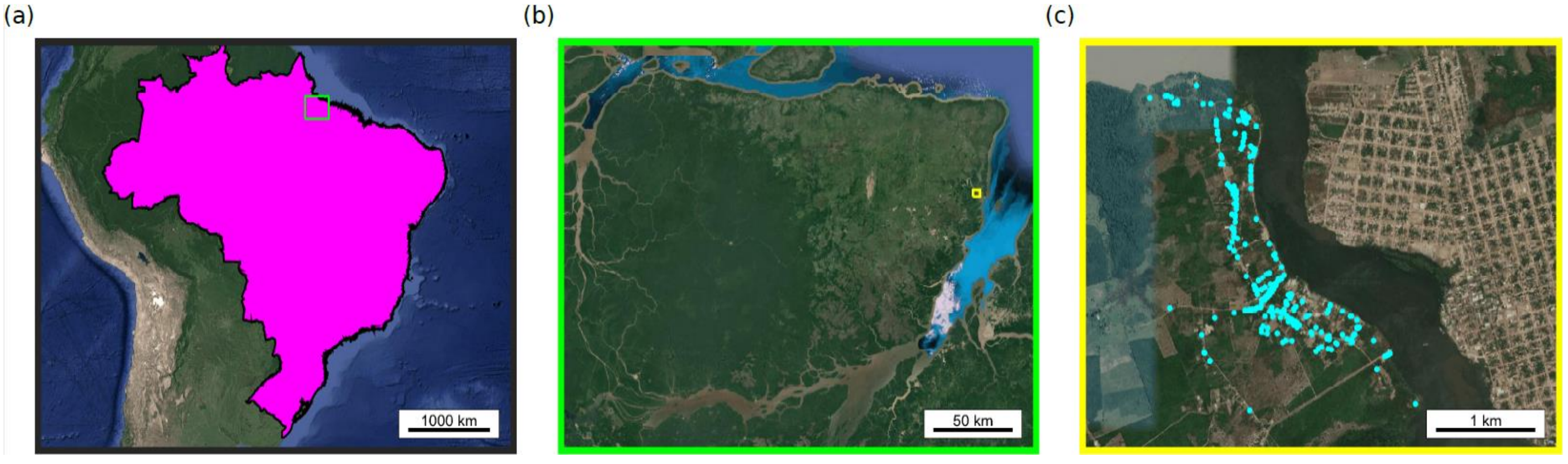
Fig. 2: **Infectious pressure surface illustration.** Greens squares denote susceptible households; red squares denote households with infectious dogs.



4. Application to data

- Used a configuration of 235 households in village of Caldeirão, north Brazil (Fig. 3).
- Host and sand fly populations obtained from Marajó region survey data.

Fig. 3: **Locator maps. (a)** Marajó, situated inside the light green box, within Brazil (shaded in magenta); **(b)** Caldeirão village site (yellow box) within Marajó; **(c)** Household locations within Caldeirão village.



- Statistic of interest was **average infection prevalence**:

$$\text{Average infection prevalence} = \frac{\sum_{t=T-364}^{T} \text{prevalence(t)}}{365}$$

- Performed two sets of analysis:
  i. Simulation study (with biological parameters fixed at baseline values, see Table 1), checking the **plausibility of infection prevalence predictions**;
  ii. Parameter sensitivity analysis, generating a parameter sensitivity ranking using **stochastic sensitivity coefficients** (calculated as outlined in Damiani et al. [6]).

Table 1: **Description of model parameters.**

Parameter ID	Symbol	Description	Baseline value	Other values tested
1	r	Interaction range of dogs (km)	0.30	0.02, 0.70, 2.00
2	π_{never}	Proportion of infected dogs that are never infectious	0.55	0.14, 0.28, 0.42
3	π_{high}	Proportion of infectious dogs that are highly infectious	0.37	0.25, 0.60, 0.80
4	ξ	Probability of a newly introduced dog being infected	0.130	0.0064, 0.2900, 0.4300
5	v	Per capita rate of progression of dogs from latently infected to a further state (days^{-1}). *1/v* is the average duration of the latent period (days)	0.0055	0.0042, 0.0047, 0.0065
6	$\mu_{NeverInf}$	Per capita mortality rate for latently infected and never infectious dogs (days^{-1})	0.0015	0.0012, 0.0023, 0.0031
7	μ_{LowInf}	Per capita mortality rate for dogs with low infectiousness (days^{-1})	0.0020	0.0012, 0.0026, 0.0031
8	$\mu_{HighInf}$	Per capita mortality rate for dogs with high infectiousness (days^{-1})	0.0021	0.0012, 0.0026, 0.0031
9	μ_{Sus}	Per capita mortality rate for susceptible dogs (days^{-1})	0.00125	0.00105, 0.00112, 0.00118
10	ψ	Average time (days) for deceased dog to be replaced	121	0, 243, 578
11	α	Biting rate[b] of sand flies (per day)	0.333	0.25, 0.40, 0.50
12	ϕ	Background proportion of sand flies that are infected	0.010	0.002, 0.100, 0.260
13	δ	Probability of *Leishmania* transmission from an infectious sand fly to a susceptible dog given that a contact bite occurs	0.321	0.10, 0.20, 0.50
14	m_{avg}	Probability of *Leishmania* transmission from an infectious dog to a susceptible sand fly given that a contact between the two occurs	0.275	0.023, 0.150, 0.450
15	ζ	Proportion of female sand fly population not observed in trapping studies	0.90	0.75, 0.80, 0.85

5. Results

Fig. 4: **Simulated daily prevalence in domestic dogs using baseline biological parameters.**

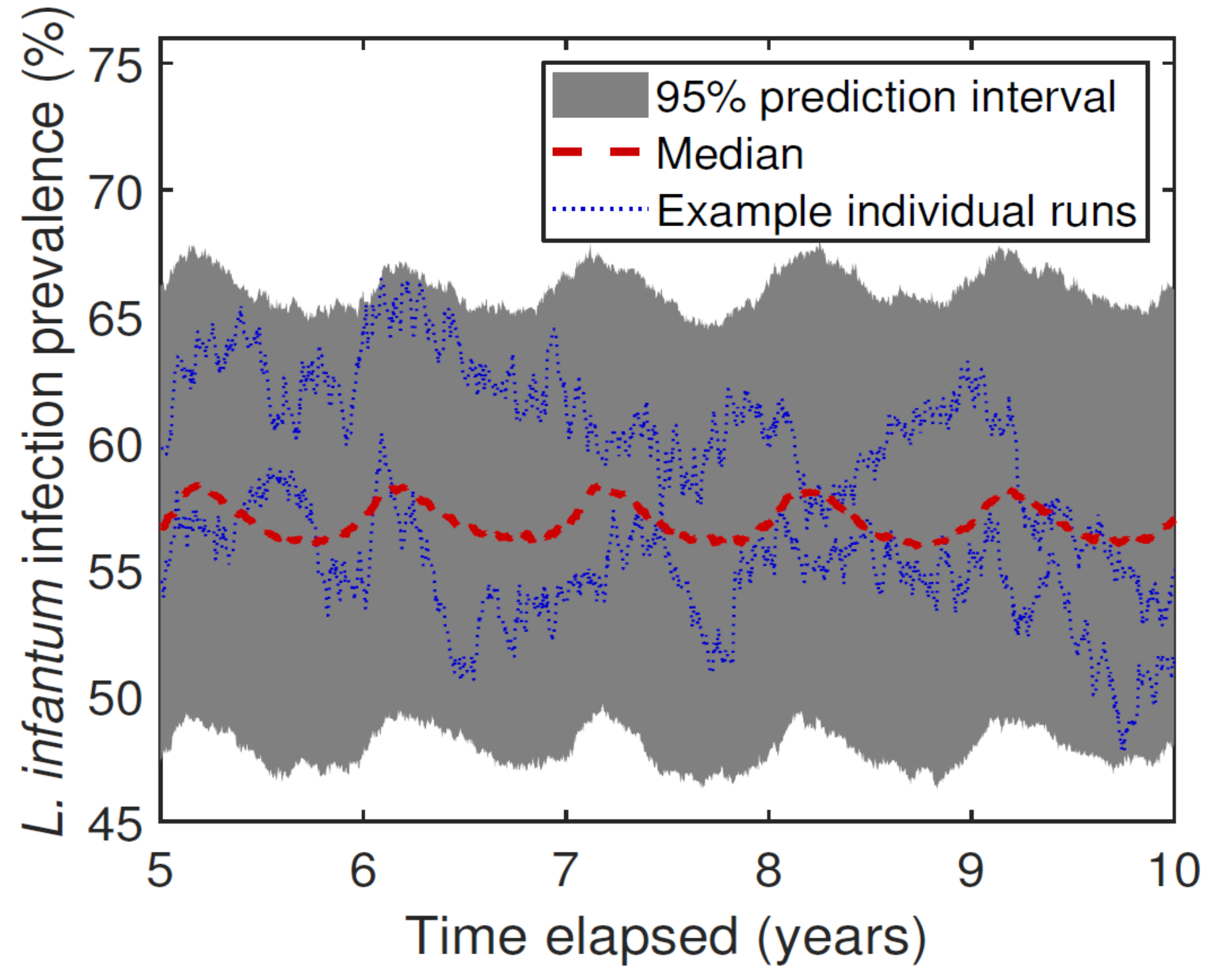
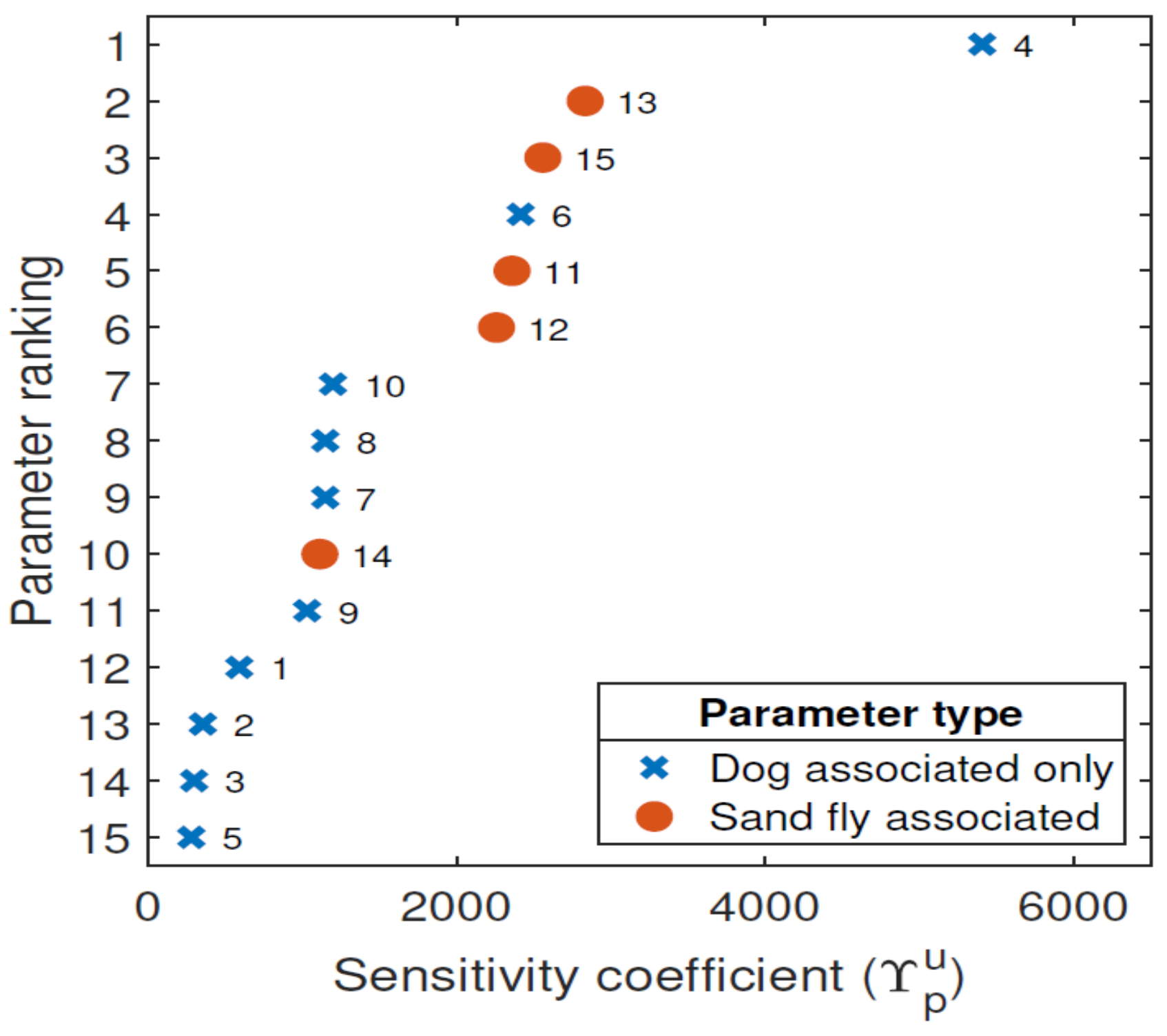


Fig. 5: **Stochastic sensitivity coefficient ranking.**



- The **median trace** for daily prevalence in dogs lay between **55–59%** (Fig. 4).
- **Top ranking parameter:** probability a newly introduced dog is infected (Fig. 5).

6. Outlook

- Modelling can contribute to decisions on where to focus data collection efforts.
- Extend the model to explore spatial patterns of zoonotic VL in humans.
- Assess spatially targeted interventions.

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