Lassa virus vaccination strategies in endemic areas

Reflections on a mathematical modelling research project

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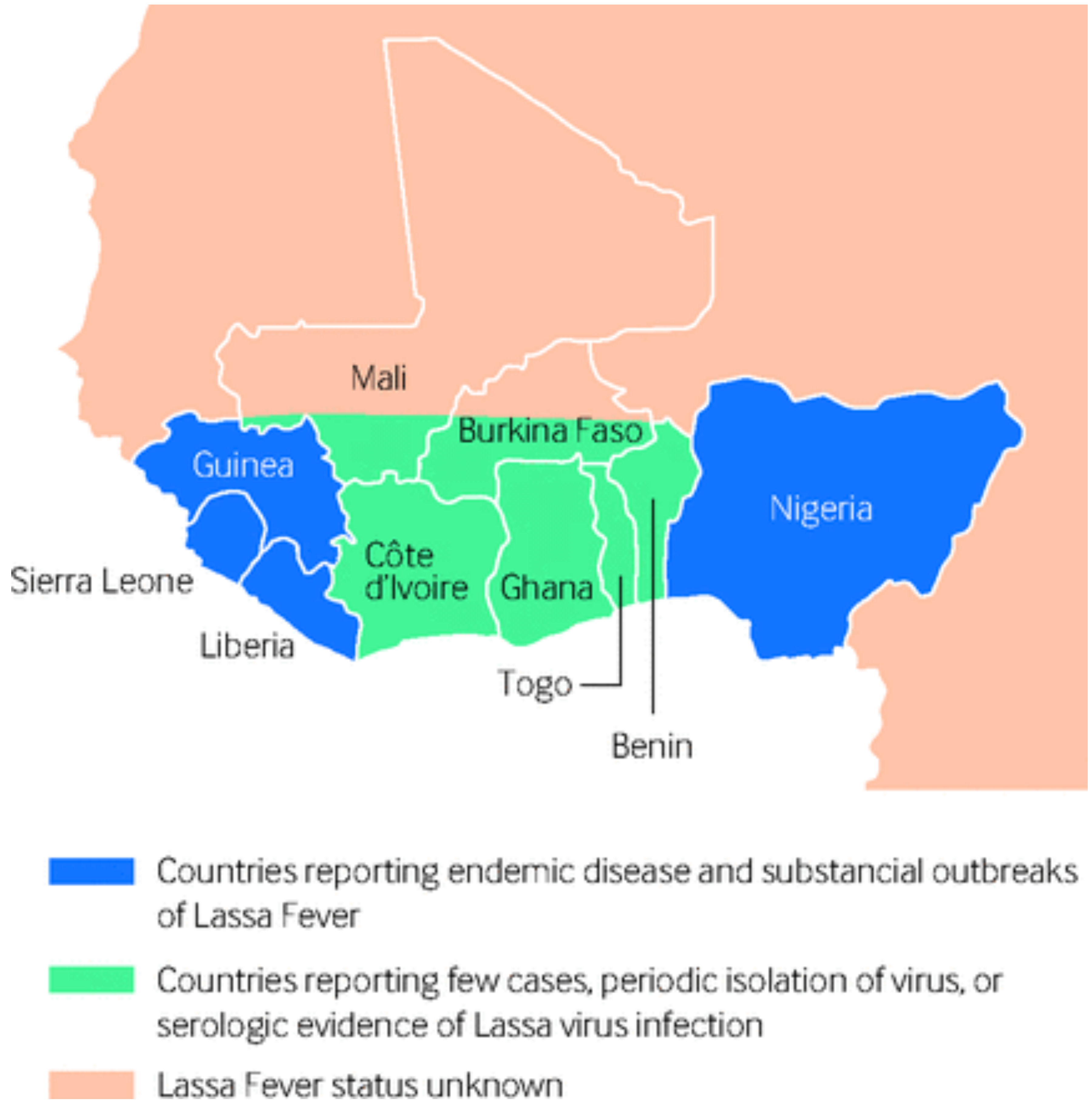
Lassa fever

- An acute viral haemorrhagic fever caused by Lassa virus (LASV), endemic to much of Sub-Saharan West Africa
- Case fatality rates are 1% overall and 15% among patients hospitalised with severe symptoms
- Clinical diagnosis challenging
- Limited treatment options



LASV control

LASV vaccination

How can we optimise vaccination strategy?

- Minimise spread of disease
- Efficient resource use

Mathematical modelling as a public health research tool

- Useful when clinical data is sparse and field experiments are impractical, costly, or unethical
- Can investigate a range of potential scenarios
- Inexpensive but requires specialist knowledge

Model development

- Deterministic SEIR mathematical model
- Simulates seasonal LASV transmission between rodents and humans
- Parametrised for Nigeria

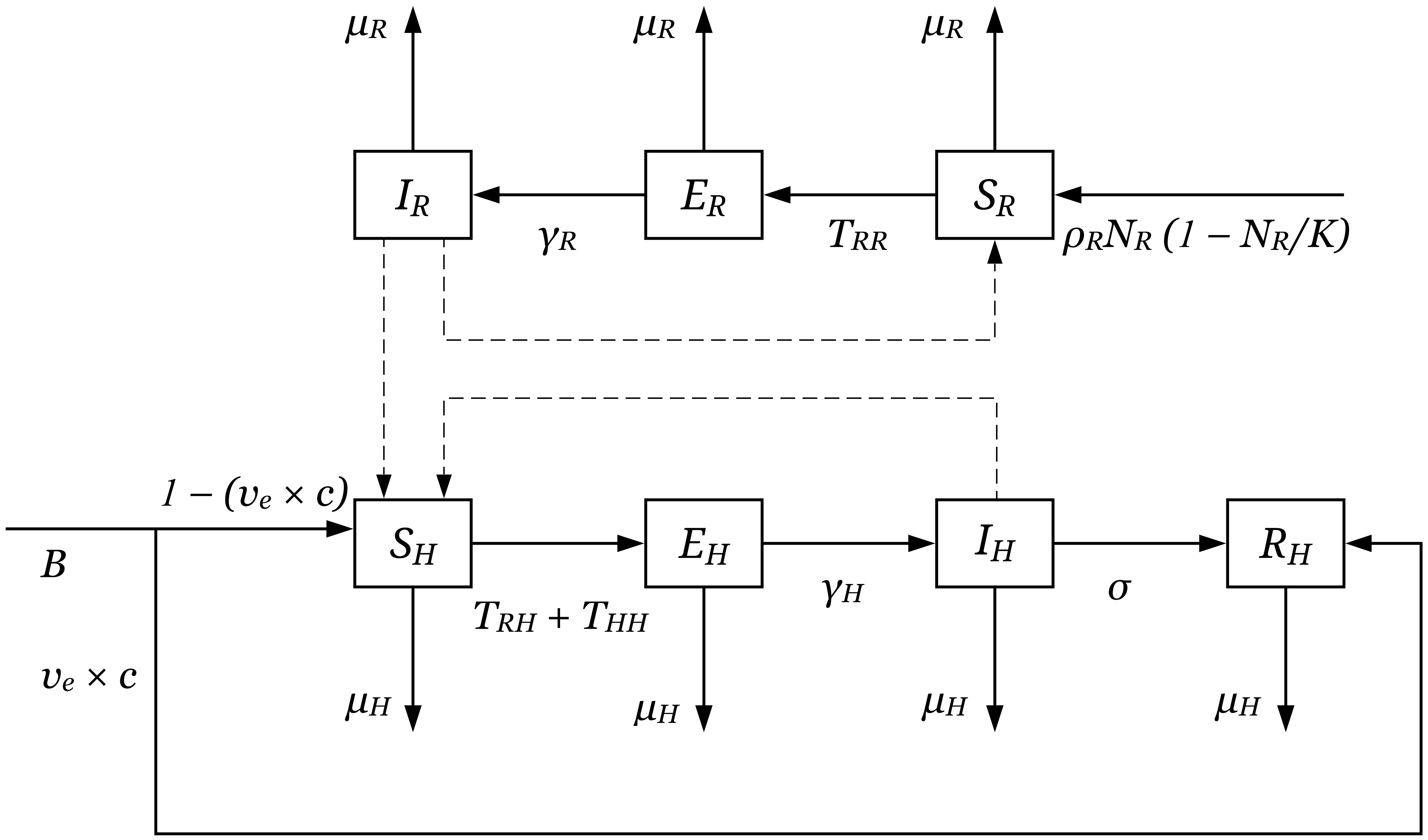


Figure 1. Structure of the LASV transmission model

Findings

- Vaccination in endemic areas could considerably reduce disease incidence
- Pulse immunisation appears to be the most efficient strategy

Reflections

AFPHM LO 3.2.7

'Analyse alternative disease prevention and control strategies in a quantitative manner'

Elements of competence
• understand the principles of quantitative modelling • understand the use of deterministic and stochastic approaches • understand applications for communicable and non-communicable diseases • understand the strengths and weakness of modelling • conduct spreadsheet-based modelling of alternative scenarios.

Reflections

AFPHM LO 1.1.9

'Advocate for timely effective action in response to important threats to public health'

Elements of competence
• prioritise public health threats based on sound public health principles • act in a timely manner on available information • use effective methods of advocacy appropriate to the issues being considered and the organisational context.

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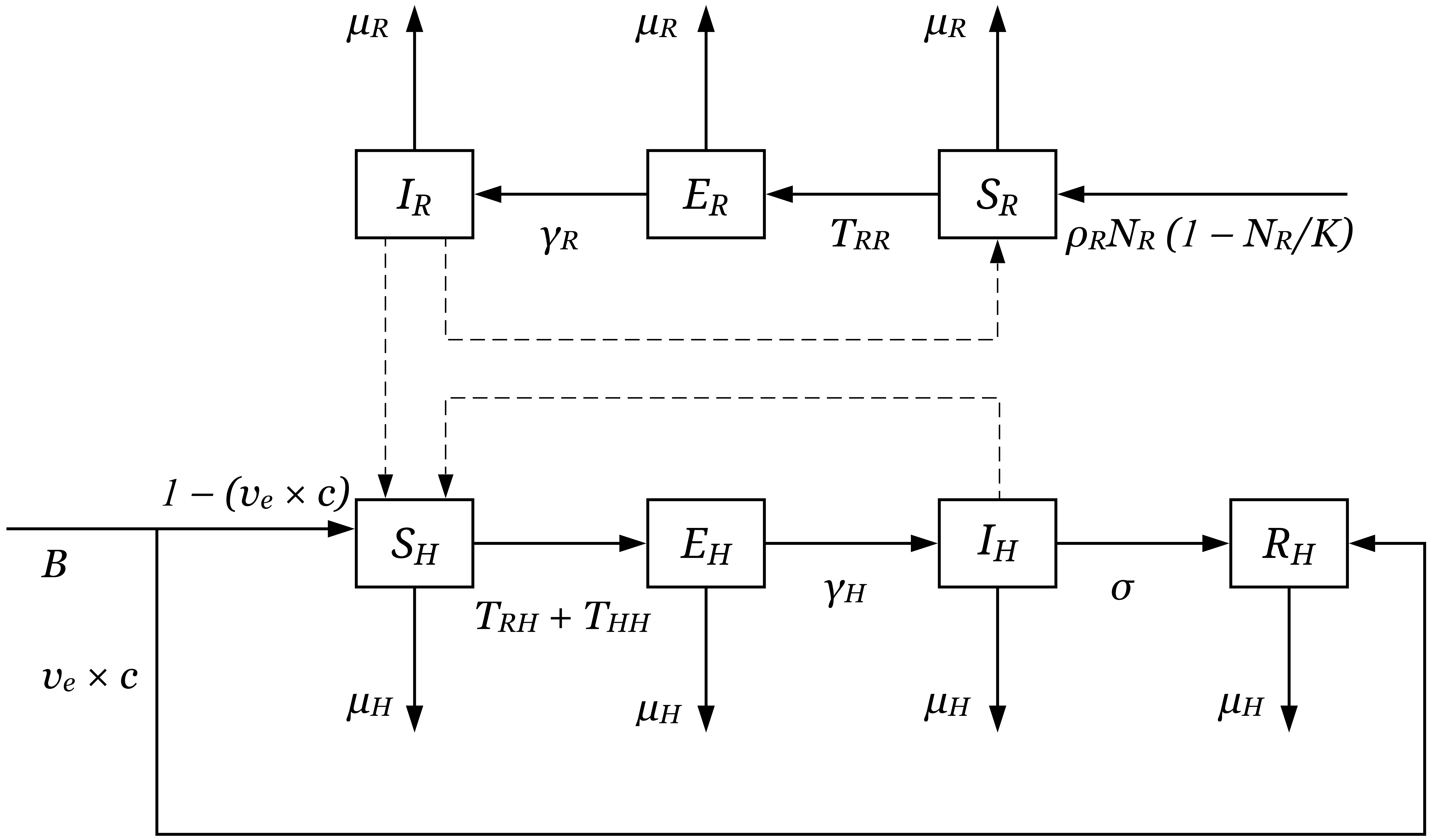
Australian National University

Model structure



Differential equations

$$\frac{dS_H}{dt} = B\,(1 - c\ ve)N_H - \frac{S_H}{N_H}(T_{RH}I_R + T_{HH}I_H) - \mu_H S_H + \alpha R_H$$

$$\frac{dE_H}{dt} = \frac{S_H}{N_H}(T_{RH}I_R + T_{HH}I_H) - \gamma_H E_H - \mu_H E_H$$

$$\frac{dI_H}{dt} = \gamma_H E_H - \sigma I_H - \mu_H I_H$$

$$\frac{dR_H}{dt} = \sigma I_H - \mu_H R_H + B\ c\ veN_H - \alpha R_H$$

$$\frac{dS_R}{dt} = \rho_R N_R \left(1 - \frac{N_R}{K}\right) - \frac{S_R}{N_R}(T_{RR}I_R) - \mu_R S_R$$

$$\frac{dE_R}{dt} = \frac{S_R}{N_R}(T_{RR}I_R) - \gamma_R E_R - \mu_R E_R$$

$$\frac{dI_R}{dt} = \gamma_R E_R - \mu_R I_R$$

Symbol and Description		Min	Default	Max	Source
N_H	Total human population	–	180,000,000	–	World Health Organization (2015)[33]
B	Human birth rate	–	1/(55×365)	–	World Health Organization (2015)[33]
μ_H	Human death rate	–	1/(55×365)	–	World Health Organization (2015)[33]
γ_H	Progression rate from exposed to infectious human	1/6	1/12	1/21	World Health Organization (2017)[34]
σ	Recovery rate of humans	1/2	1/10	1/21	World Health Organization (2017)[34]
T_{RH}	Transmission rate from rodent to human	0	0.00001	1	Default value selected to produce a seroprevalence of LASV in humans of 21.3%[2], and so that 80% of human infections are due to contact with rodents[21]
T_{HH}	Transmission rate from human to human	0.01	0.015	0.02	
T_{RR}	Transmission rate from rodent to rodent	0.005	0.007	0.014	Agbonlahor et al. (2017)[35]
ρ_R	Rodent growth rate	–	0.02	–	Default value selected to produce a ratio of 1.2:1 rodents to humans at equilibrium
K_{av}	Average carrying capacity of the environment for the rodents	–	$1.5N_H$	–	
μ_R	Death rate of rodents	–	1/(1×365)	–	Demartini et al. (1975)[26]
γ_R	Progression rate from exposed to infectious rodent	1/1	1/3	1/5	Default value selected such that the number of infectious humans is approximately 25% higher in the dry season than in the wet season
η	Amplitude of seasonality	0	0.6	1	Default value selected to produce 25% higher prevalence in the dry season
ω	Phase	0	300	365	Default value selected to produce peaks in February
c	Proportion of infants vaccinated at birth	0	Varied	1	Varied
d	Proportion of the population vaccinated through pulse vaccination	0	Varied	1	Varied
ve	Vaccine effectiveness		0.7, 0.9		Based on World Health Organisation Target Product Profile (TPP) [29]

Table 1. Parameter descriptions, values and ranges, units and sources.

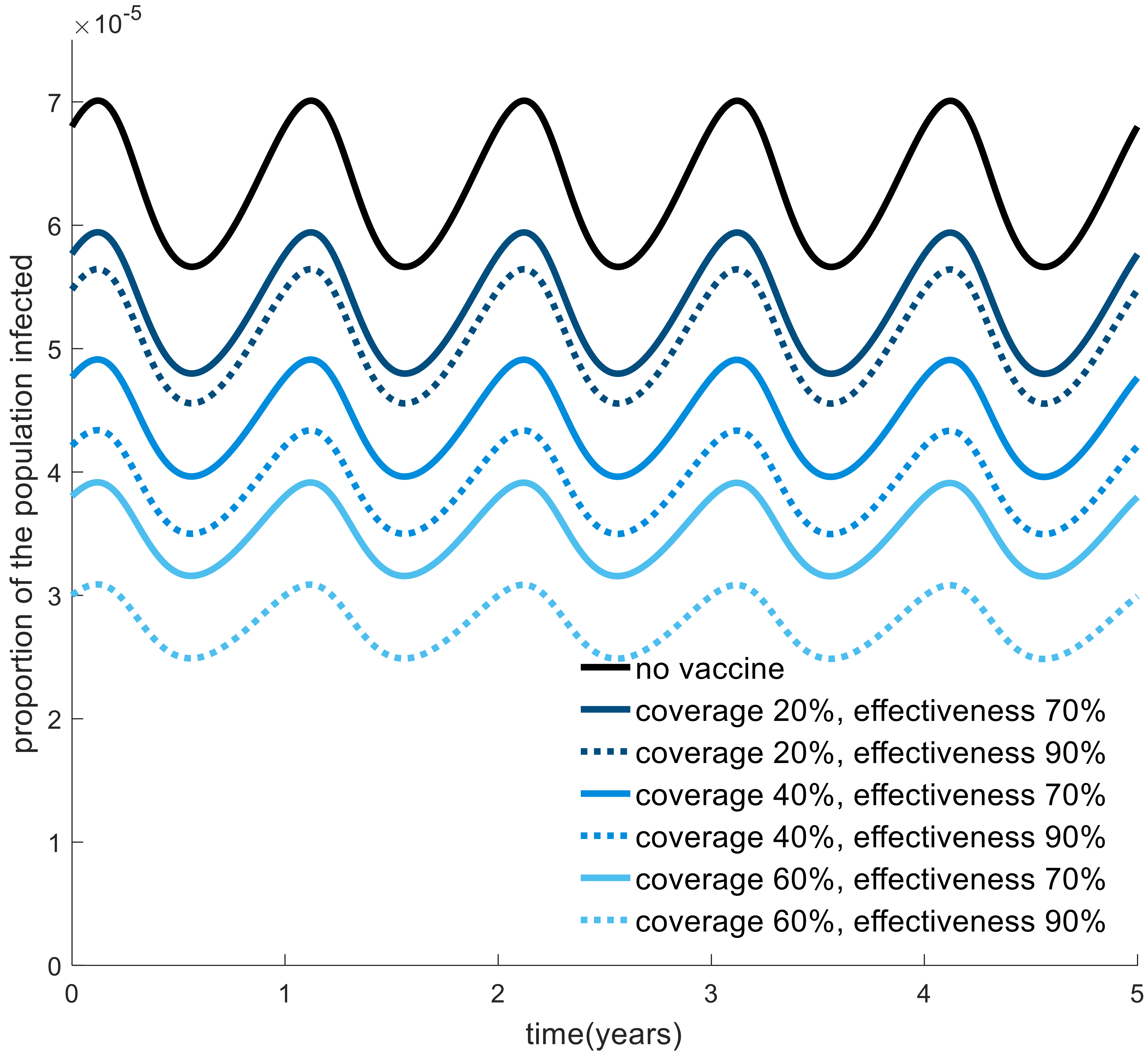


Figure 2. Time-dependent variation in the proportion of the population infected for different levels of coverage and vaccine effectiveness.

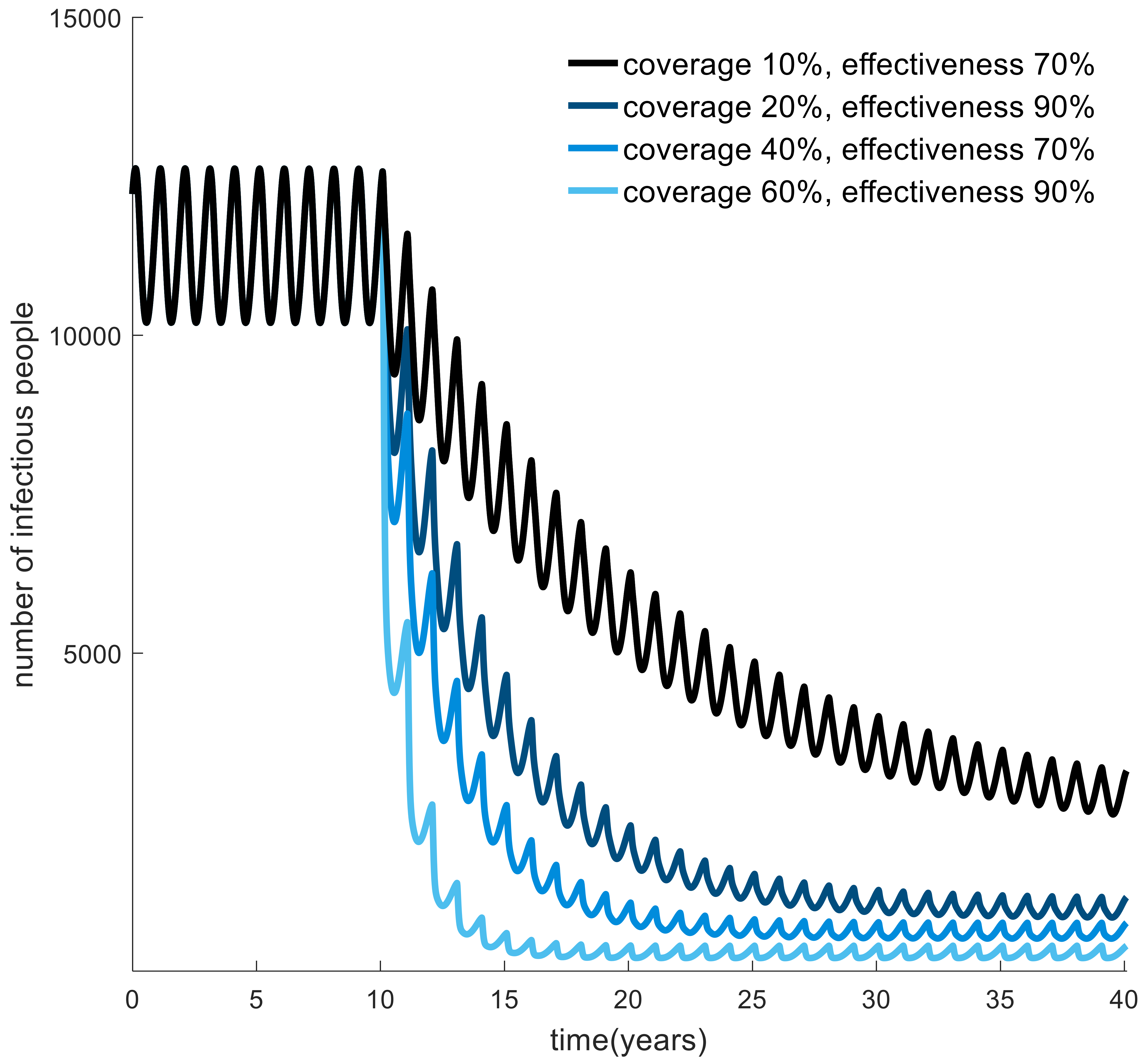


Figure 3. The number of infectious people over time with yearly pulse vaccination introduced after 10 years of transmission. Vaccination takes place in February each year, with vaccine coverage and effectiveness varied.

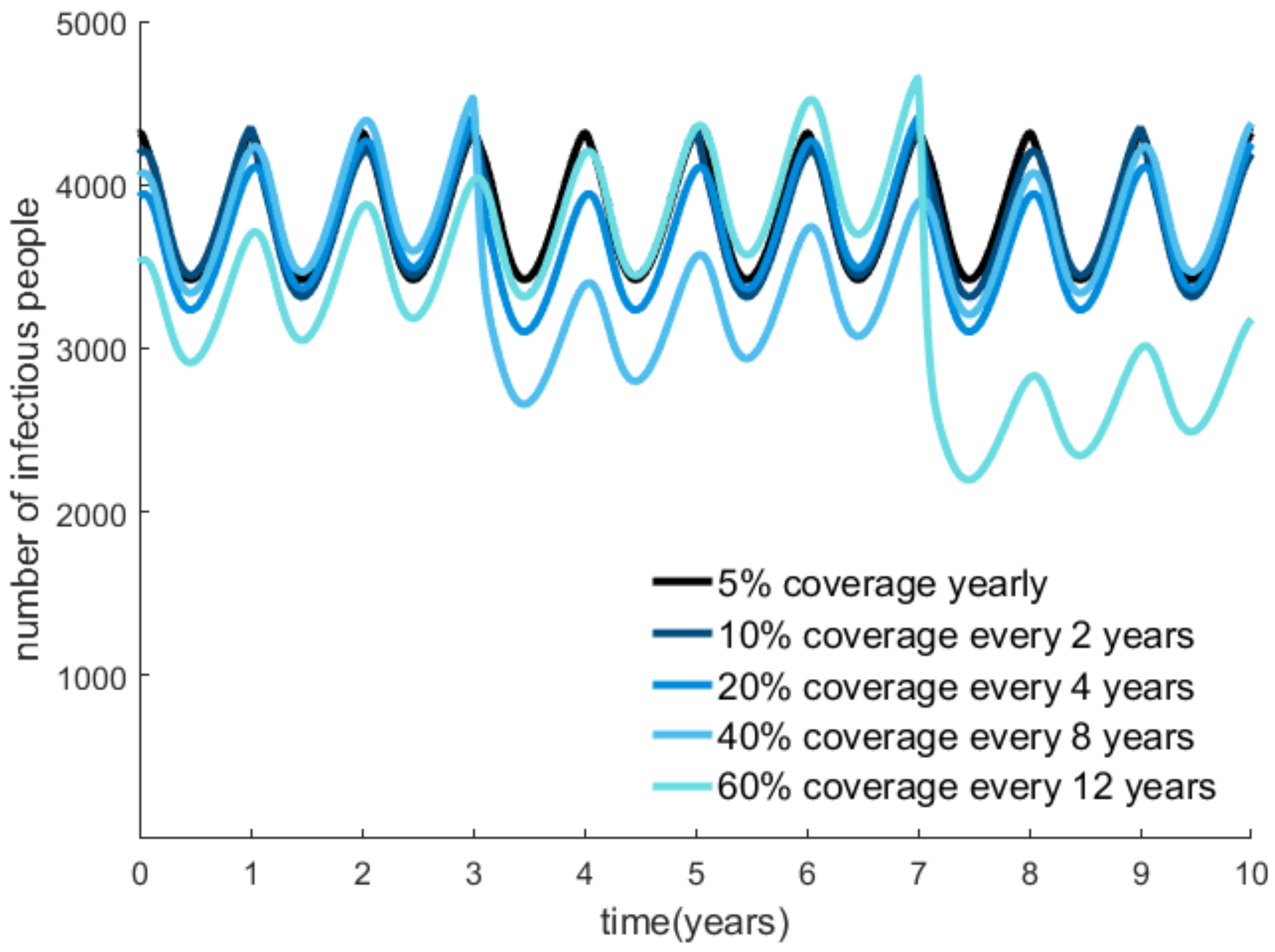


Figure 4. The number of infectious humans over time with pulse vaccination in February at different levels of vaccine coverage and pulse interval length with 70% vaccine effectiveness.

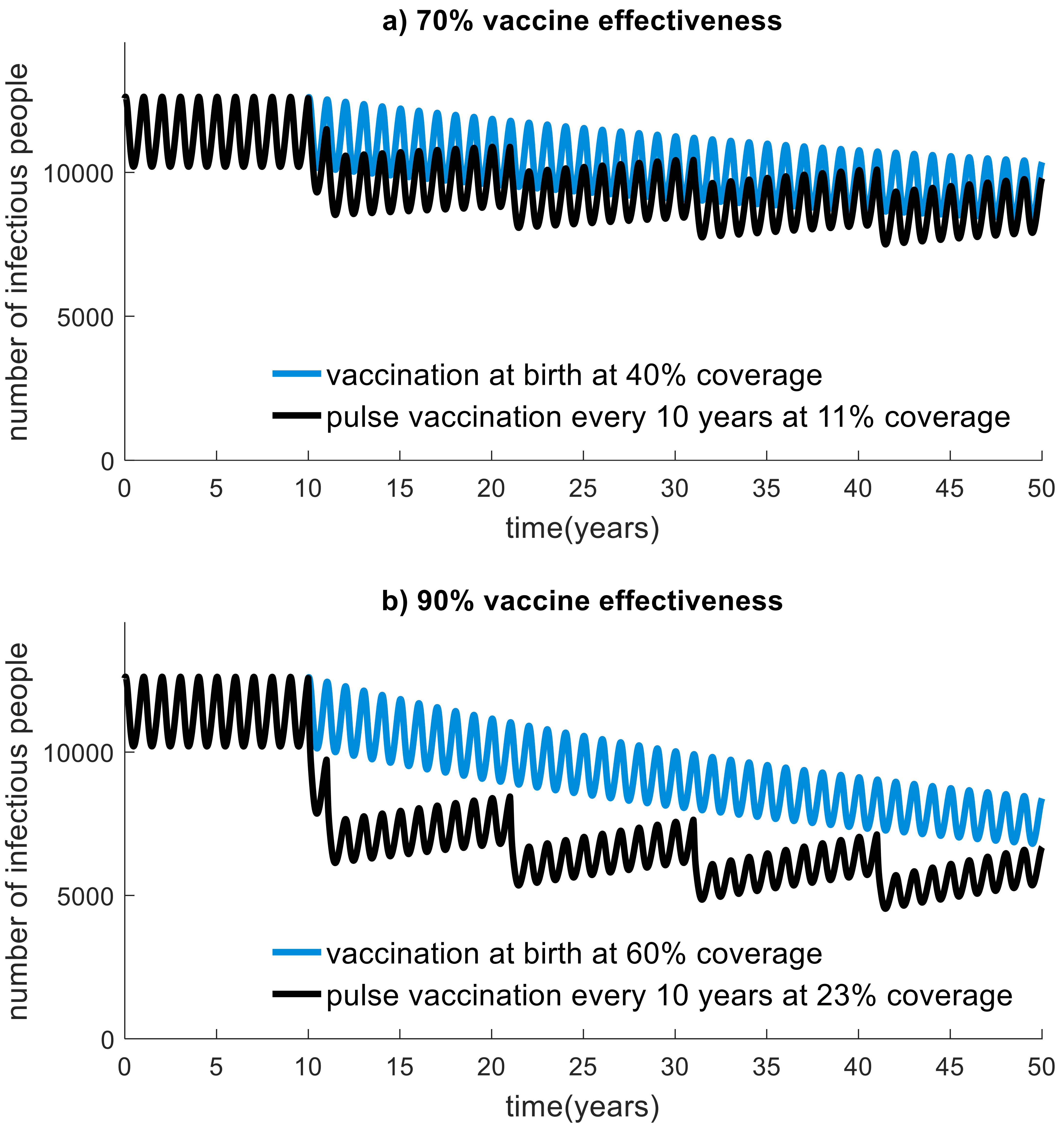


Figure 5. Comparison of vaccination at birth and pulse vaccination strategies that lead to the same final reduction in infected people.