Assessing the effect of social contact structure on the impact of pneumococcal conjugate vaccines

2 Oct 2024

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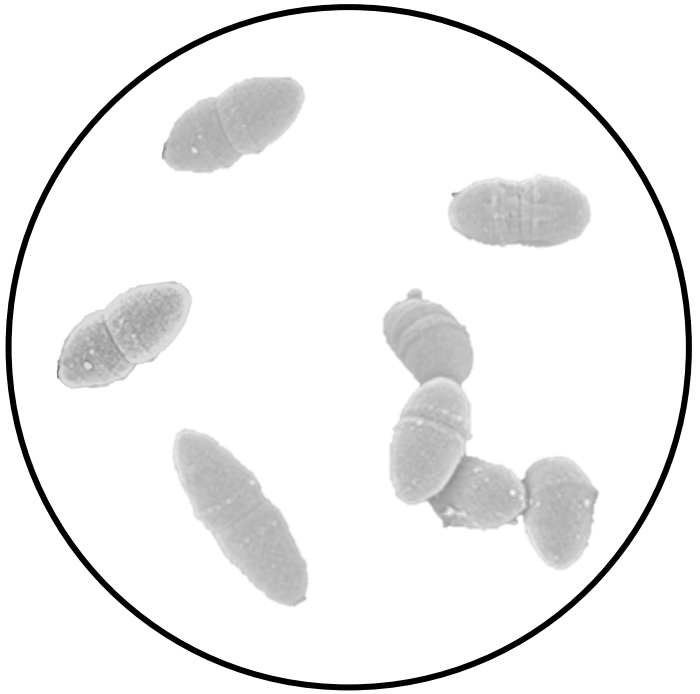
Infectious Disease Epidemiology Group (PI: Matthieu Domenech de Cellès)
Max Planck Institute for Infection Biology

Streptococcus pneumoniae **causes**
pneumonia and invasive diseases

Colonization is key for transmission



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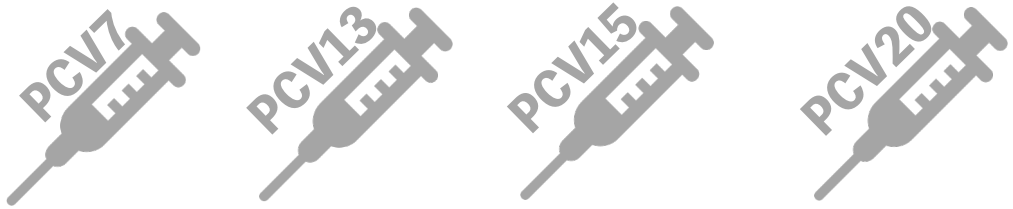
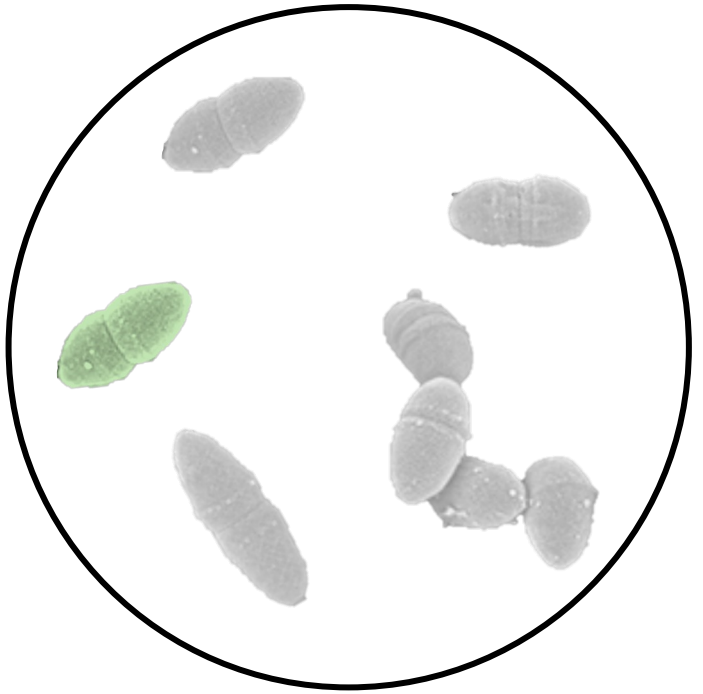
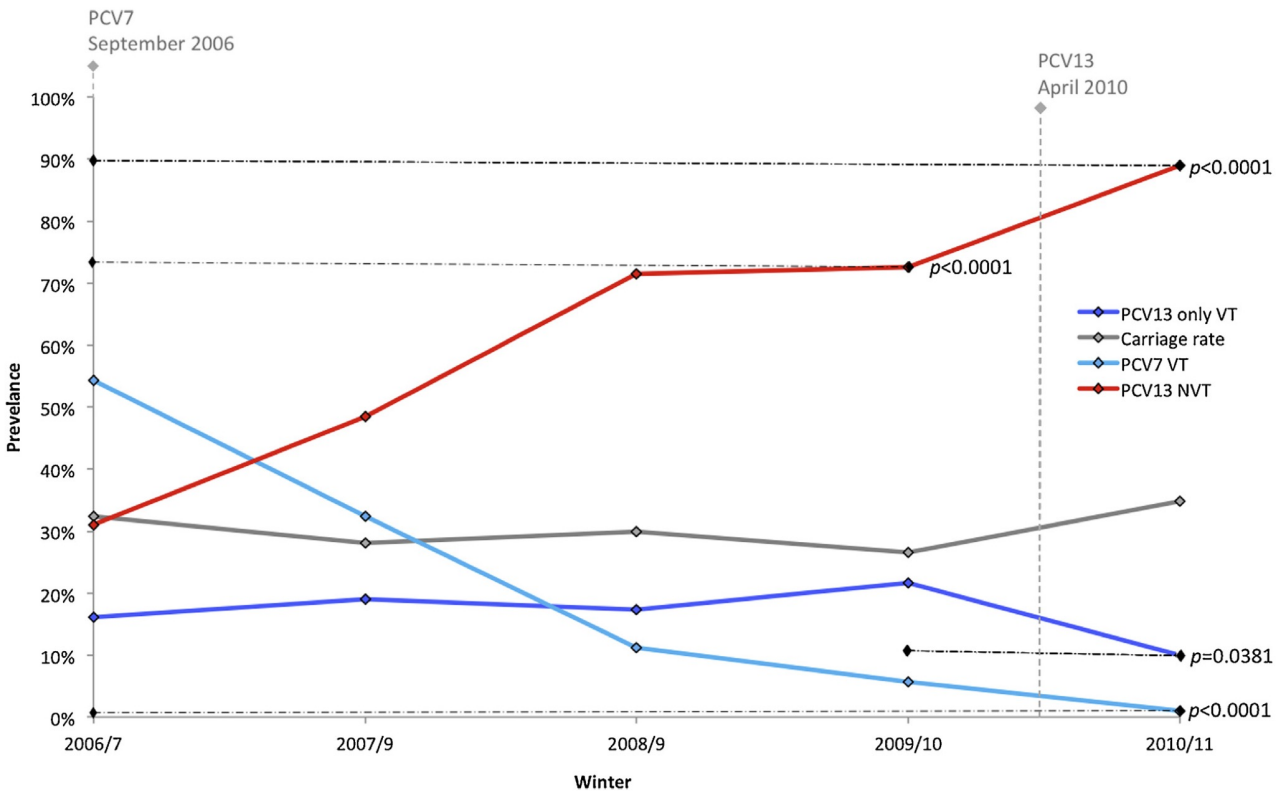


PCVs cover up to 15 / 20 out of 100 serotypes[1]



1. Ganaie et al. (2020) *mBio*

Serotype replacement observed in carriage

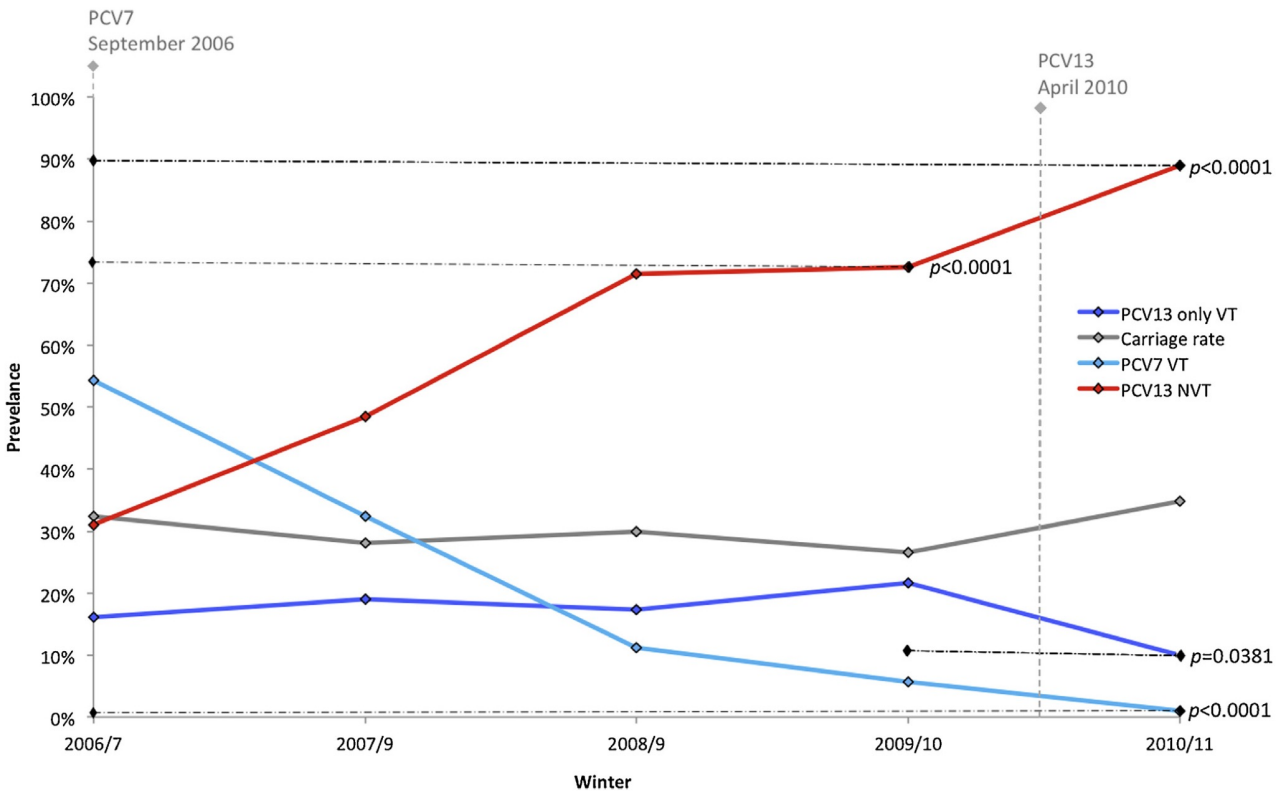


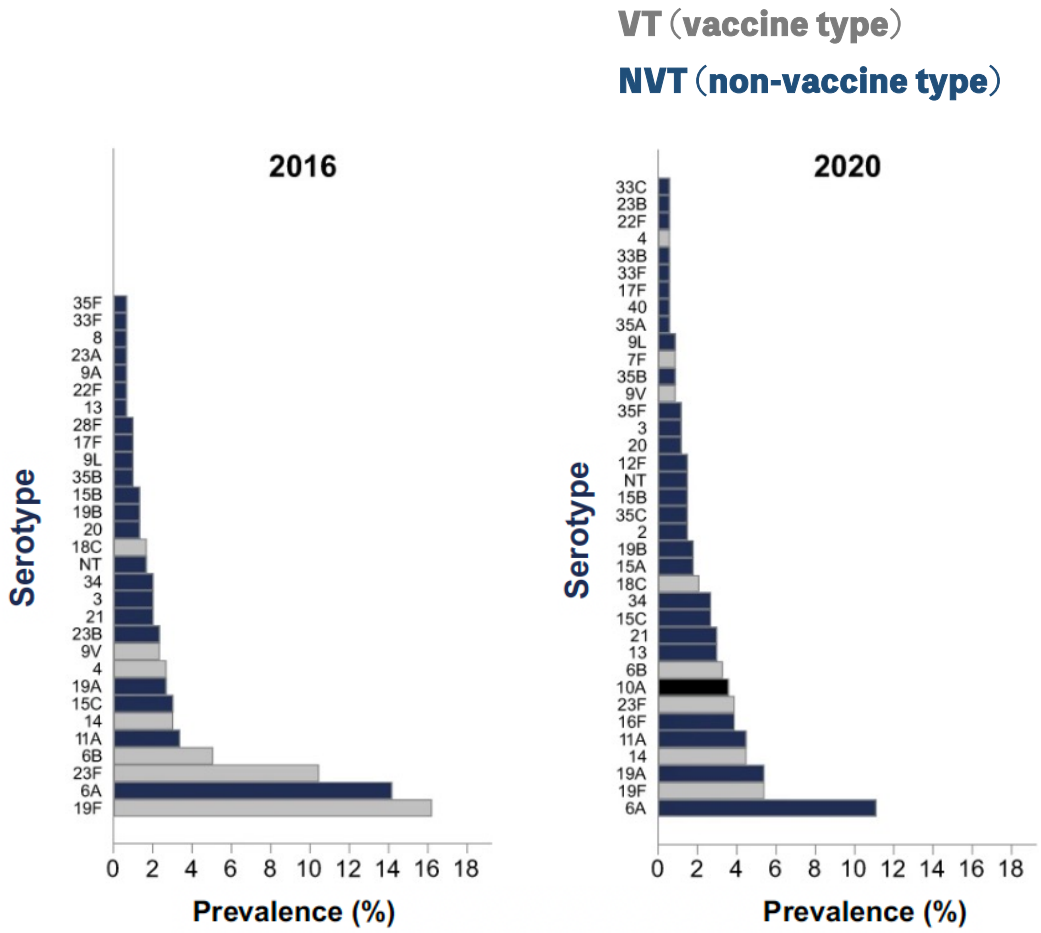
NVT（non-vaccine type）

VT（vaccine type）

1. Gladstone et al. (2015) *Vaccine*

Serotype replacement observed in carriage across settings[1,2]





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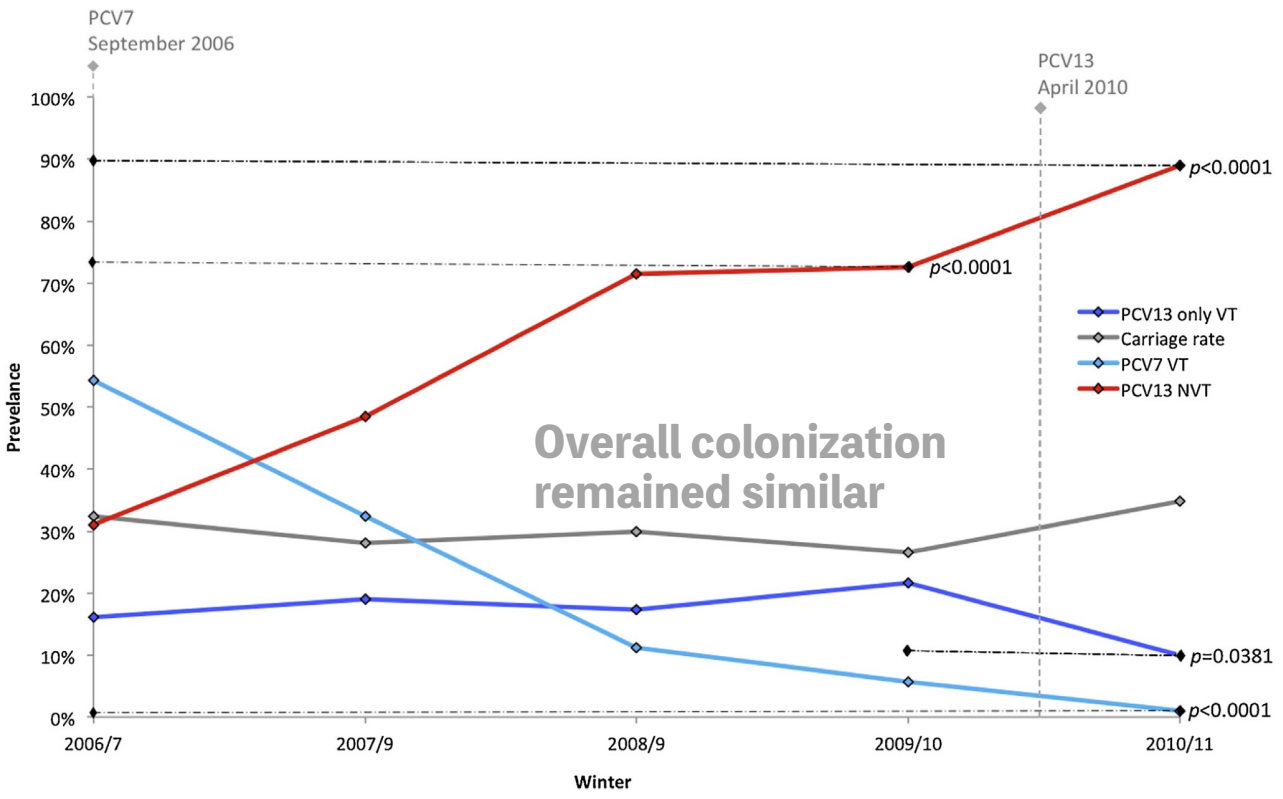

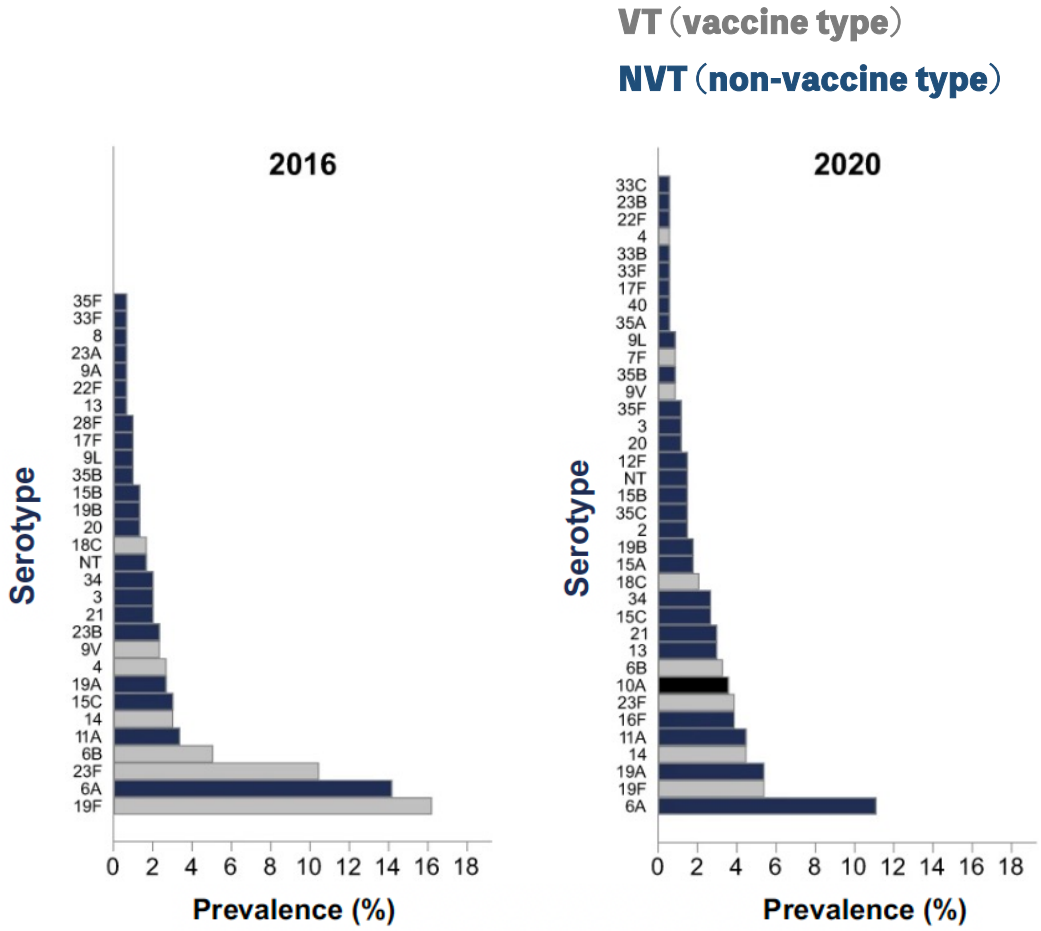

1. Gladstone et al. (2015) *Vaccine*
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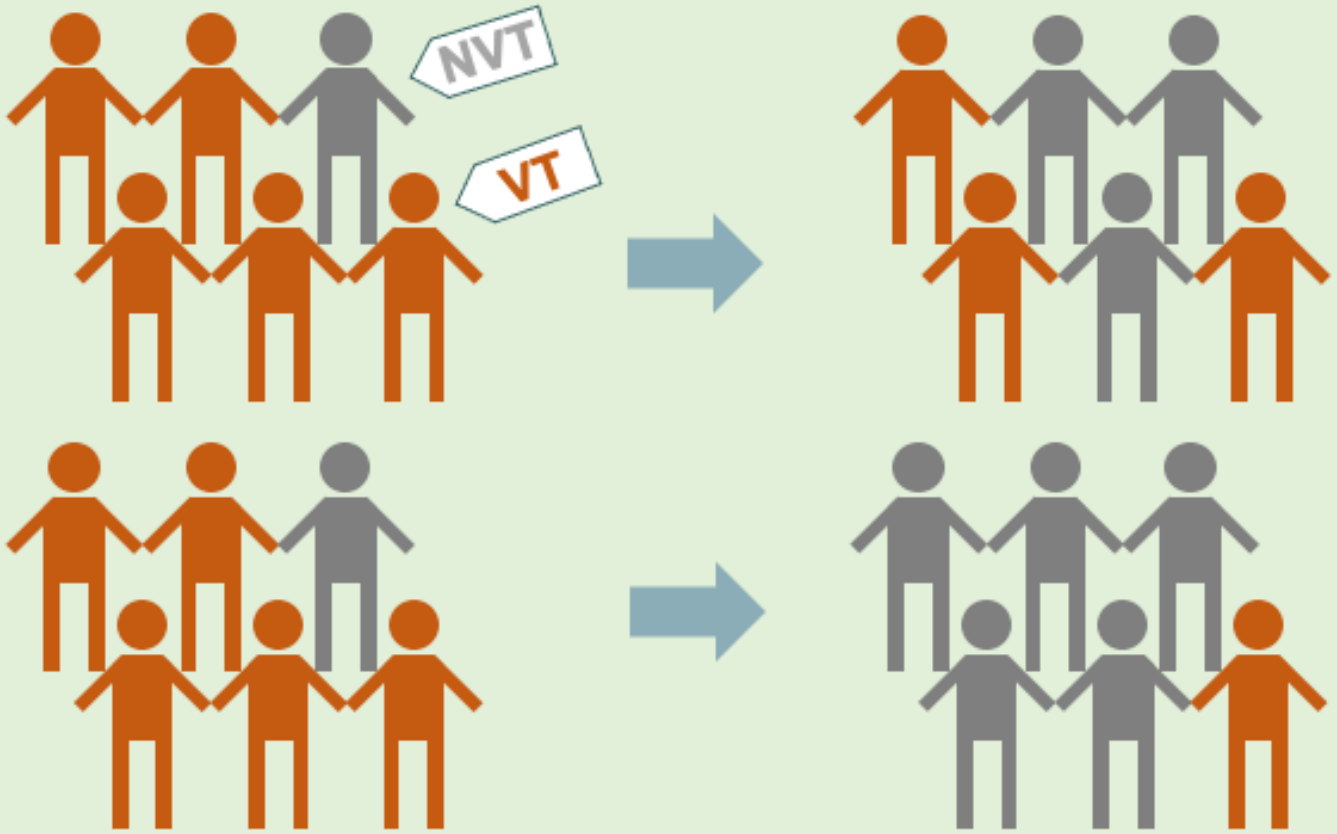
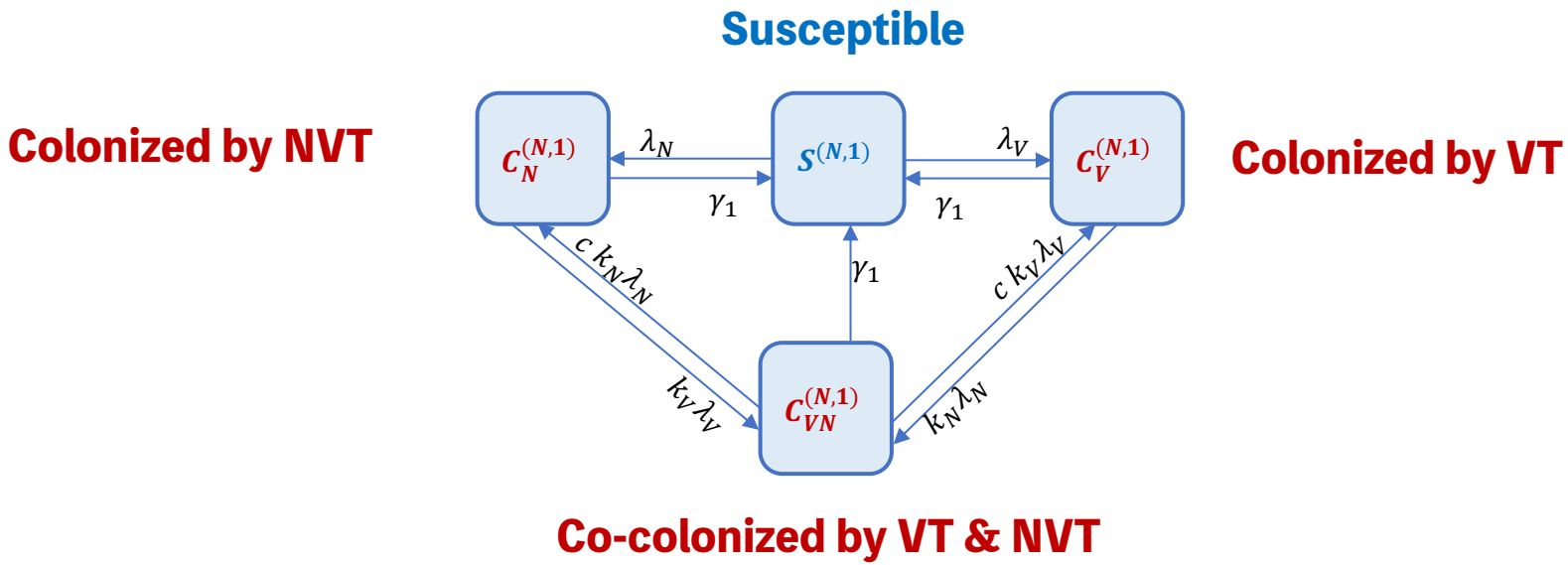
Can the social contact structure affect these dynamics?



We developed a neutral[1] transmission model



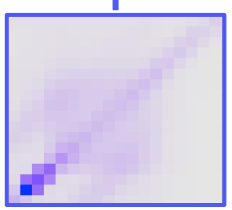
1. Lipsitch et al. (2009) *Epidemics*

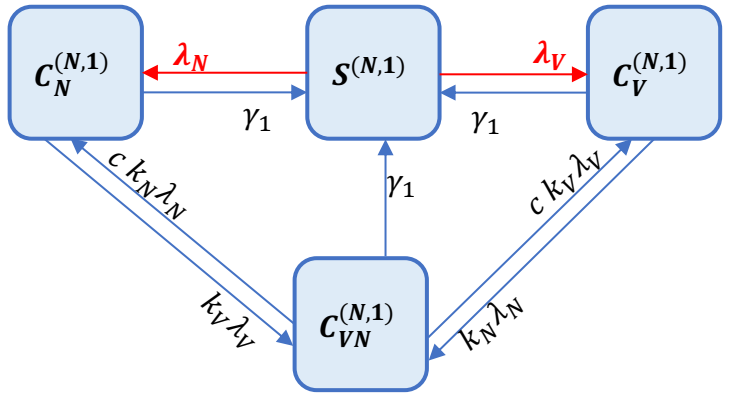
We developed a neutral[1] transmission model

Susceptibility **Total no. of colonized**

$$\lambda_V^{(i)} = \beta_V^{(i)} \sum_{j=0}^{A-1} \widetilde{m}_{ij} CC_V^{(j)}$$

$$\lambda_N^{(i)} = \beta_N^{(i)} \sum_{j=0}^{A-1} \widetilde{m}_{ij} CC_N^{(j)}$$





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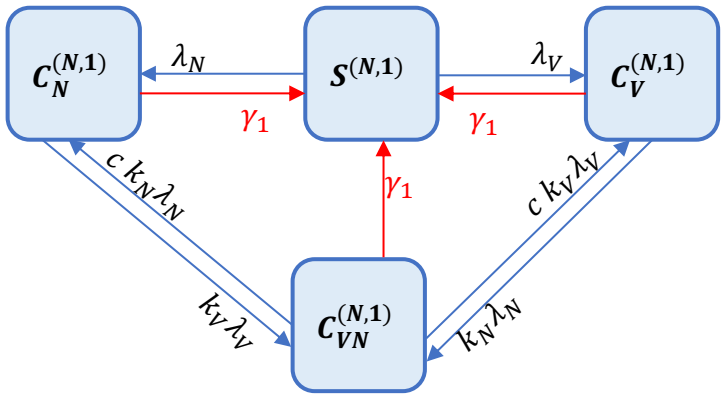

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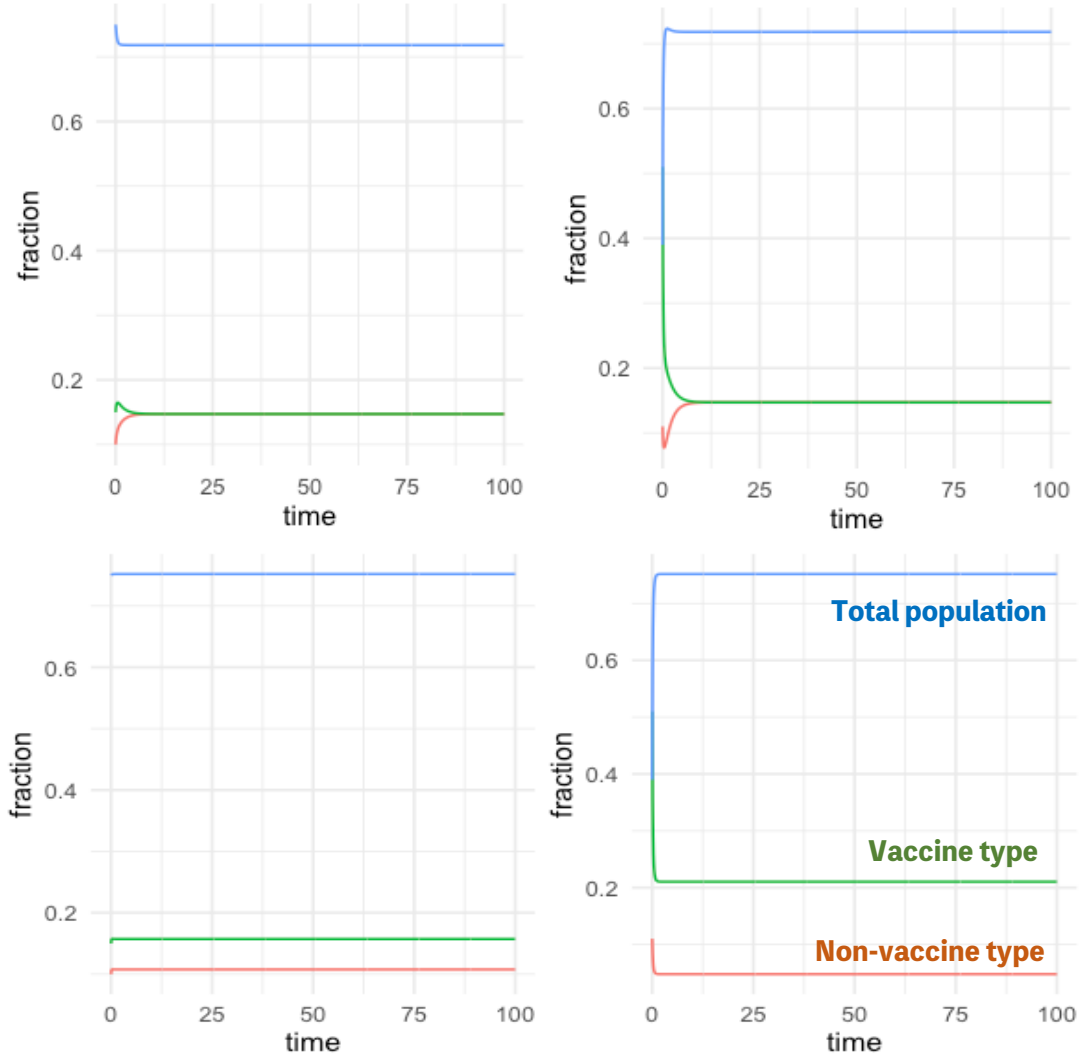


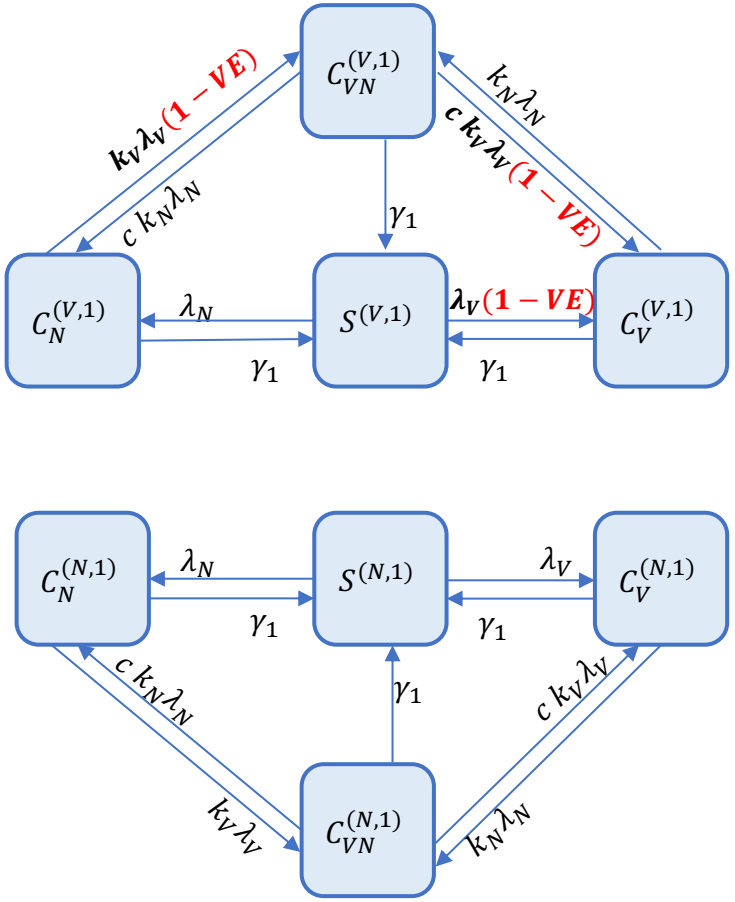
Non-neutral model

Intrinsically favours co-existence

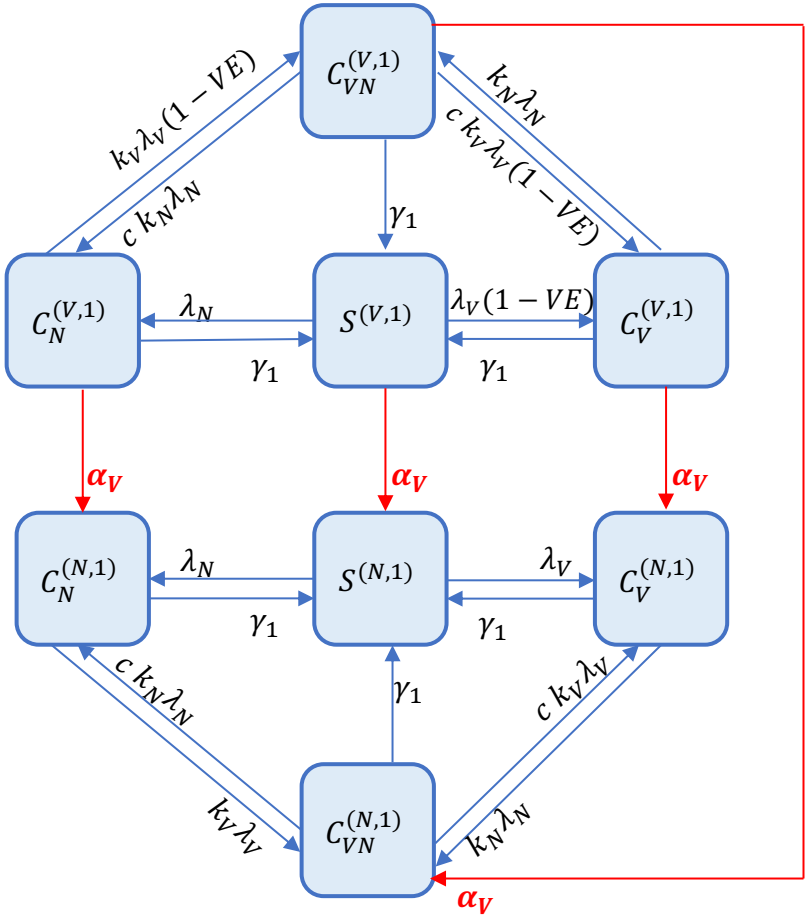
Neutral model

Can fix any prevalence

1. Lipsitch et al. (2009) *Epidemics*



Duplicate compartments for vaccinated individuals

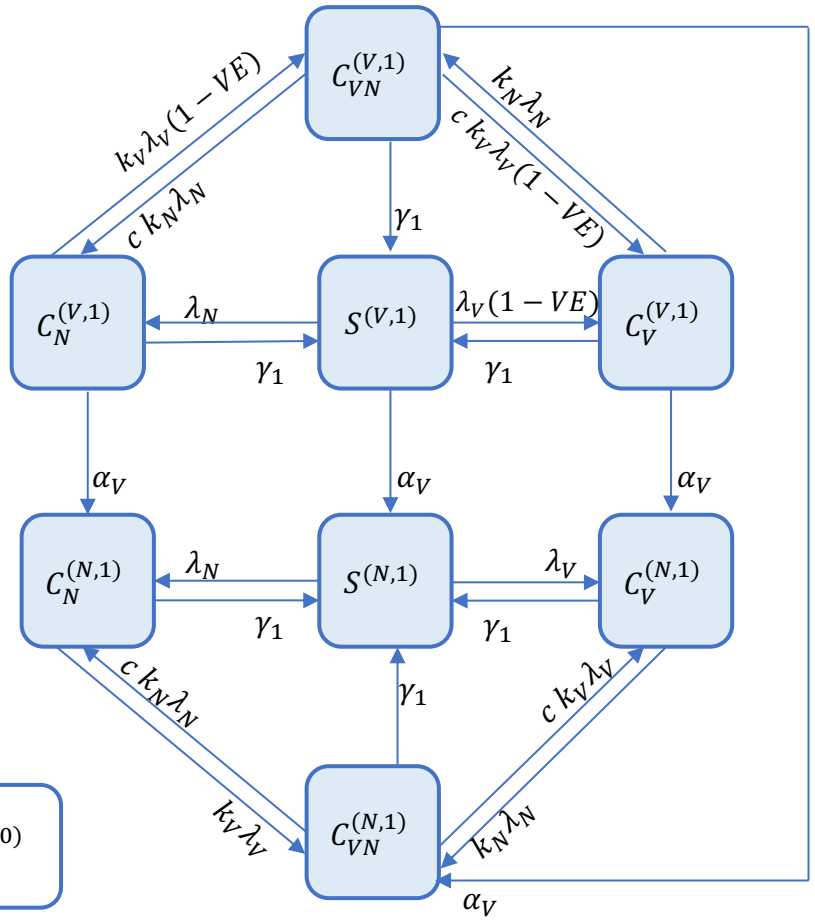


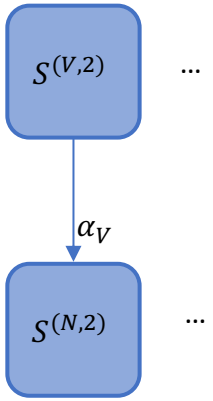
Allow vaccine protection to wane over time

Add age structure

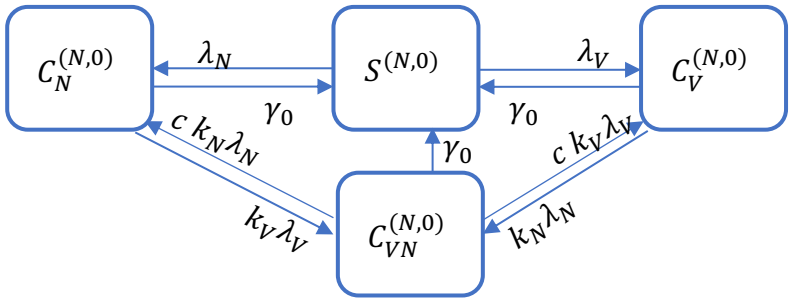
Age 1

Age 2,3,⋯,84





Age 0



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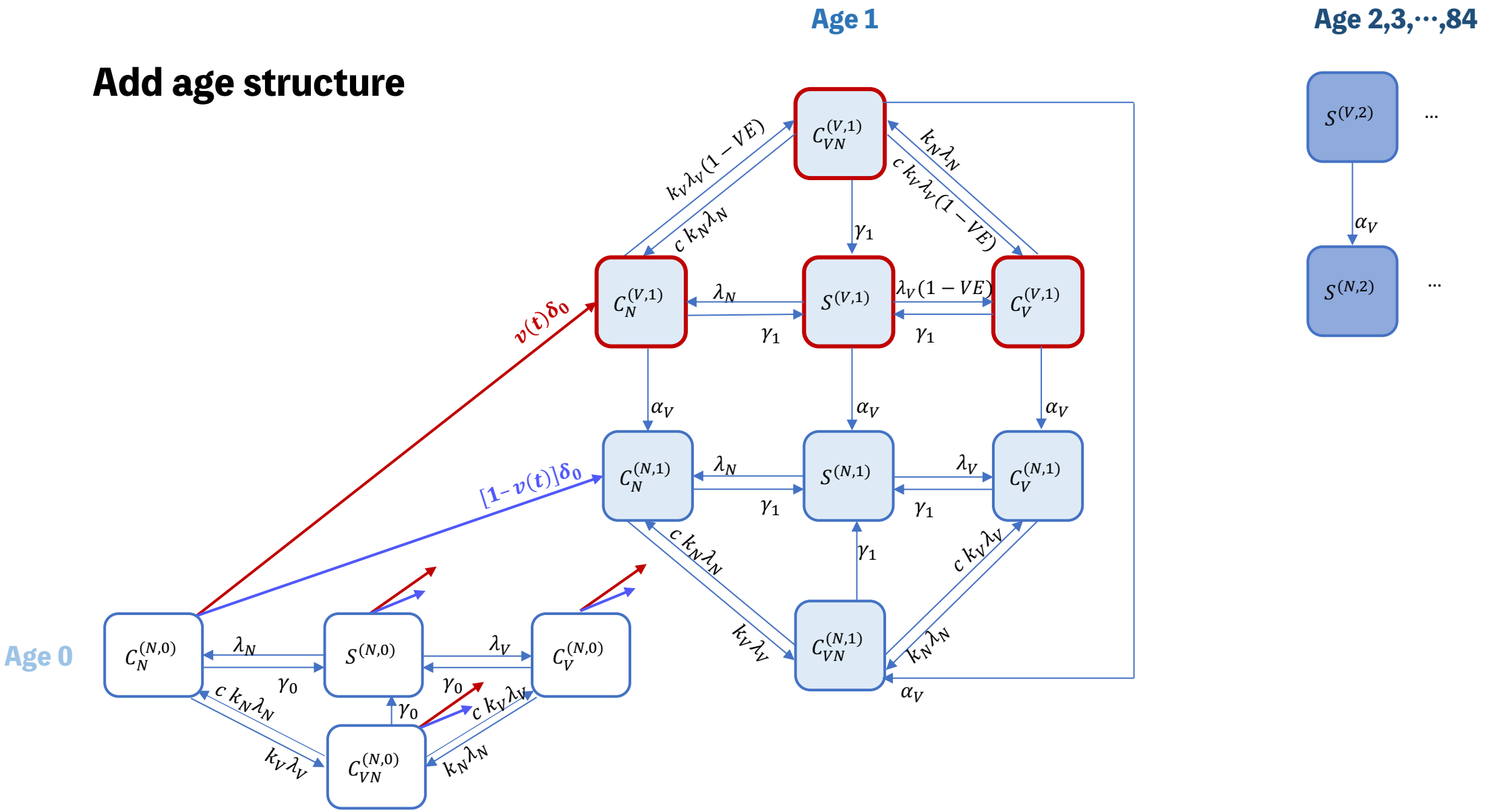

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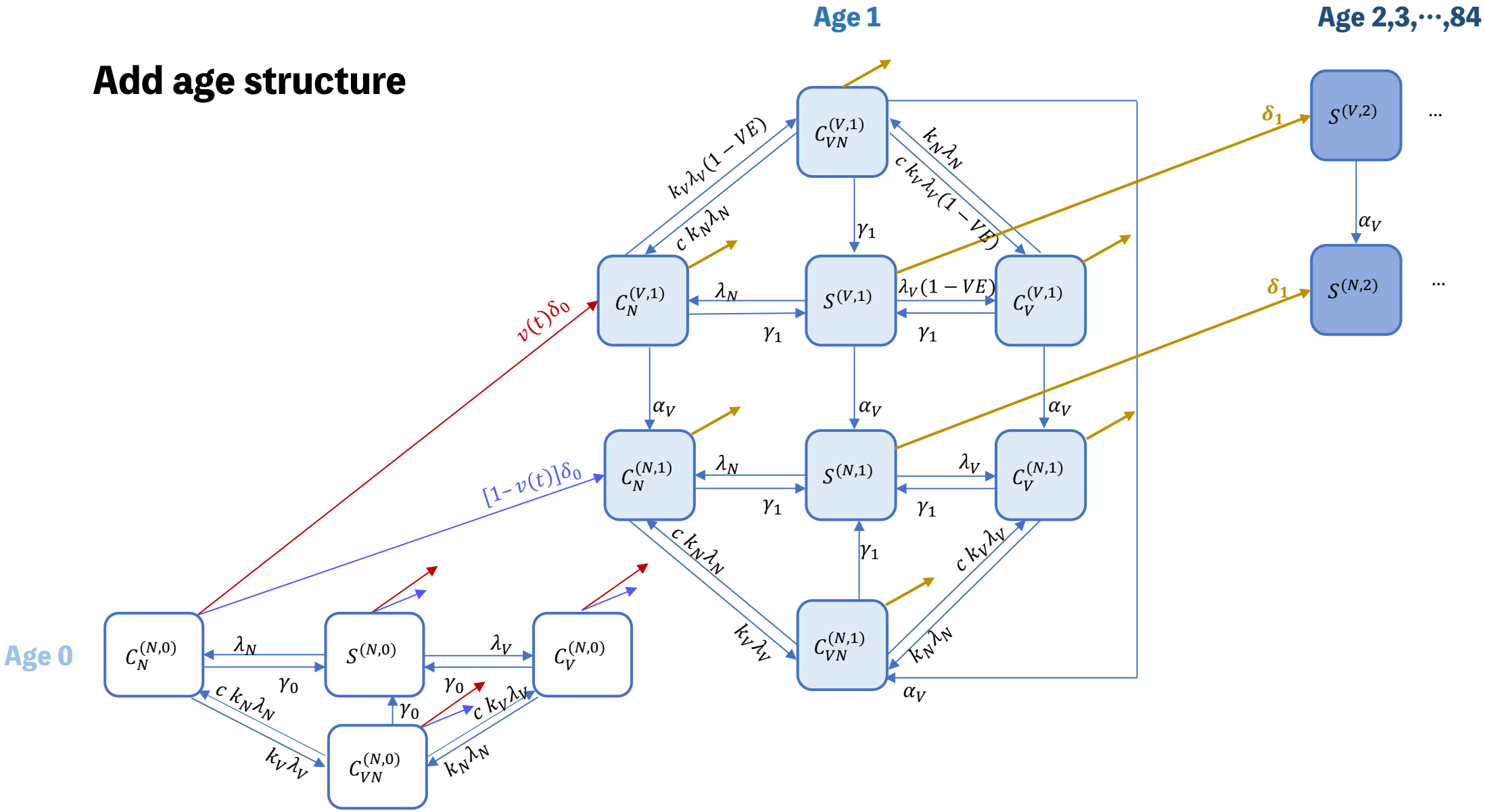
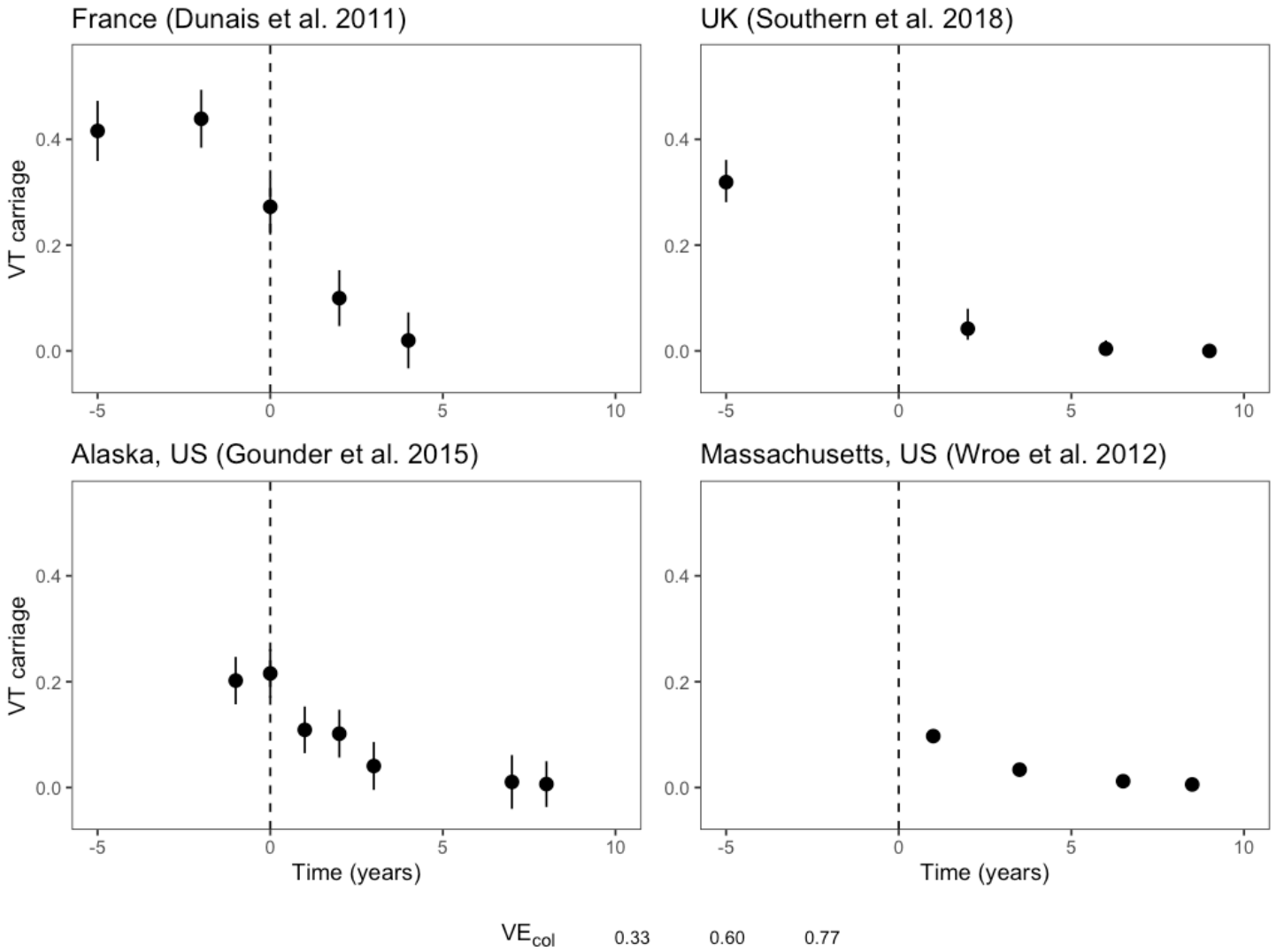


1）Our model can reproduce real-world VT colonization decline



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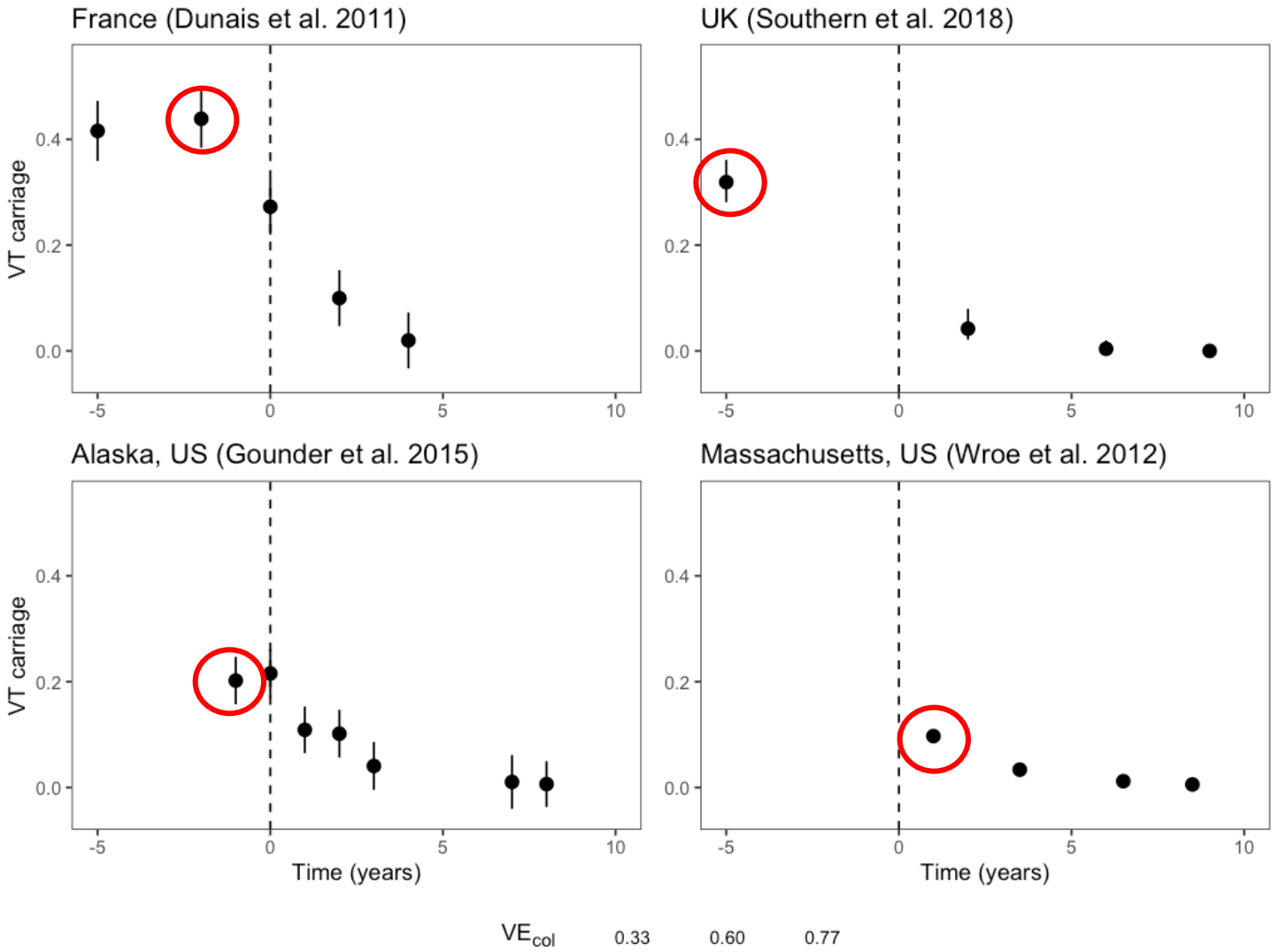

Fixed:

- **Vaccine coverage**
- **Overall prevalence**
- **Initial VT:NVT ratio**

Estimated:

- **Susceptibility $\beta^{(i)}$**

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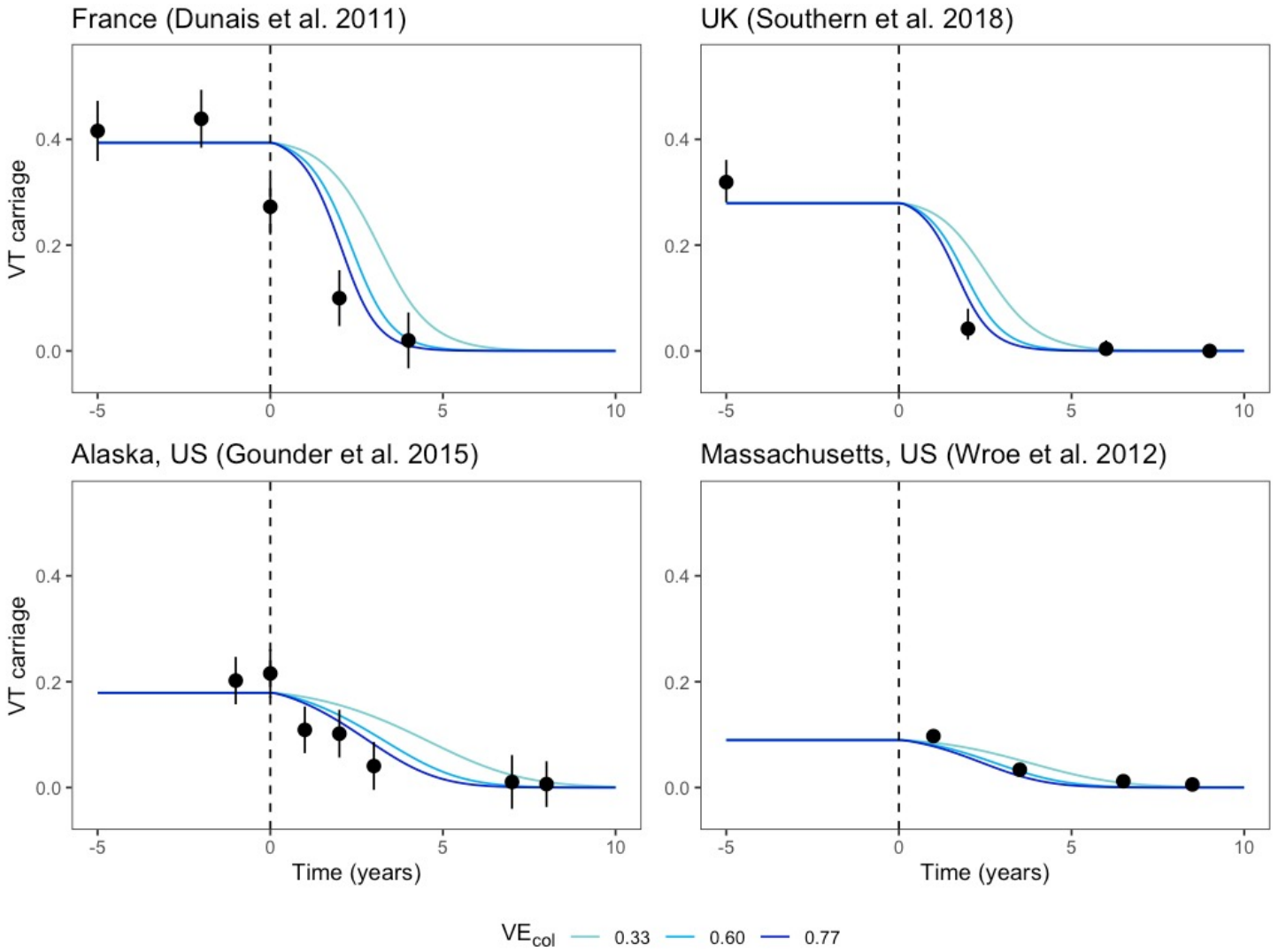


JOURNAL ARTICLE

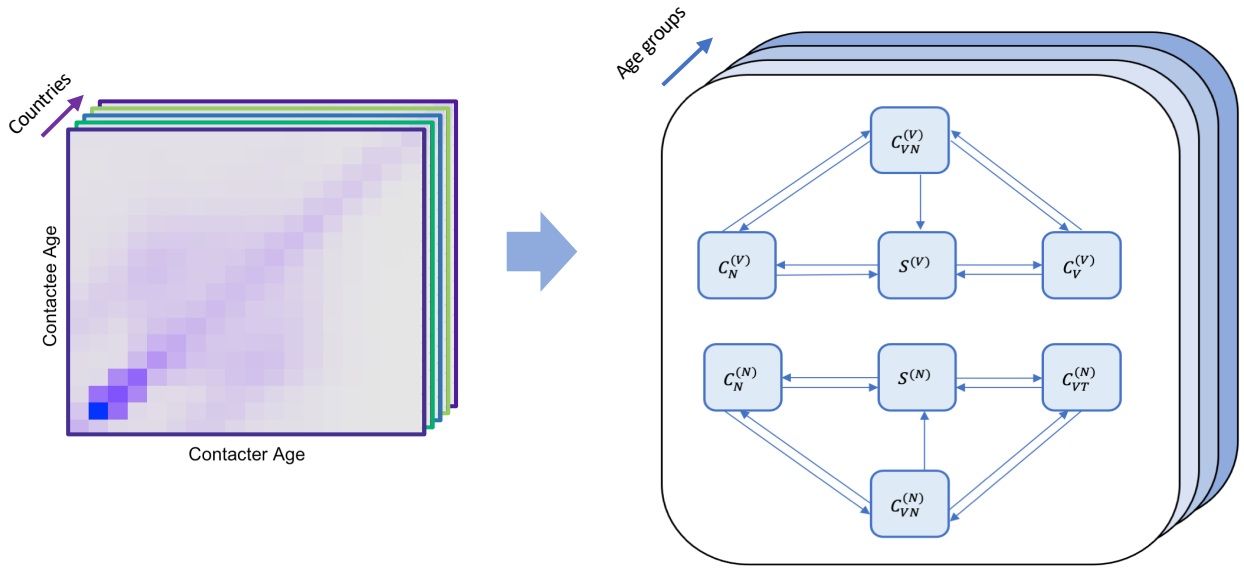
Effect of Pneumococcal Conjugate Vaccine on Nasopharyngeal Colonization among Immunized and Unimmunized Children in a Community-Randomized Trial

Katherine L. O'Brien, Eugene V. Millar, Elizabeth R. Zell, Melinda Bronsdon, Robert Weatherholtz, Raymond Reid, Jocelyn Becenti, Sheri Kvamme, Cynthia G. Whitney, Mathuram Santosham Author Notes

The Journal of Infectious Diseases, Volume 196, Issue 8, 15 October 2007, Pages 1211–1220, https://doi.org/10.1086/521833
Published: 15 October 2007 **Article history**

2) Contact matrices led to different time-to-elimination

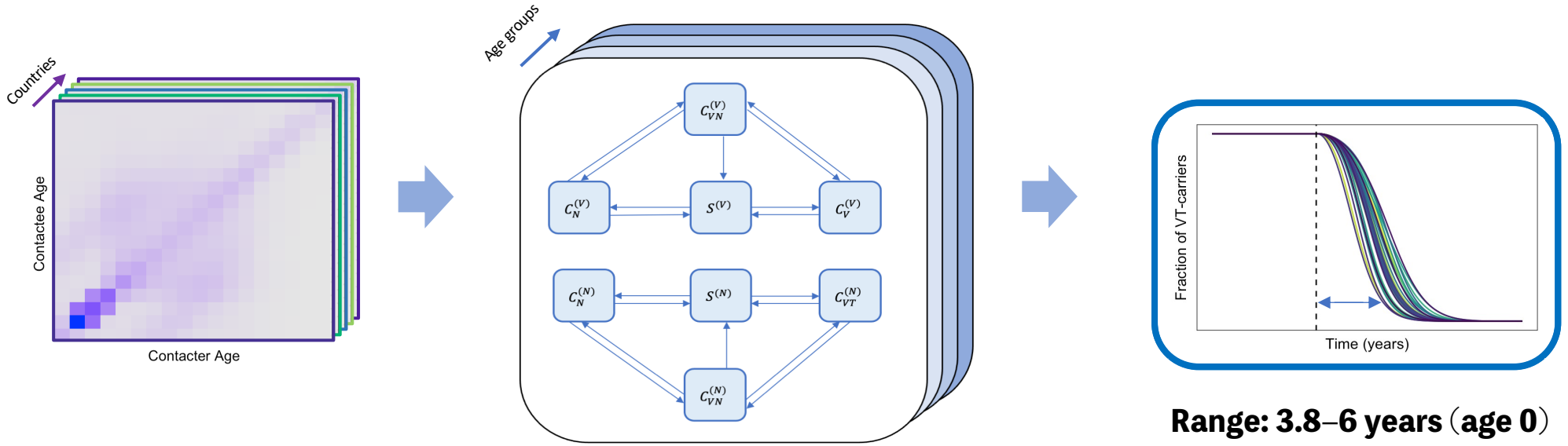
- **Simulate transmission using different contact matrices[1]**



1. Mistry et al. (2021) *Nat Comm*

2) Contact matrices led to different time-to-elimination

- **Simulate transmission using different contact matrices[1]**
- **Measure time-to-elimination**



Range: 3.8–6 years (age 0)

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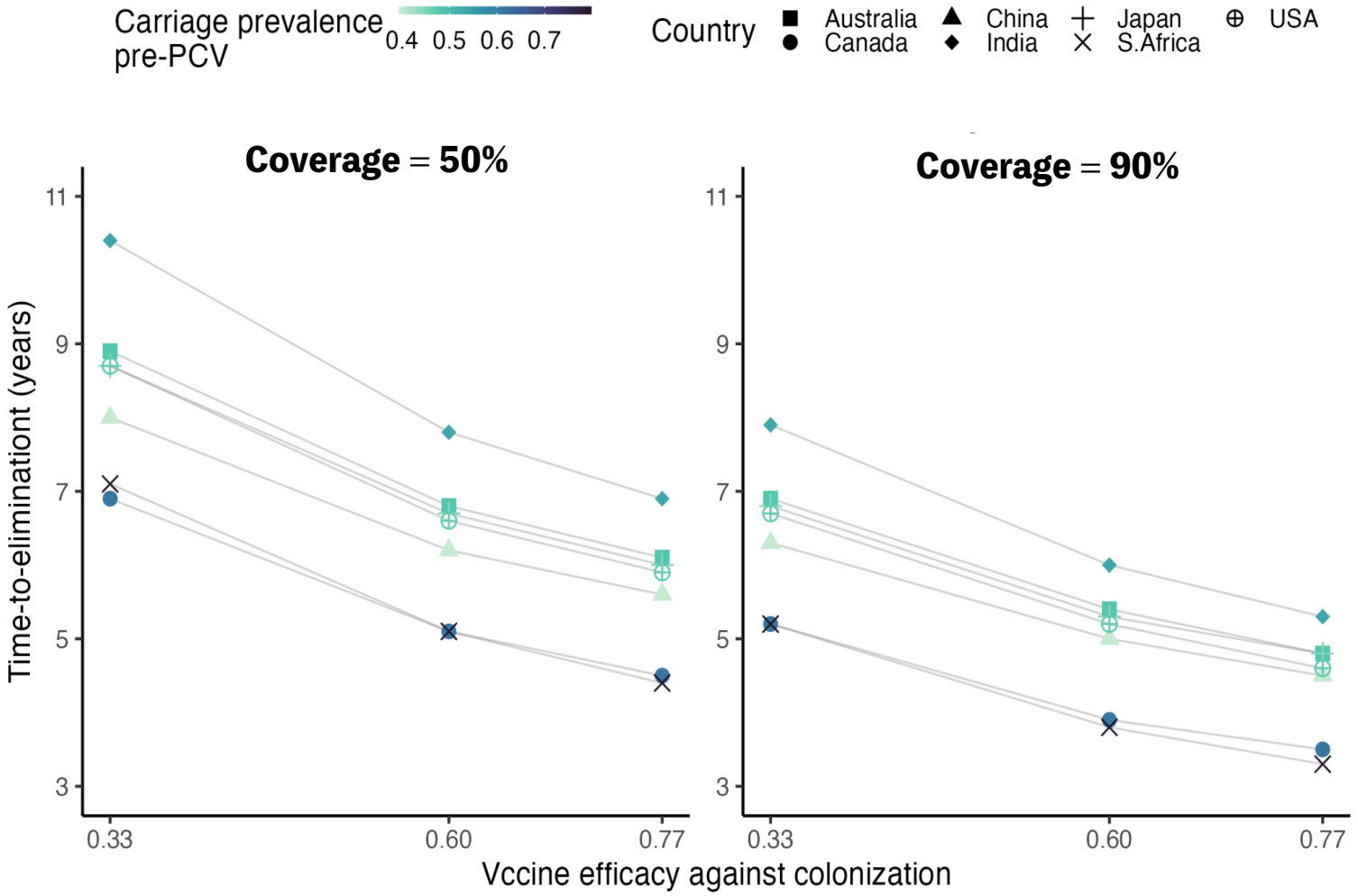
3) Vaccine factors were the most influential parameters



We tested:

- **Vaccine efficacy**
- **Vaccine coverage**
- Waning rate
- Initial VT:NVT ratio
- Population susceptibility

4) Effect of various features of contact structure:

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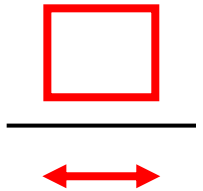
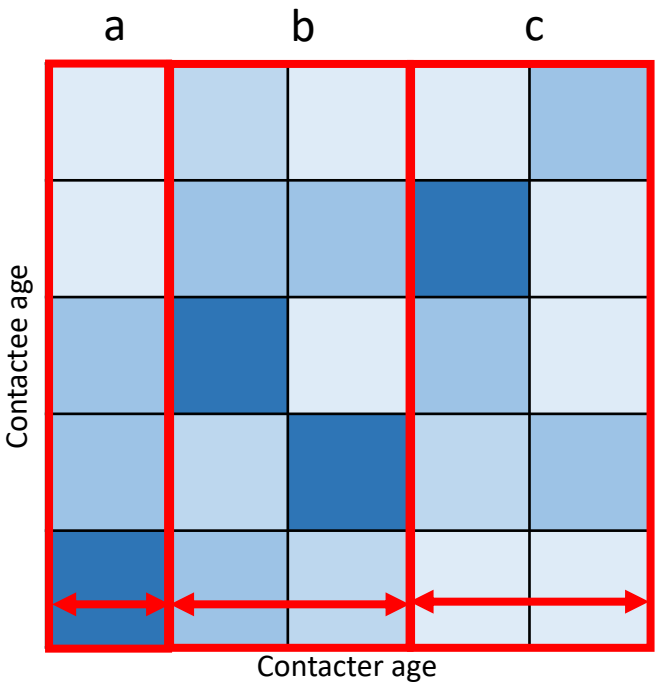
- **Features[1]**
  - **Total contact =** 



1. Sage et al. (2021) *PLoS ONE*

4）Effect of various features of contact structure:

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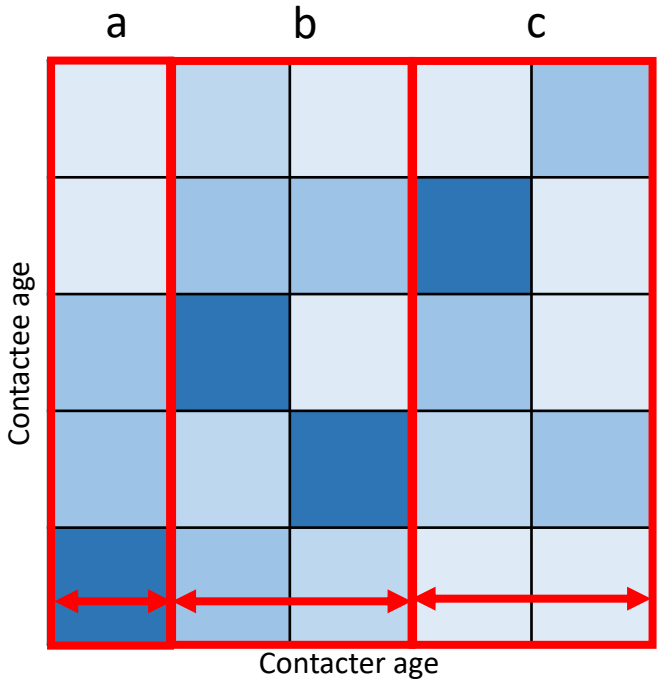

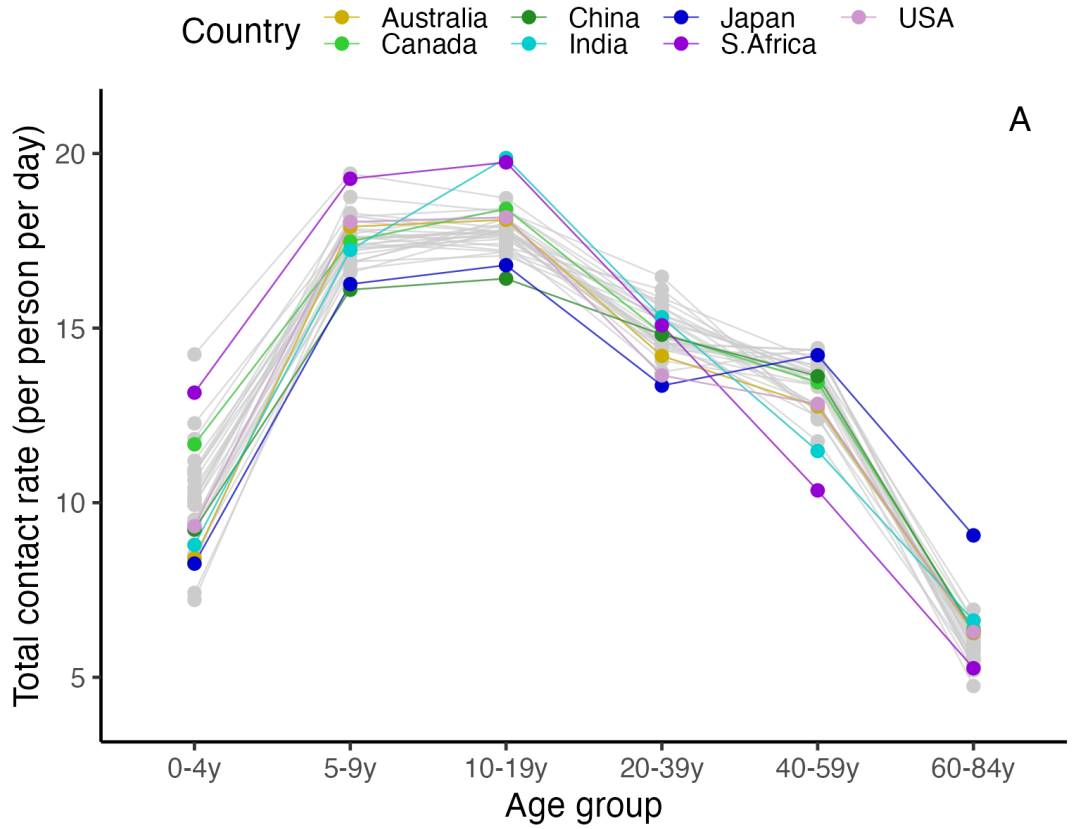

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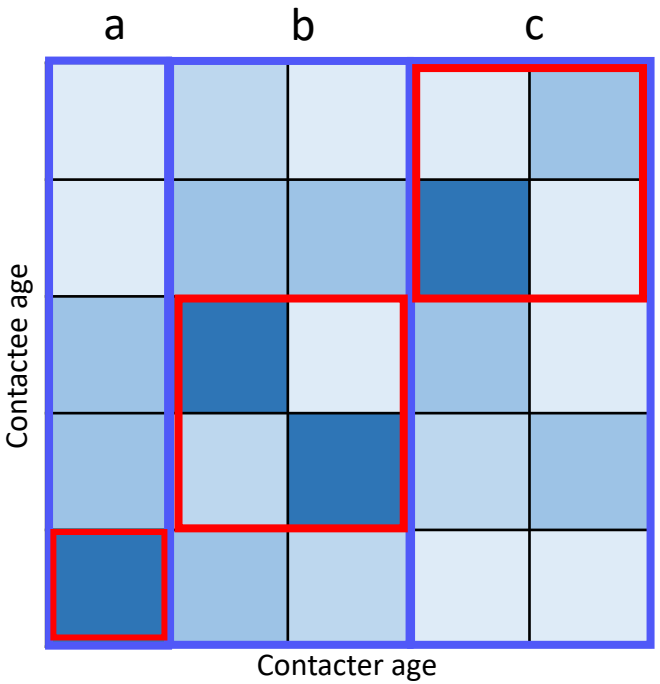

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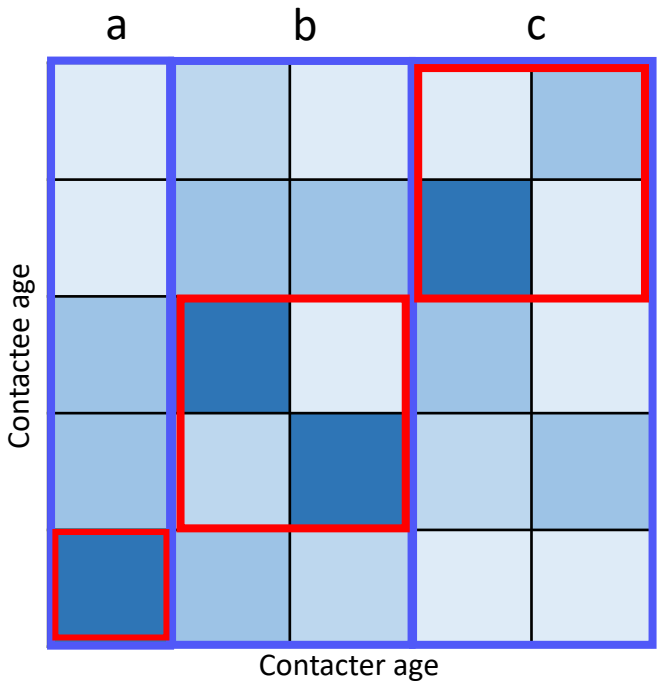

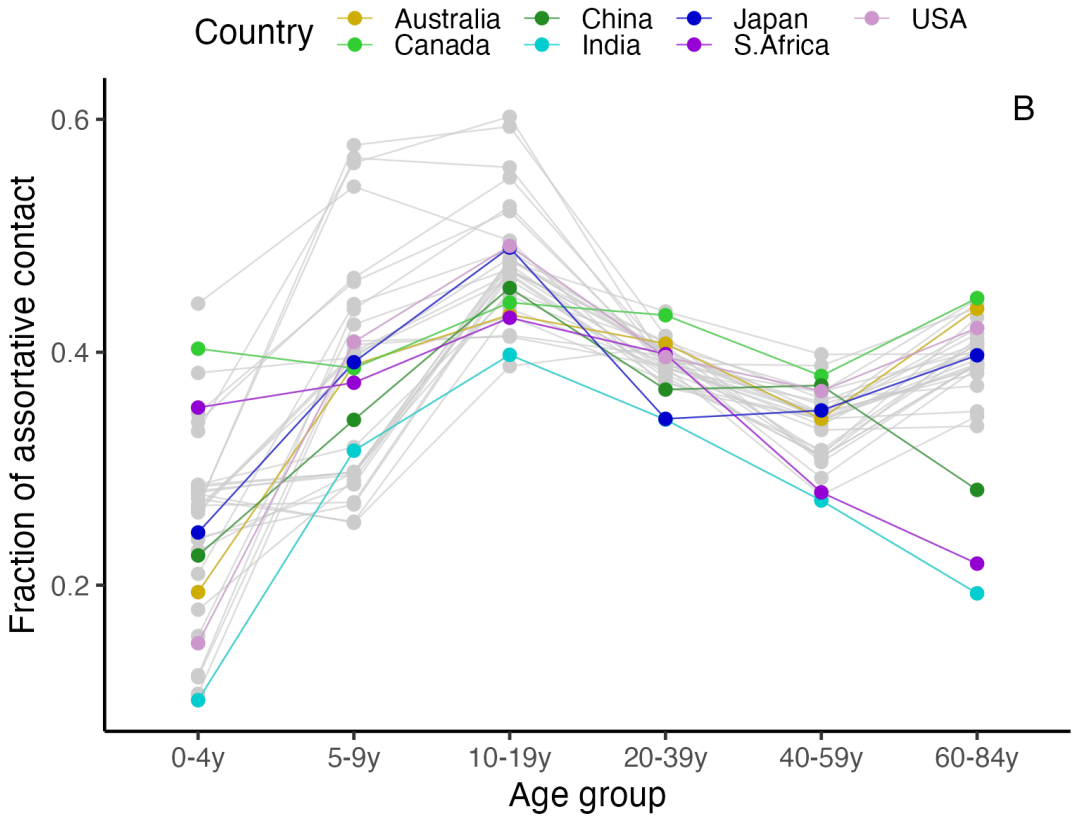

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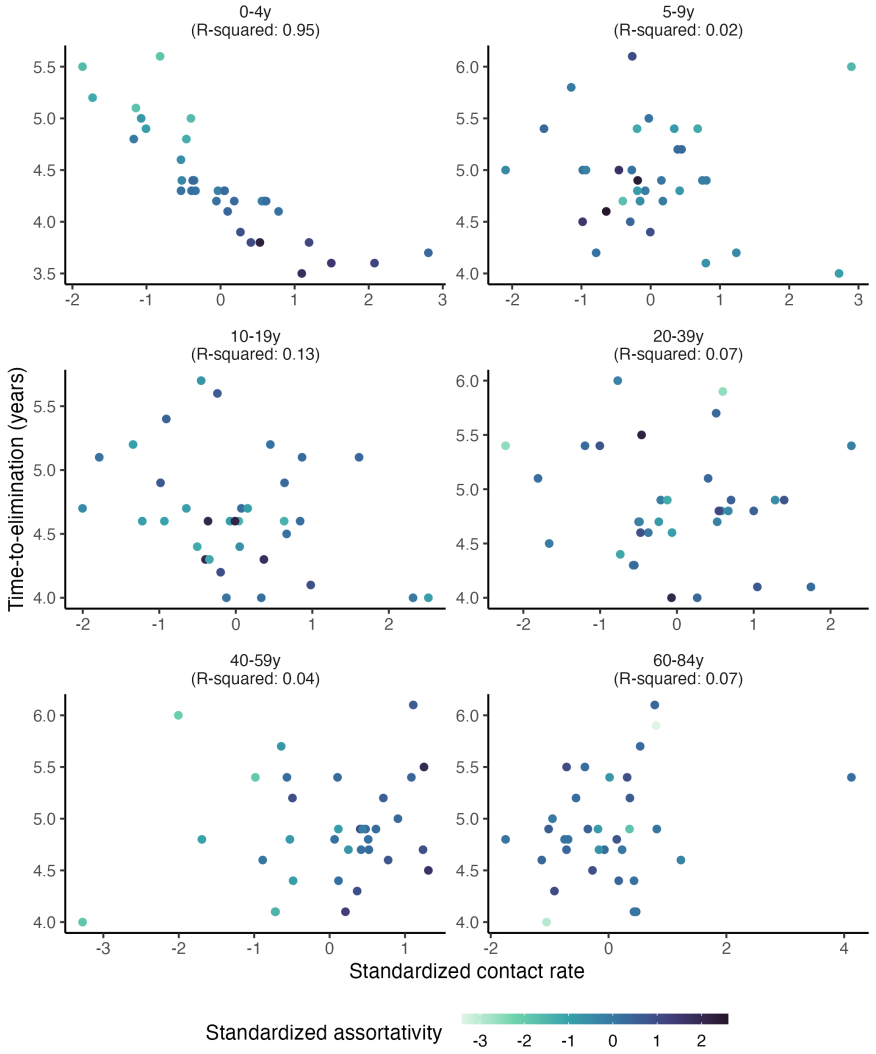
Time-to-elimination was highly dependent on contact patterns in children under 5



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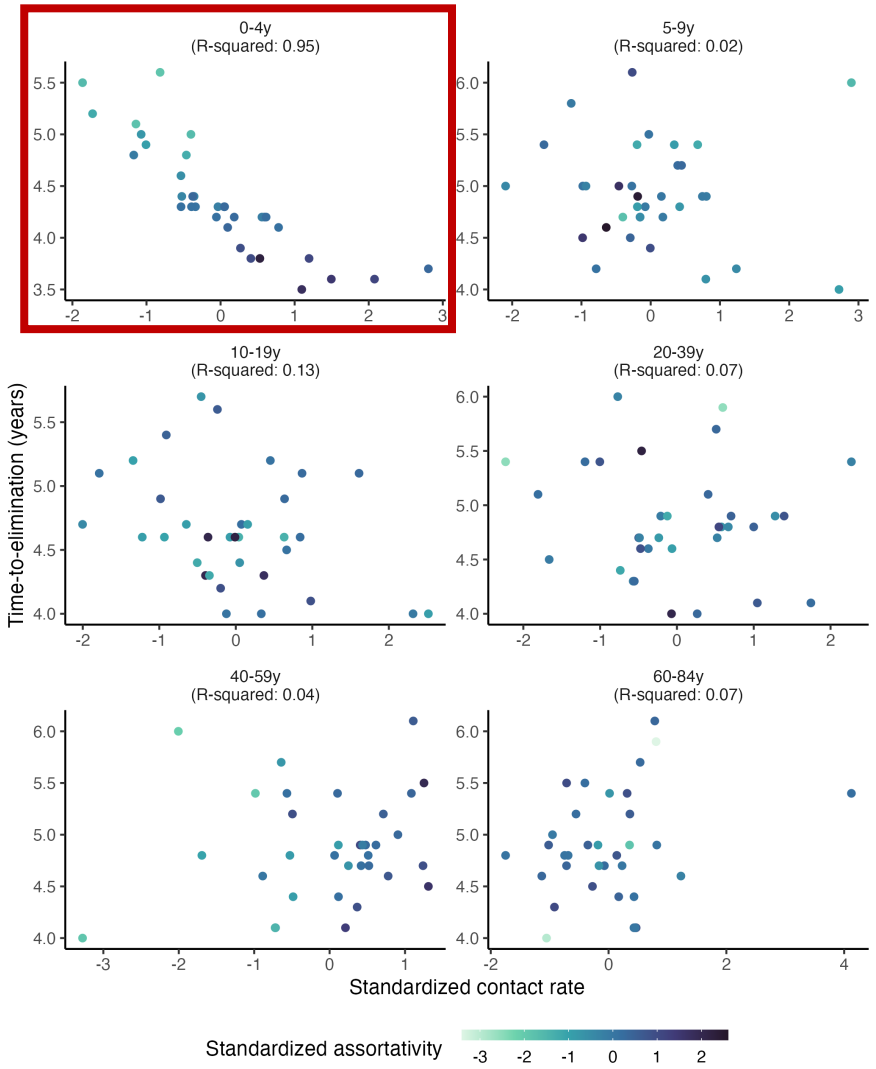

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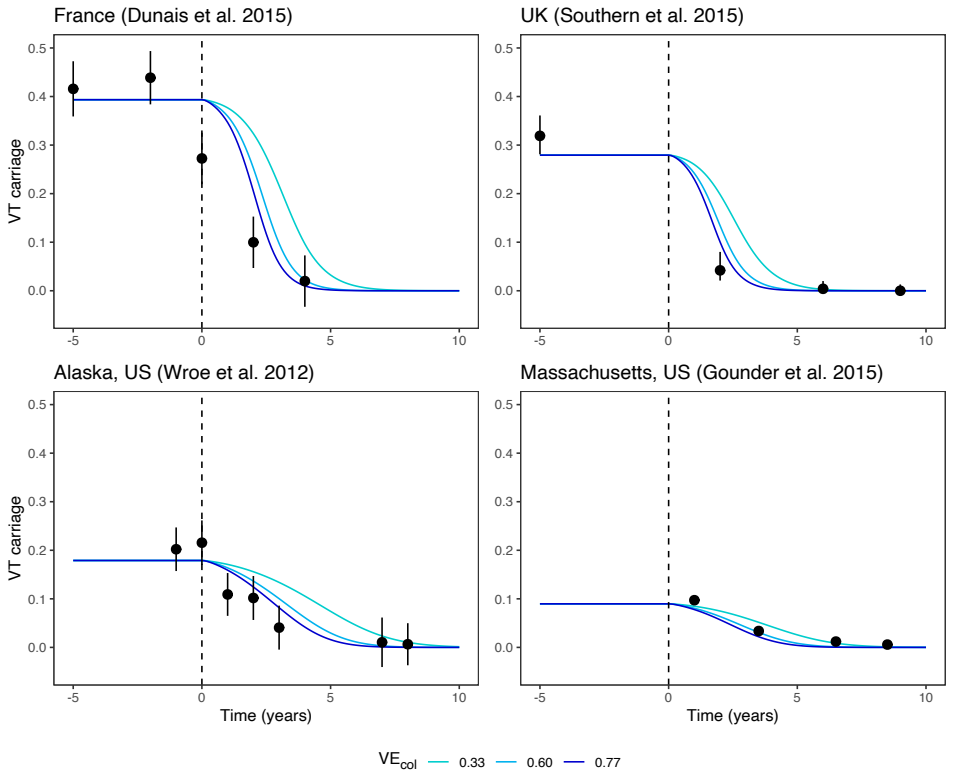

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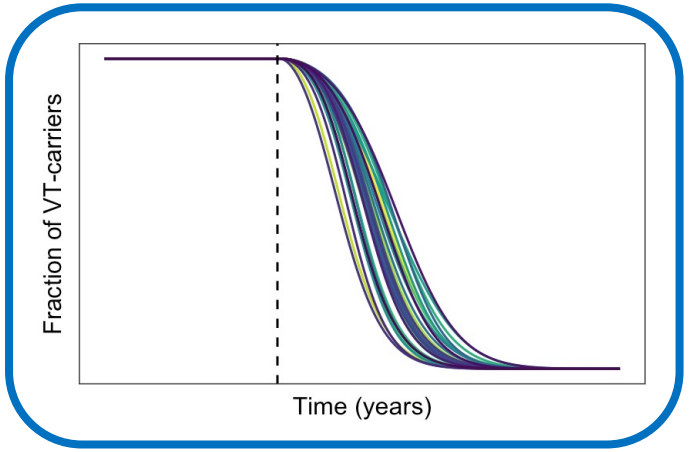

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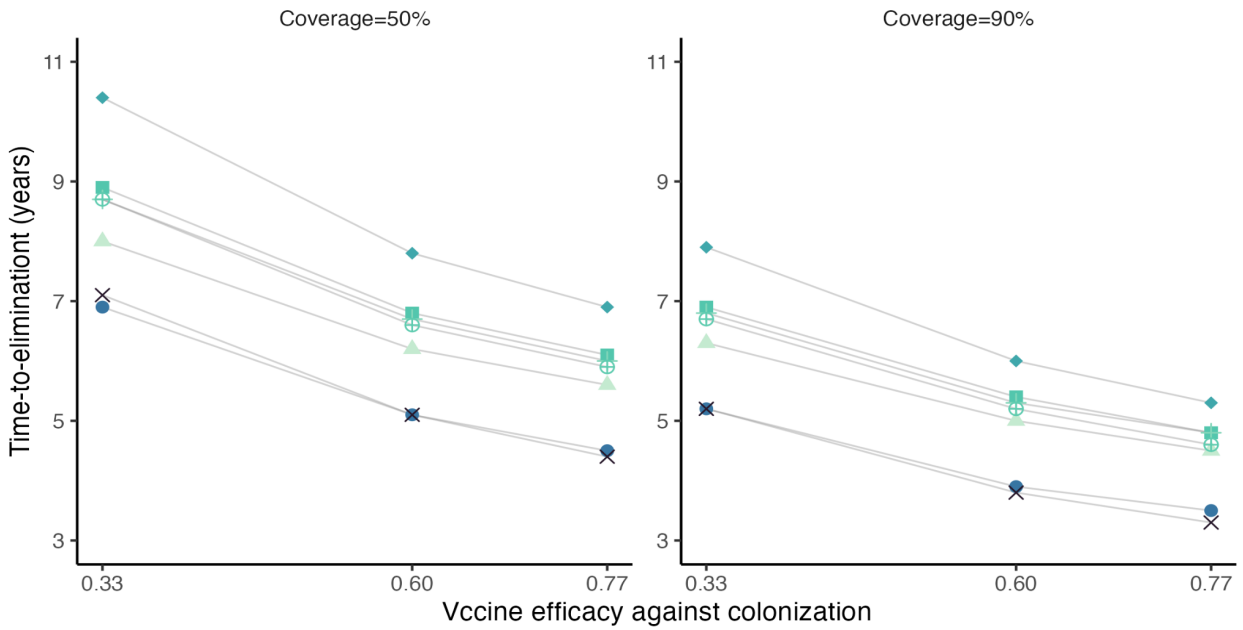

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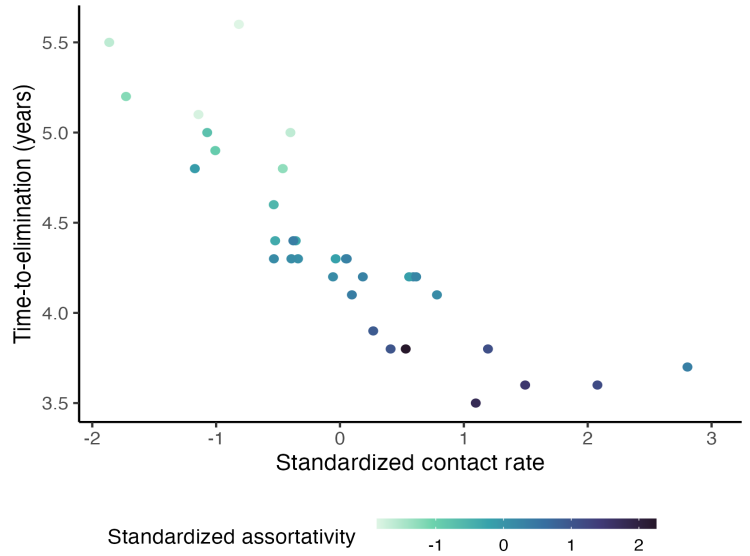

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Anabelle Wong, Sarah C. Kramer, Daniel M. Weinberger, Matthieu Domenech de Cellès

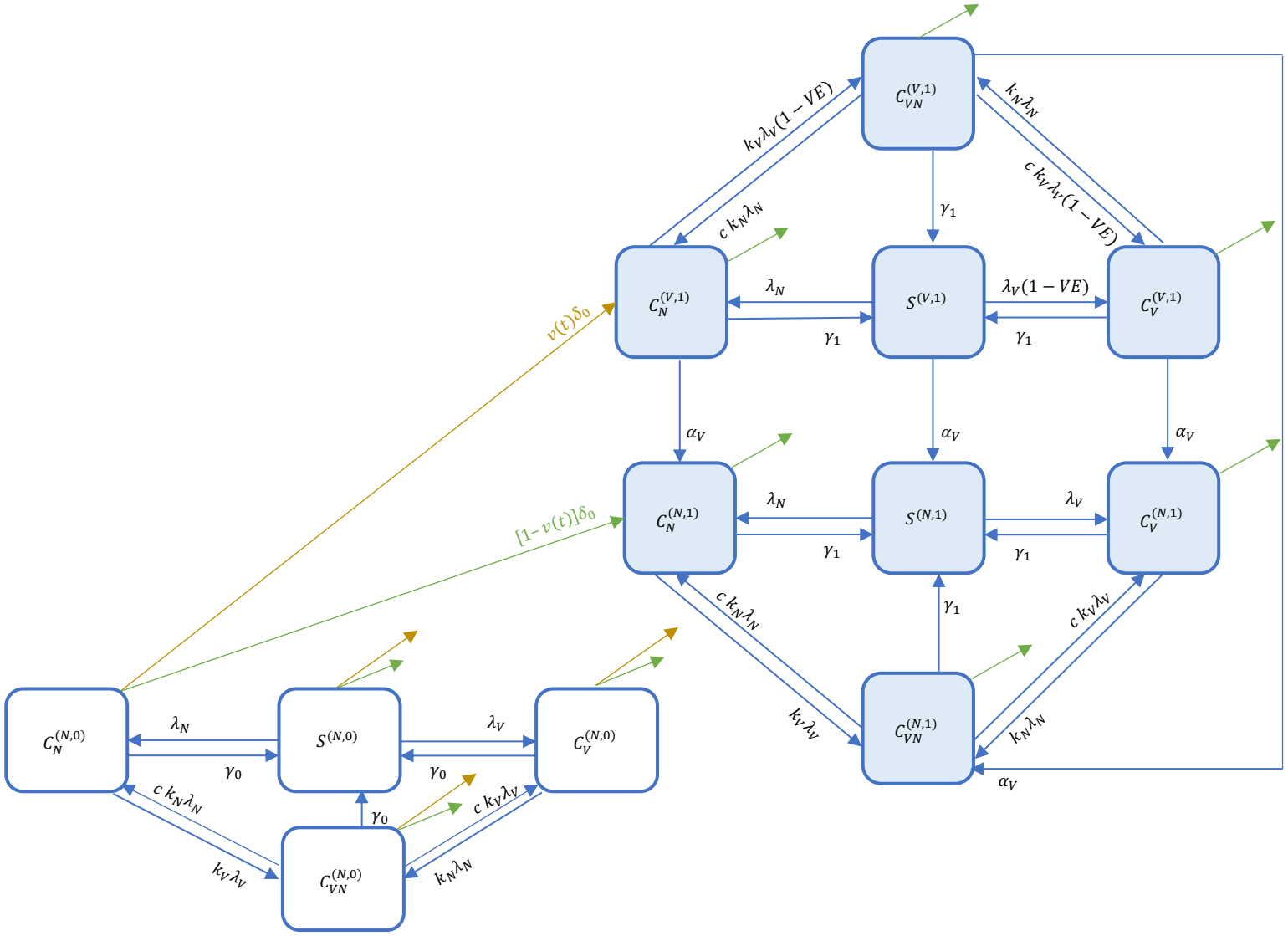
doi: https://doi.org/10.1101/2024.08.13.24311931

Thank you!

Q&A

Parameters

Parameter	Interpretation	Value	Source
$\beta_V^{(i)}(=\beta_N^{(i)})$	Age-specific susceptibility to carriage acquisition	$\beta^{(0,\ldots,4)}=0.015$ $\beta^{(5,\ldots,19)}=0.004$ $\beta^{(20,\ldots,59)}=0.003$ $\beta^{(60,\ldots,84)}=0.005$ *$\pm$20% for high and low population susceptibility respectively	[48]
$1/\gamma_i$	Age-specific average duration of carriage	See Supplementary Figure 1	Fitted to observed data (Supplementary Data 1)
$k_N(=k_V)$	Competition parameter: Effect of existing VT (NVT) carriage on acquiring NVT (VT) carriage	0.5	[36]
c	Fraction of co-carriers returning to C_V (C_N) upon reinfection with VT (NVT)	0.5	[15]
q	Relative infectiousness with each serotype for co-carriers	0.5	[15]
ϵ_V	Vaccine efficacy against carriage acquisition	33%, 60%, 77%	[40]
p_V	Vaccine coverage	50%, 90%	[10]
α_V	Waning rate of vaccine-conferred immunity	0, 0.1, 0.2, 0.3 per year	[42,43]
$f_C^{(i)}(0)$	Initial prevalence of carriers in age group i	$f_C^{(0,\ldots,4)}(0)=0.5$ $f_C^{(5,\ldots,19)}(0)=0.2$ $f_C^{(20,\ldots,59)}(0)=0.1$ $f_C^{(60,\ldots,84)}(0)=0.1$	[23], observed data (Supplementary Data 2)
$f_V(0), f_N(0)$	Initial proportions of VT-, NVT-carriers	$f_V(0)$: 0.2–0.8 $f_N(0)$: 0.2, 0.4 where $f_V(0)+f_N(0)\leq 1$	Observed data (Table 2)



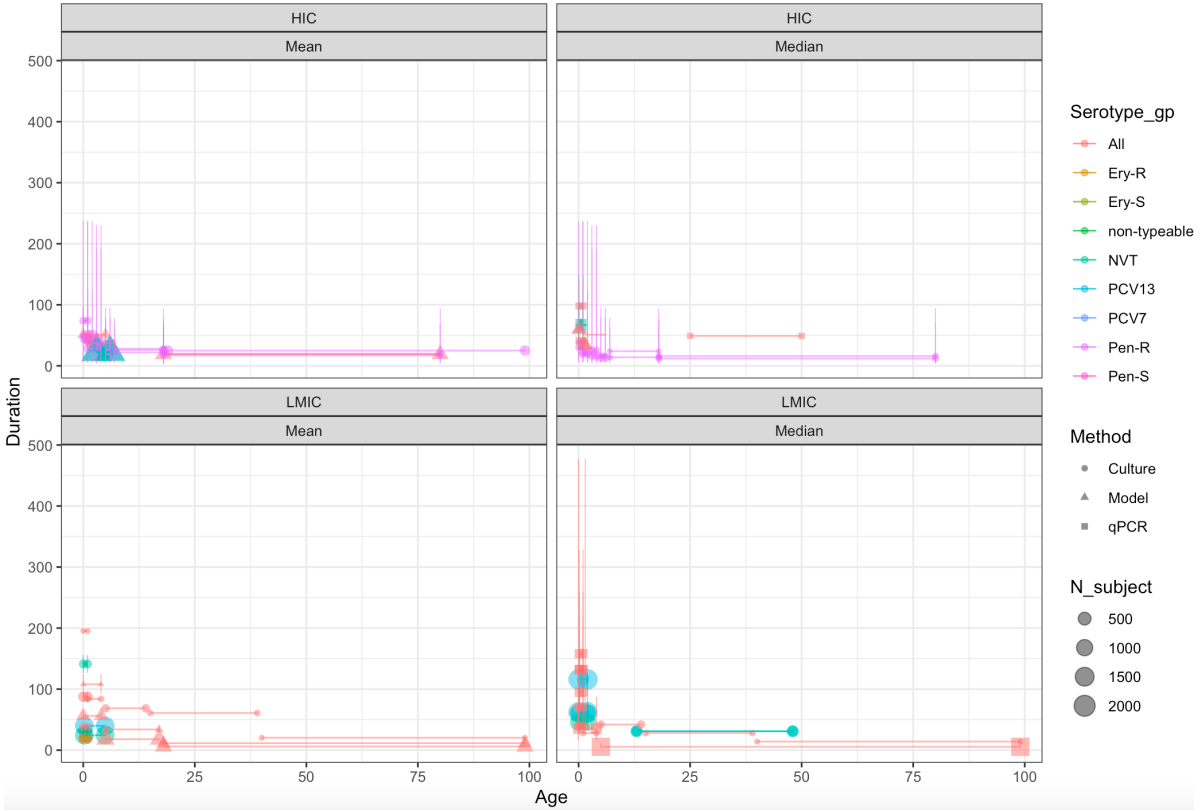
Parameters: Clearance rate (γ)

- **Fit clearance rate (to extracted estimates from literature)**

23 studies

Culture only: 15/23 studies

- **HIC (7/12) – pre: 4/7, post: 3/5**
- **LMIC (8/11) – pre: 6/7, post: 2/4**



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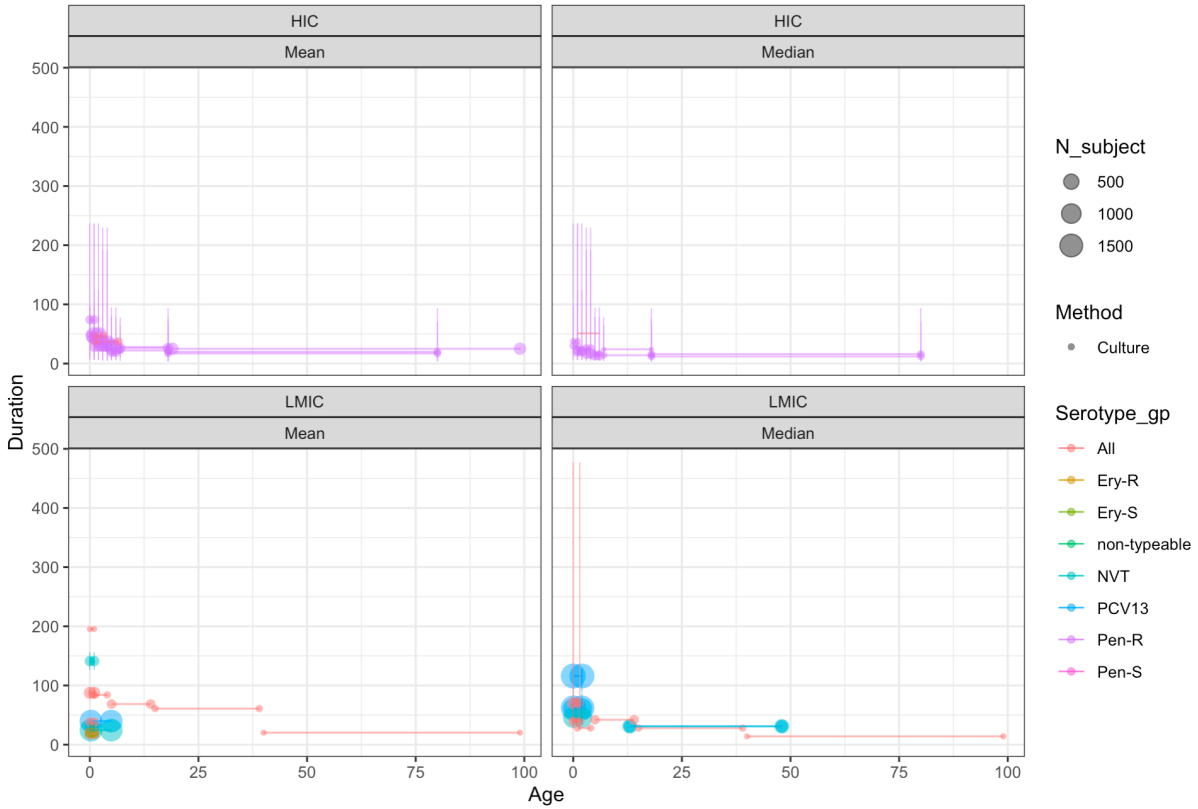
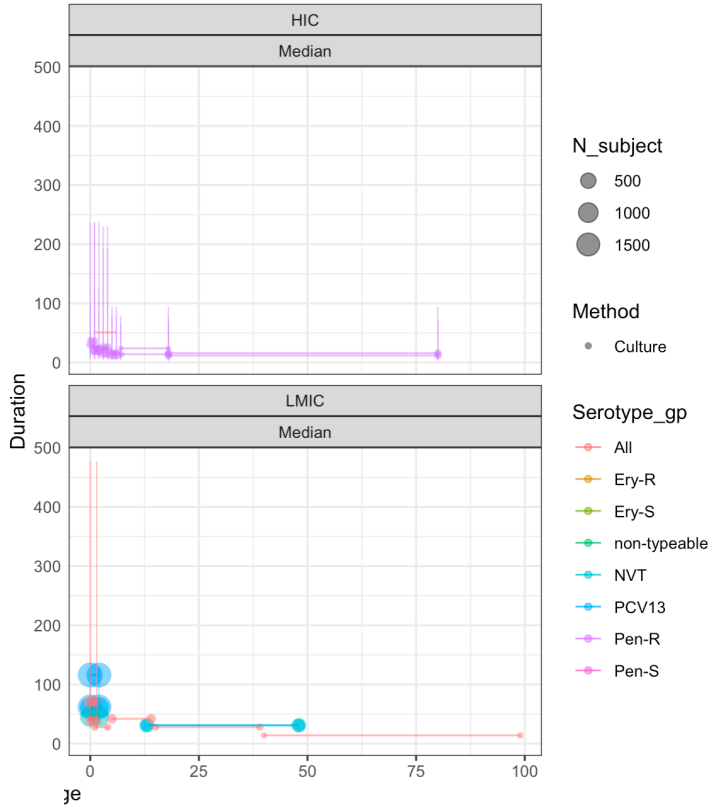


Parameters: Clearance rate (γ)

- **Fit clearance rate (to extracted estimates from literature)**

23 studies
→ culture only = 15
→ take median only = 8

Culture only: 15/23 studies
• **HIC (7/12) – pre: 4/7, post: 3/5** • **LMIC (8/11) – pre: 6/7, post: 2/4**
Reported median: 8/15 studies
• **HIC (4/7) – pre: 1/4, post: 3/3** • **LMIC (4/8) – pre: 4/6, post: 0/2**

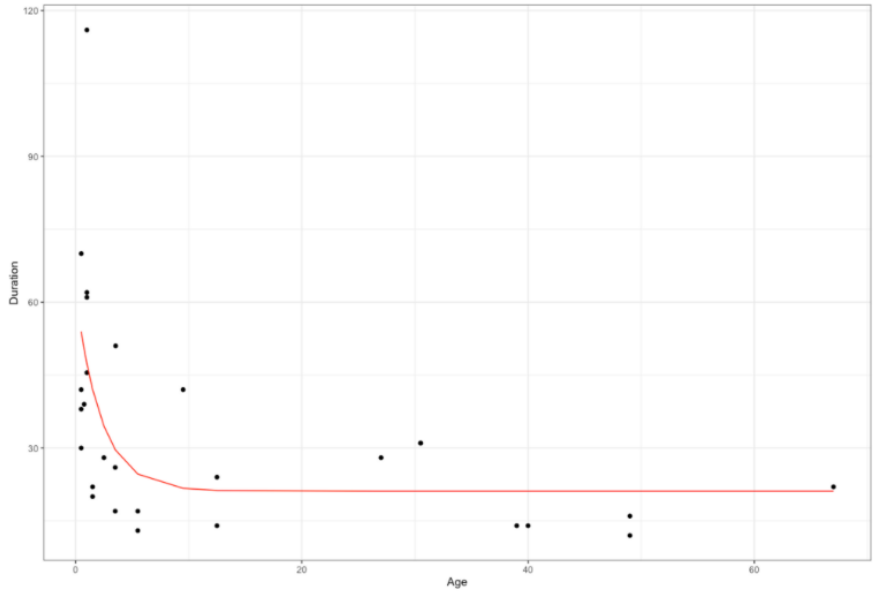


Parameters: Clearance rate (γ)

- **Fit clearance rate (to extracted estimates from literature)**

23 studies
→ culture only = 15
→ take median only = 8

Formula: Duration ~ k + (b - k)*exp(-c*Age)



Parameters: Contact matrices $(\tilde{m}_{ij})$

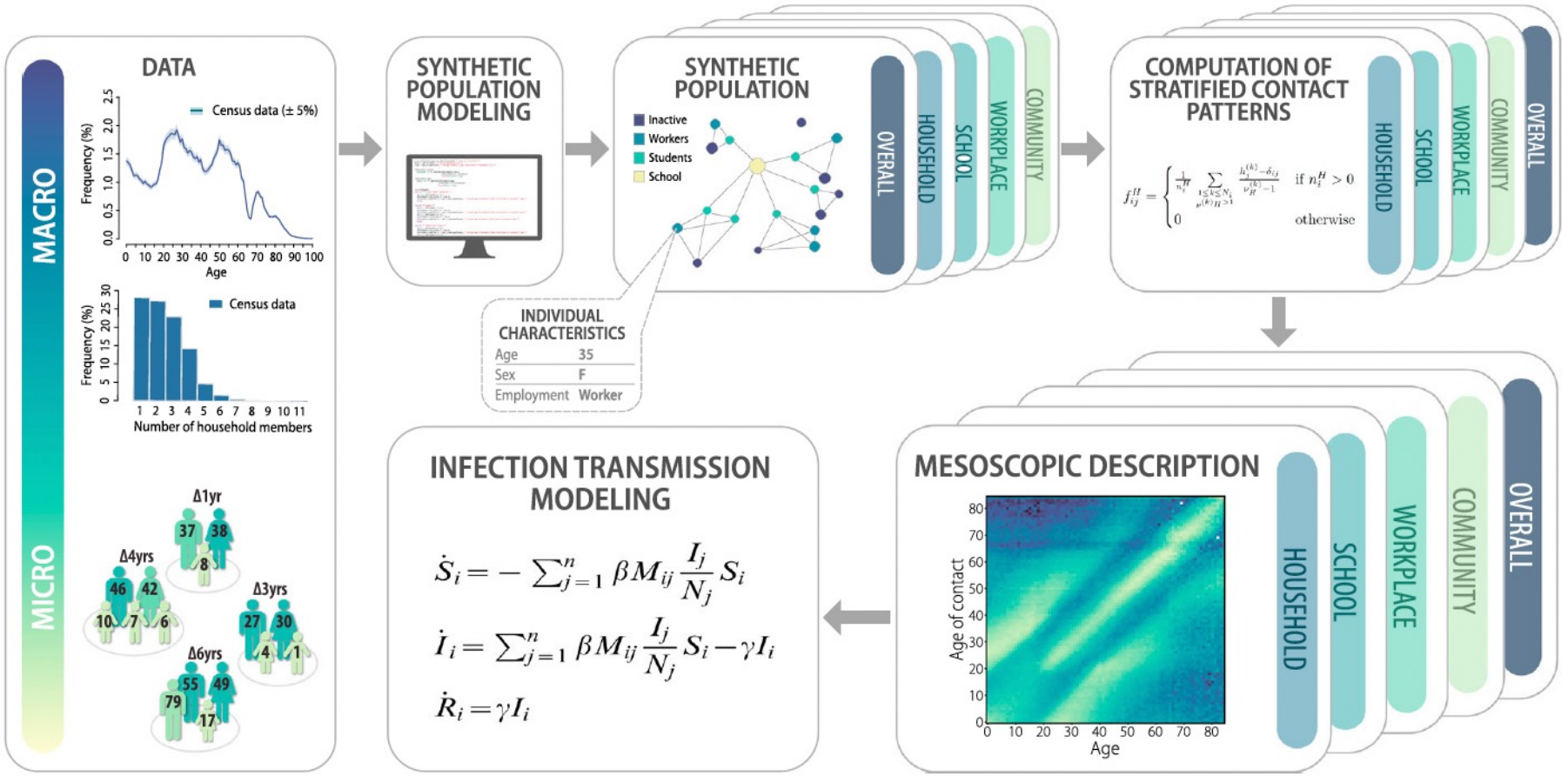


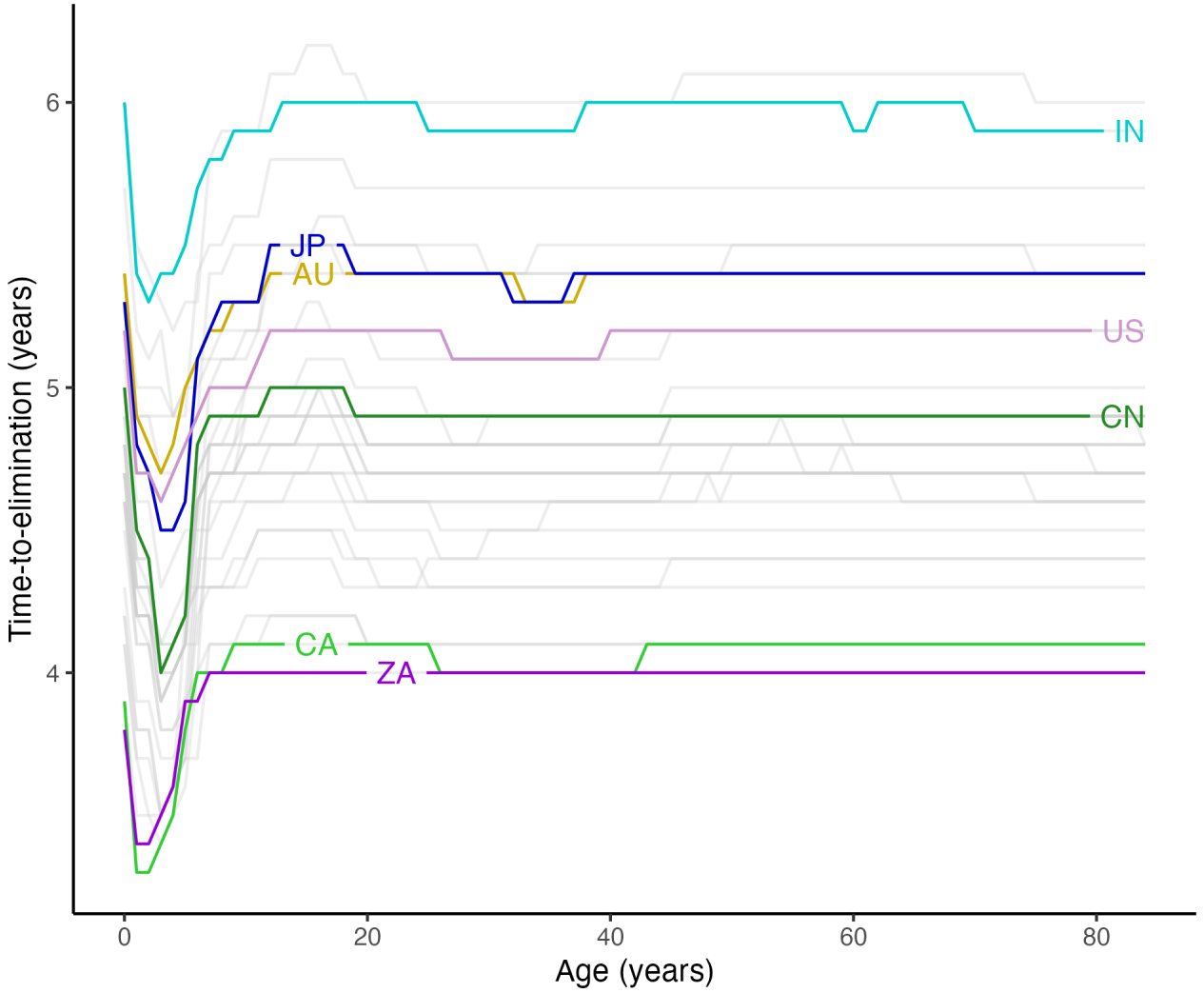
Fig. 1 Modeling framework. Schematic representation of the workflow for modeling human-mixing patterns and infection transmission dynamics.

Mistry et al. (2021) *Nat Comm*

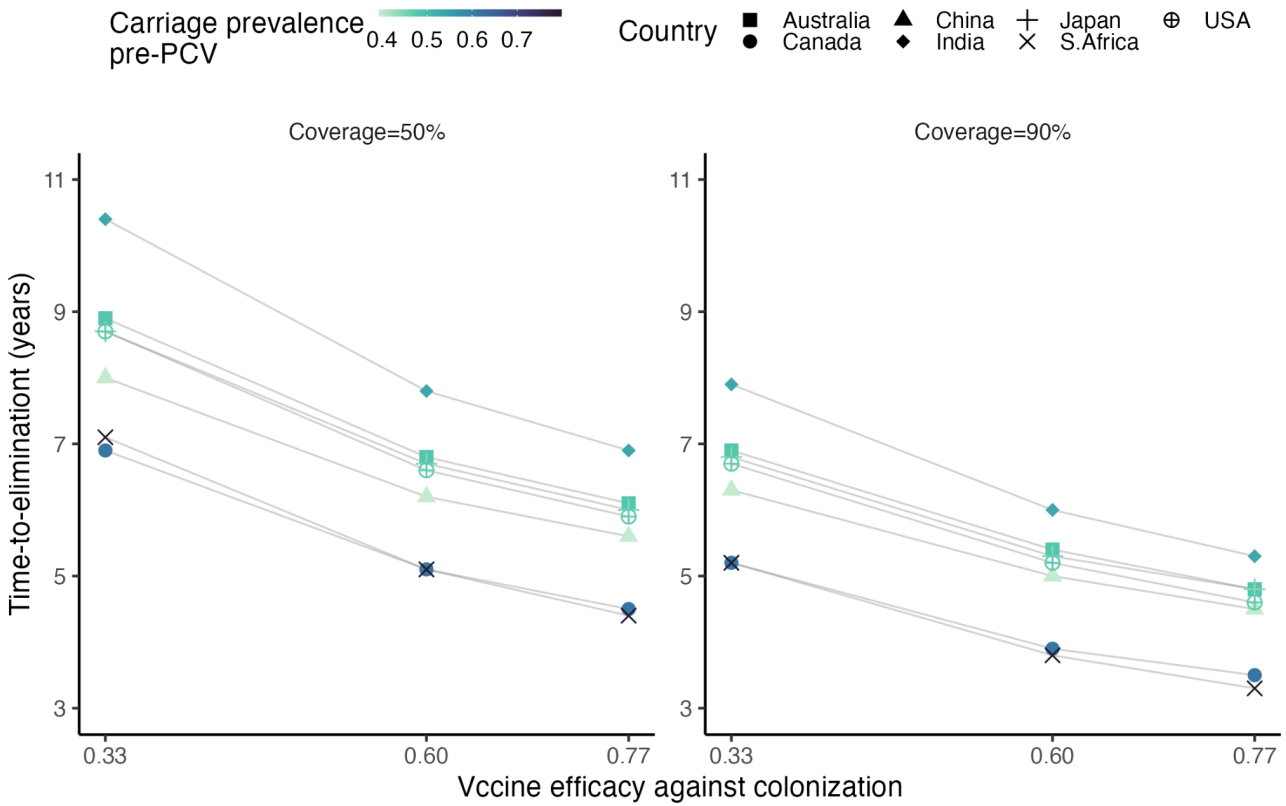
1）Verify model against real-world VT-decline

Location	Sample characteristics	Overall carriage (age 0, 1-4, 5-17, 18-39, 40-59, 60-84)	Initial proportions of VT-, NVT-carriers	Vaccine coverage
France [16]	Children 3–40 months attending daycare center	0.59, 0.59, 0.30, 0.10, 0.10, 0.10 [16,23]	0.75, 0.25 [16]	2004-05: 61% 2005-05: 74% 2006-07: 86% 2007-08: 90% [30]
UK [17]	Children 1–5 years attending primary care practices	0.49, 0.49, 0.21, 0.08, 0.08, 0.08 [17]	0.659, 0.341 [17]	90% [49]
Alaska, US [18]	Children 3 months–5 years attending primary care practices	0.38, 0.38, 0.30, 0.10, 0.10, 0.10 [18,23]	0.53, 0.47 [18]	60% [18]
Massachusetts, US [19]	Children 3 months–7 years attending primary care practices	0.28, 0.28, 0.28, 0.10, 0.10, 0.10 [19,23]	0.36, 0.64 [19]	85% [19]

2) Contact matrices led to different time-to-elimination



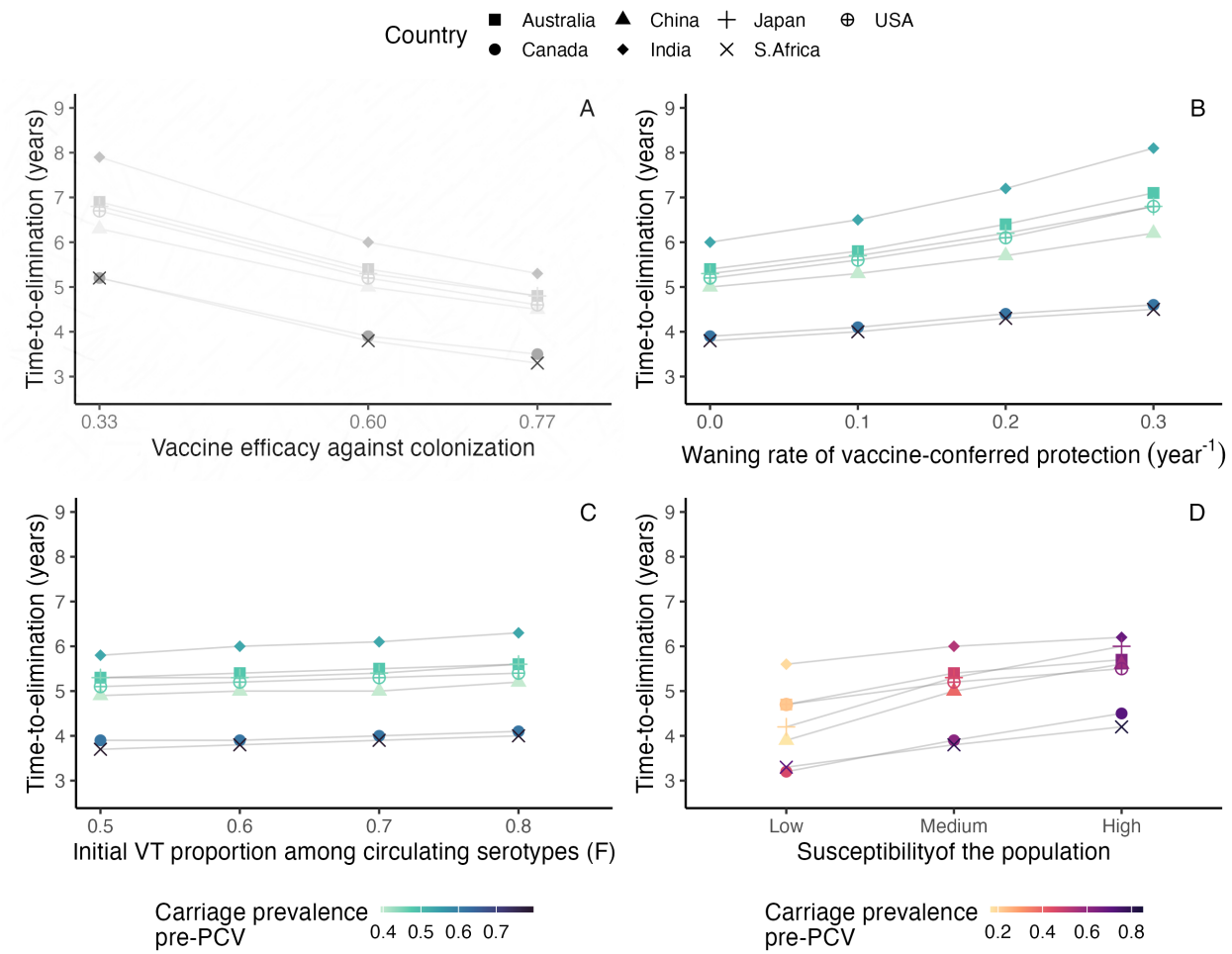
3）Effect of other factors



We tested:

- **Vaccine efficacy**
- **Vaccine coverage**
- Waning rate
- Initial VT:NVT ratio
- Population susceptibility

3）Effect of other factors

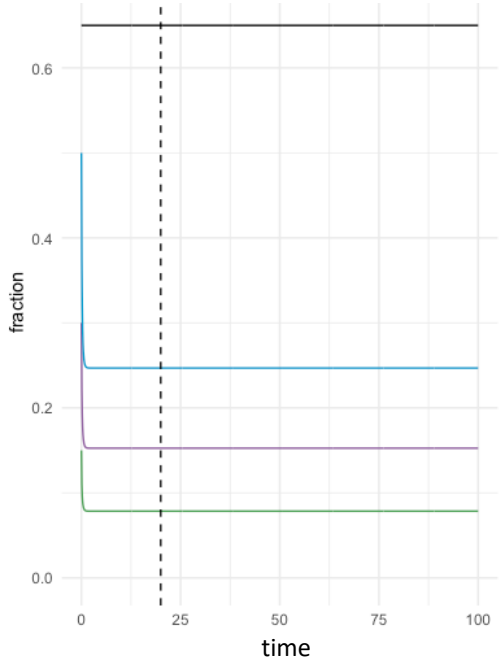


We tested:

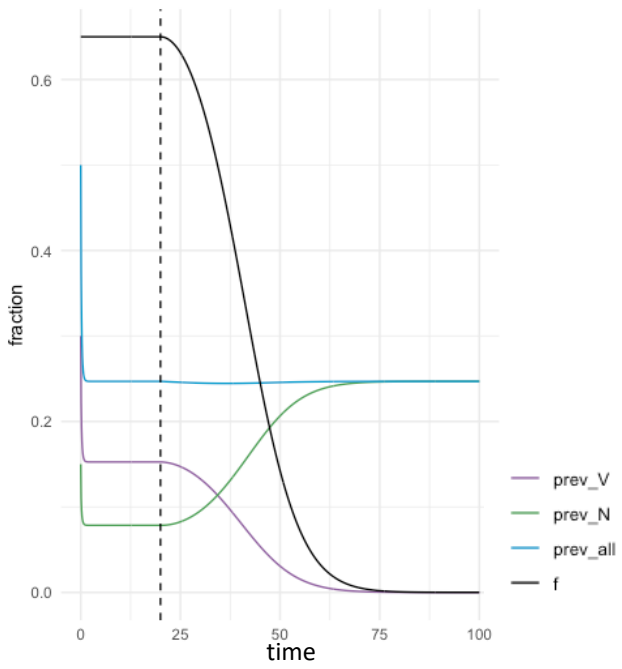
- Vaccine efficacy
- Vaccine coverage
- **B）Waning rate**
- **C）Initial VT:NVT ratio**
- **D）Population susceptibility**

A neutral, S–C transmission model

Null-impact vaccine



Effective vaccine



- **Neutral model :**
  does not assume one serotype to have fitness advantage over the other

- **To check neutrality, track fraction of VT-carriers among all carriers (f)[1]**

$$f = \frac{C_{VT}^{NV} + q \times C_{VT,NVT}^{NV} + C_{VT}^{V} + q \times C_{VT,NVT}^{V}}{C_{VT}^{NV} + C_{NVT}^{NV} + C_{VT}^{V} + C_{NVT}^{V} + 2q(C_{VT,NVT}^{NV} + C_{VT,NVT}^{V})}$$

1. Lipsitch et al. (2009) *Epidemics*