

Quantifying Key Parameters of Environmental Transmission and Age-Specific Susceptibility for MAP

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1. Introduction

- ❖ **Paratuberculosis (Johne's disease)** is a chronic disease in ruminants caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP).
- ❖ **Transmission** occurs horizontally and vertically.
- ❖ **Age-specific susceptibility** with higher risk in younger animals.
- ❖ **Shedding patterns** vary depending on the stage of infection.





2. Objective

- ❖ Develop an age-specific dose-response model to estimate susceptibility decrease rate (g) and median infectious dose (ID_{50}).
- ❖ Construct two compartmental model to quantify key parameters such as shedding rates (sh), transmission rates (β), and MAP decay rates (de).
- ❖ Explore scenarios involving exposure timing, exposure duration, and recipient age.

3. Materials & Method

Age-Specific Dose-Response Model:

- **Data source:** 14 published experiments
- **Statistical method:** Maximum Likelihood Estimation



$$p(dose, age) = 1 - e^{-\left(rS(age) \times \frac{\ln(2)}{ID_{50}}\right) \times dose}$$

with $rS(Age) = e^{-g \times Age}$

*Older individuals need a higher dose of MAP to get infected compared to younger individuals.

Environmental Transmission Models:

- **Data source:** Transmission experiments by van Roermund et al., 2007.

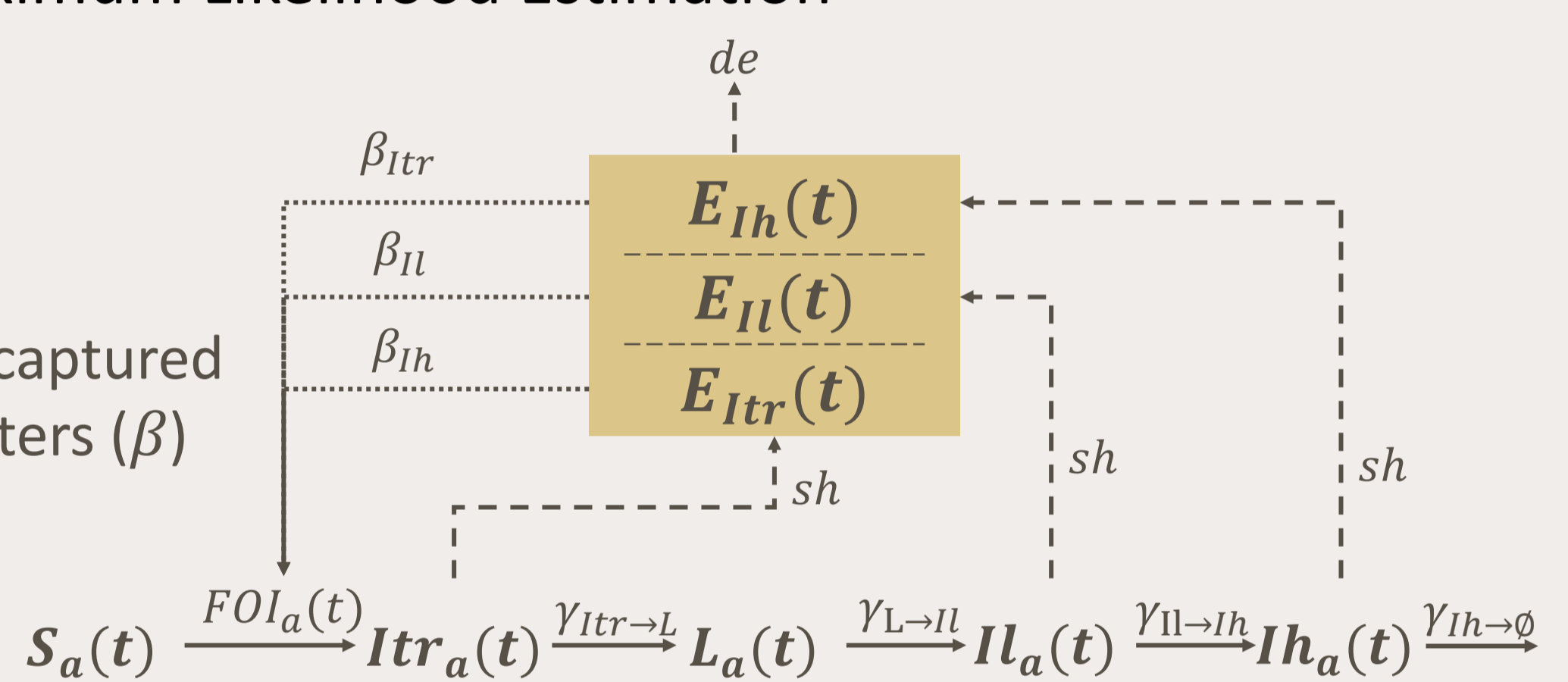


* 12 cows
20 calves

Statistical method: Maximum Likelihood Estimation

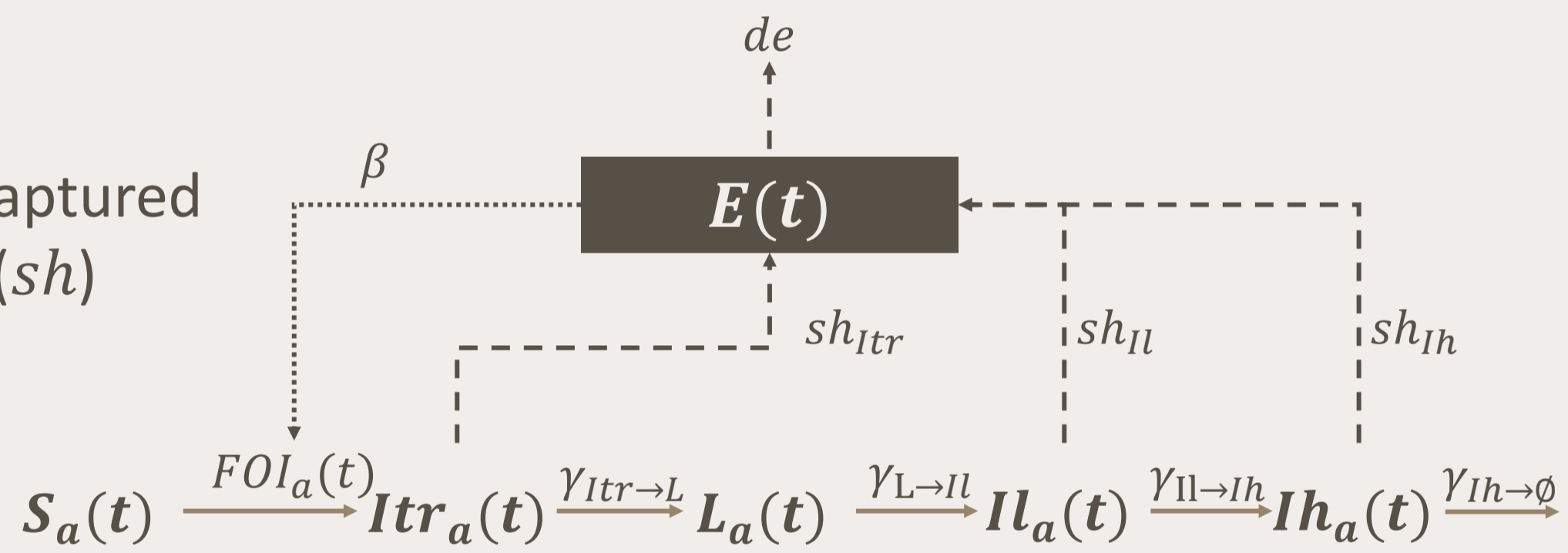
Model A

* Infectivity differences are captured in transmission rate parameters (β)



Model B

* Infectivity differences are captured in shedding rate parameters (sh)



where:

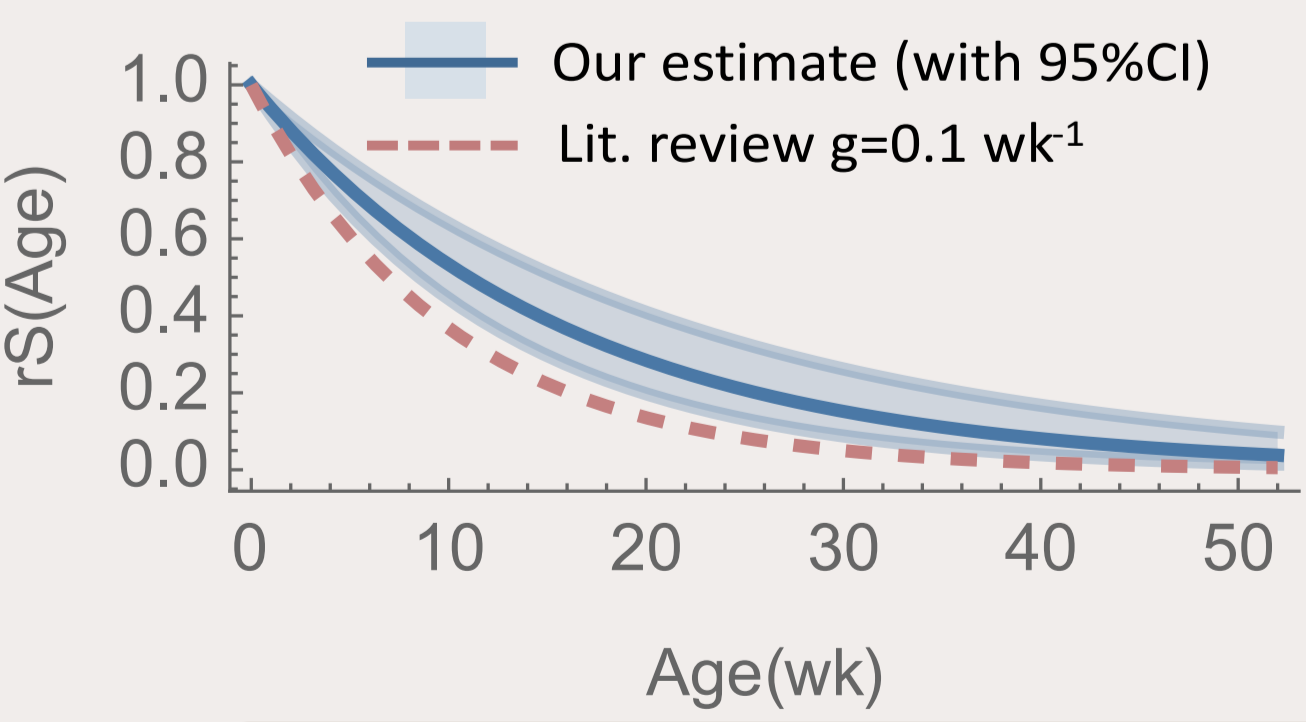
- $E(t)$ represent environmental contamination level at time t .
- $S_a(t), Itr_a(t), L_a(t), Il_a(t), Ih_a(t)$ represent number of susceptible, transient shedder, latently infected, low shedder, high shedder aged a at time t .
- $FOI_a(t)$ represent force of infection rate for a recipient aged a at time t ; $\gamma_{x \rightarrow y}$ represent transition rate from x to y .

4. Results

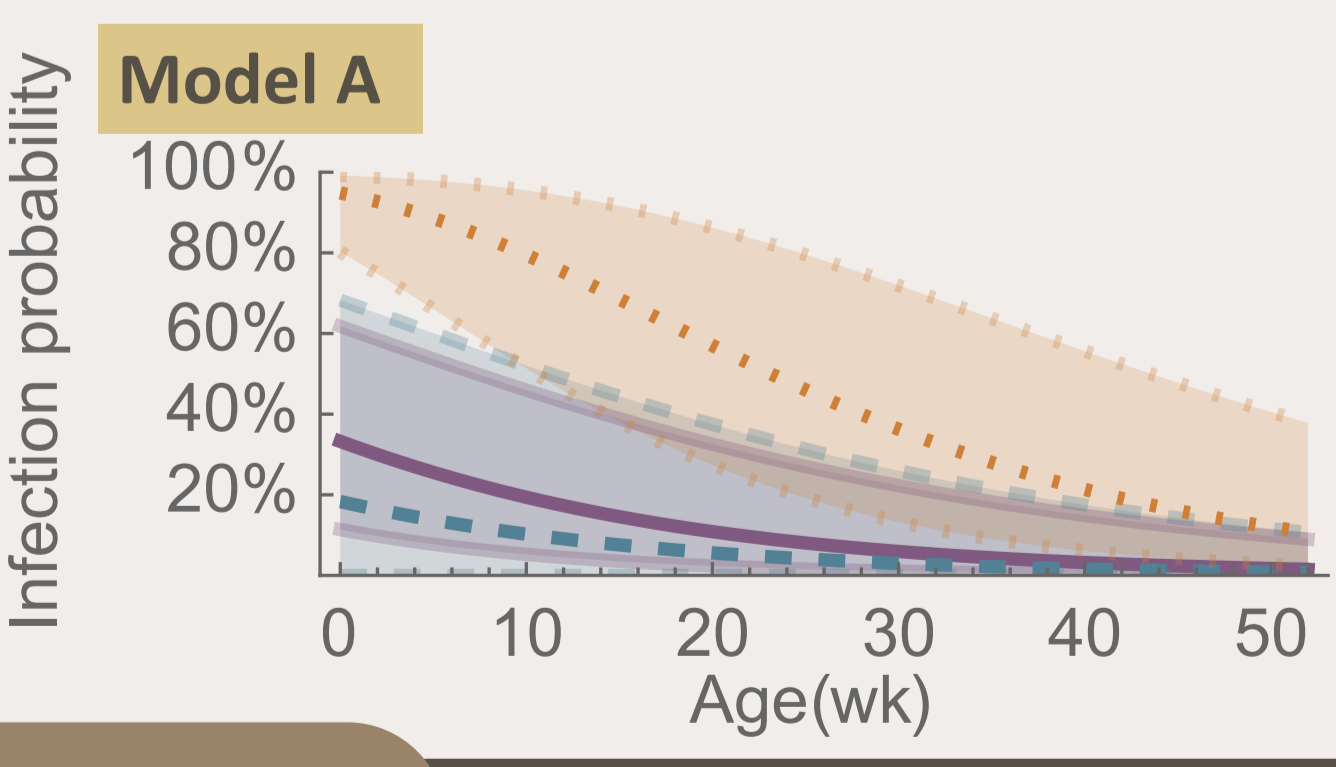
Parameters Estimates

Median Infectious Dose (ID_{50}) (unit:CFU)				Susceptibility Decrease Rate (\hat{g}) (unit:wk ⁻¹)				
2.75×10 ⁶				0.0629				
Model	Transmission Rate ($\hat{\beta}$) (unit:wk ⁻¹)			Shedding Rate (\widehat{sh}) (unit:wk ⁻¹)			Decay Rate (\widehat{de}) (unit:wk ⁻¹)	AIC
	$\widehat{\beta}_{Itr}$	$\widehat{\beta}_{Il}$	$\widehat{\beta}_{Ih}$	\widehat{sh}_{Itr}	\widehat{sh}_{Il}	\widehat{sh}_{Ih}		
A	0.0299	0.0150	0.219	2.10			0.150	72.6
B	0.0299			2.10	1.05	15.4	0.150	72.6

Susceptibility change over Age

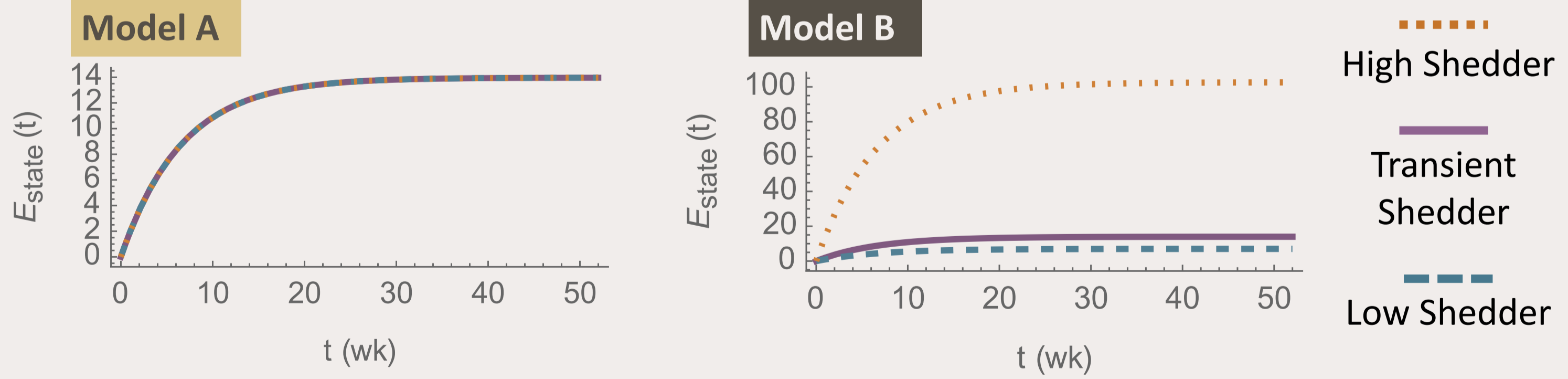


Infection Probability change over Age

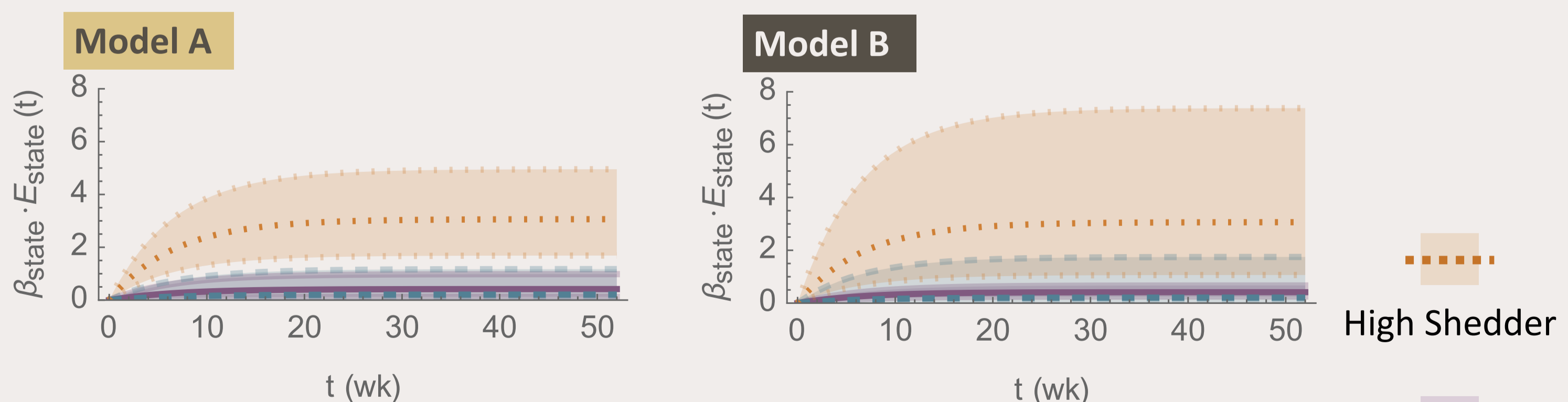


Comparison of MAP Infectivity in Transient, Low, and High Shedders

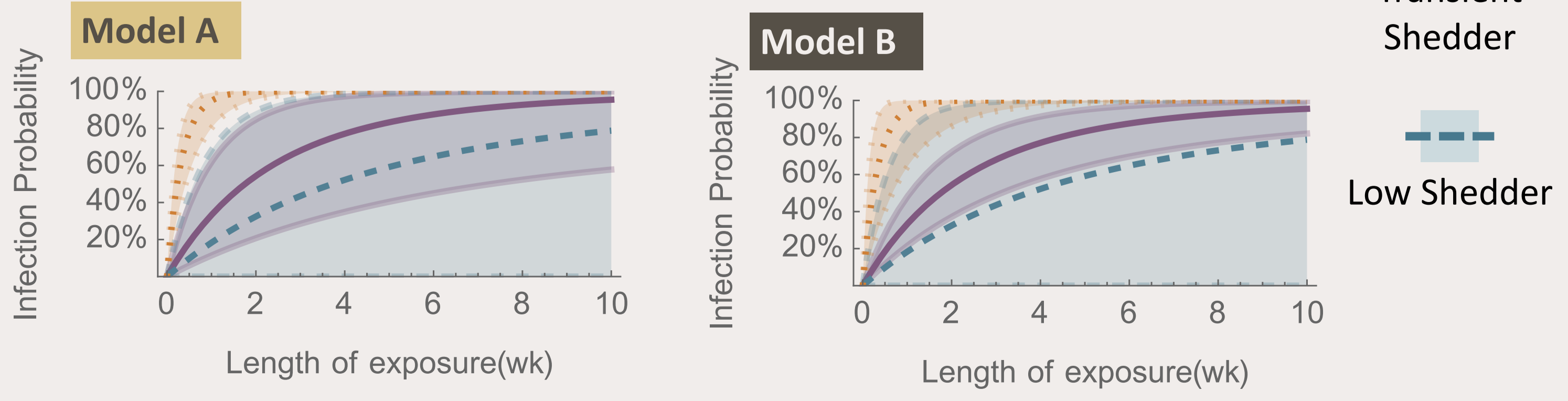
Environmental Contamination Level change over Time



Hazard Rate (with 95%CI) change over Time



Infection Probability (with 95%CI) change over Length of Exposure



5. Take home messages

- ❖ **Susceptibility decrease rate** with age has been **overestimated**, while the **infection risk** has been **underestimated**.
- ❖ It's **not reliable** assume only animals under **one year** are susceptible.
- ❖ Although both model A and B have **identical** best estimates and AIC values, Model B has wider 95% CI, indicating greater uncertainty.
- ❖ Transmission / Shedding rates: **High-shedding (Ih) > Transiently infectious (Itr) > Low-shedding (Il).**