

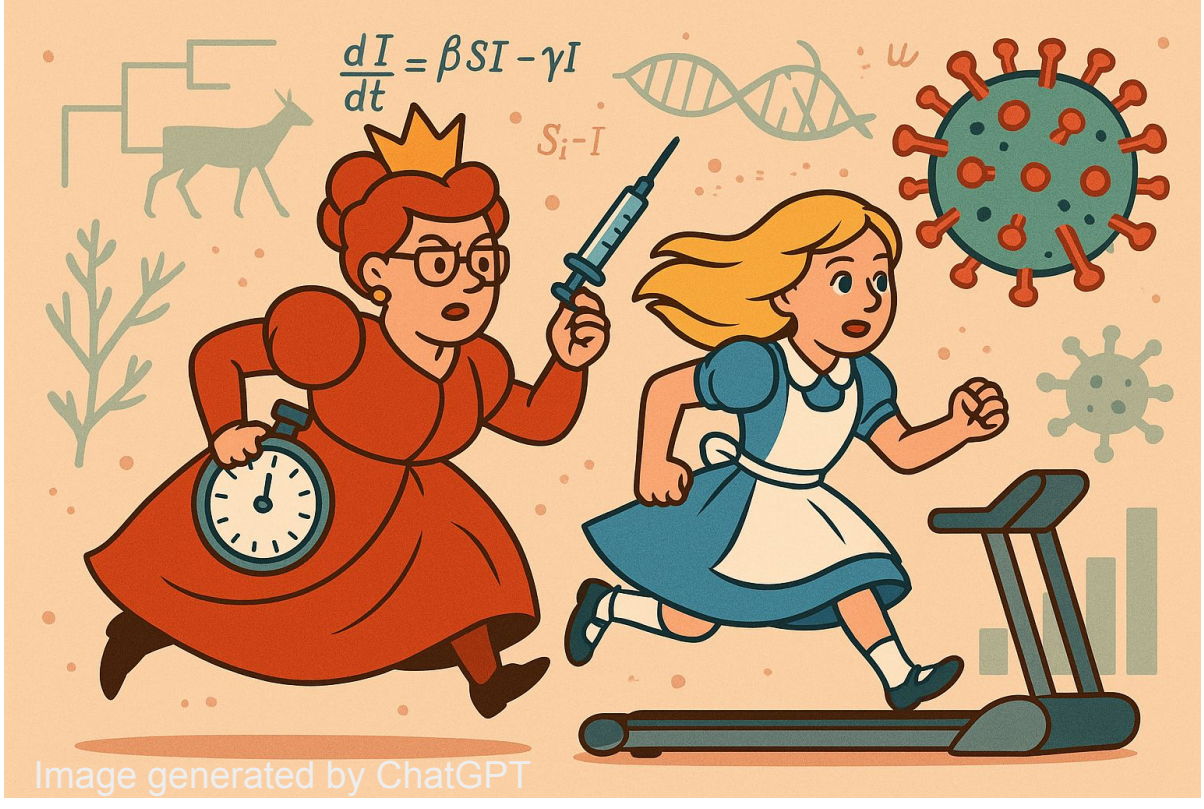

Modelling **vaccine escape:** ecology and evolution

Maria A. Gutierrez

University of Cambridge

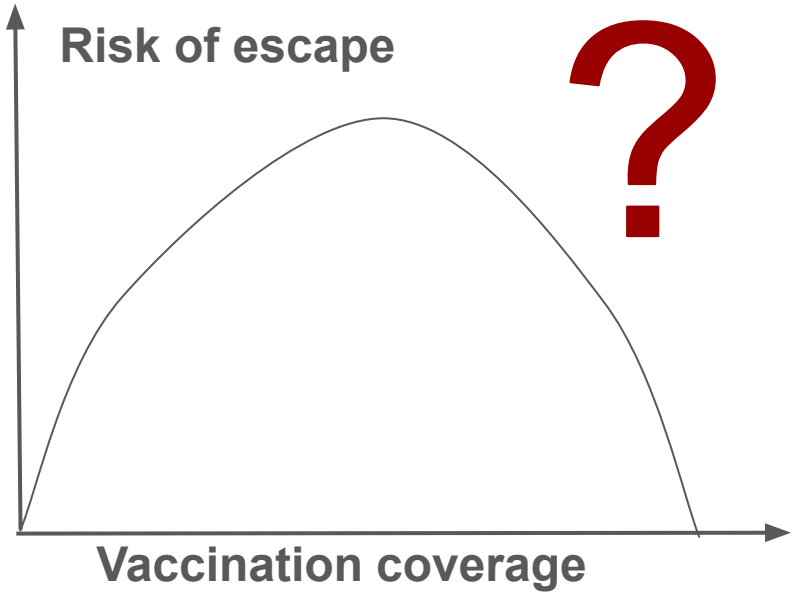
Soon postdoc with P. Rohani (UGA)

“Now, here, you see, it takes all the running you can do, just to keep in the same place.”



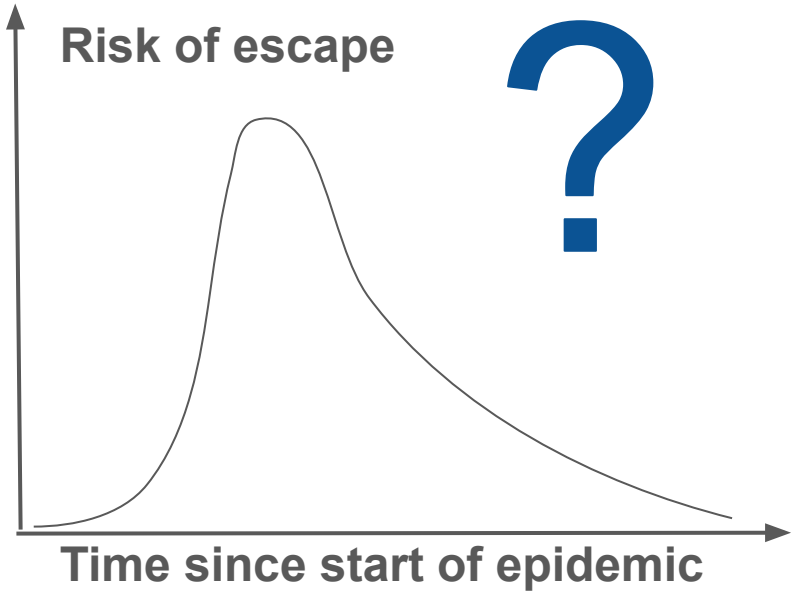
Red Queen
to Alice in
Through the Looking Glass
(Lewis Carroll)

Question #1:



Do intermediate vaccination coverages always maximise the risk of escape?

Question #2:



Does the highest escape risk occur when the prevalence is at its peak?

Outline

1. Generation of escape strains

J. Theoretical Biology, 2023, Gutierrez and Gog

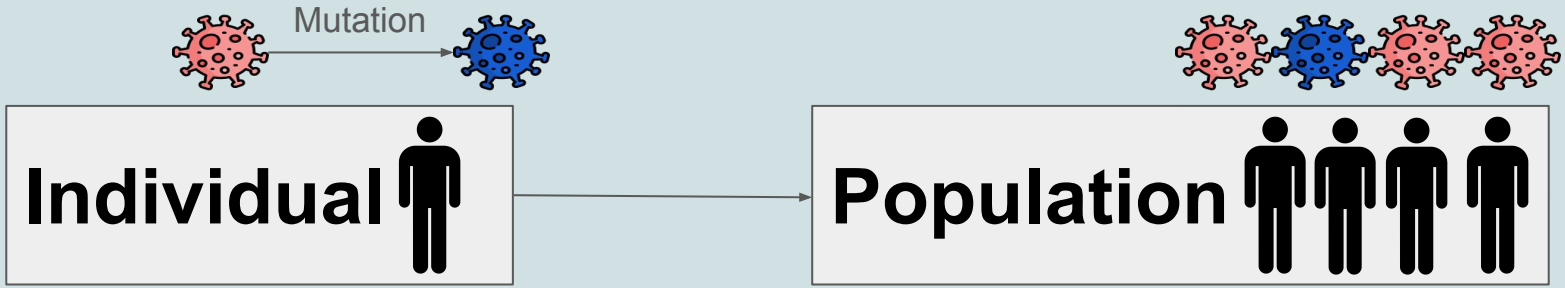
2. Establishment of escape strains

Submitted in PhD thesis, manuscript in preparation

Epidemic/impact of escape strains

Not in today's talk, but ask me about it

Simplified scales of selection for the *appearance* of strains



$$P(t) \propto (I_U(t) + \theta_E I_V(t))$$

Immune escape pressure

infections in unvaccinated hosts

Relative selection in vaccinated hosts

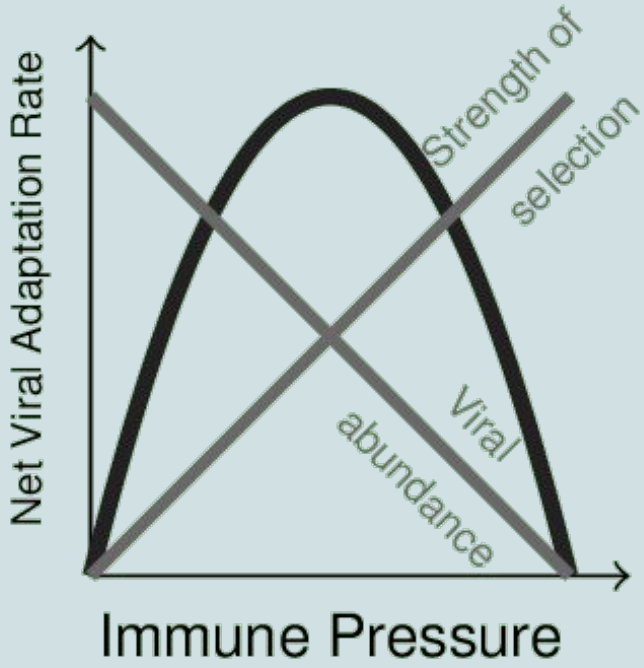
infections in vaccinated hosts

Within-host selection by vaccination status

$$P(t) \propto (I_U(t) + \theta_E I_V(t))$$

$\theta_E > 1?$

If infected, **who is more likely to generate an escape strain?** Vaccinated or unvaccinated?



Grenfell et al, *Science* 2004

Transient SIR epidemic wave

vaccination coverage *c*:
vaccines given before outbreak,
permanent partial immunity
against infection θ_S and transmission θ_I

$$\dot{S}_U = -S_U \lambda$$
$$\dot{S}_V = -S_V \lambda$$
$$\dot{I}_U = S_U \lambda - I_U$$
$$\dot{I}_V = S_V \lambda - I_V$$

$$\lambda = R_0 (I_U + \theta_I I_V)$$

reduced transmissibility

$$S_U(0) = 1 - c$$
$$S_V(0) = c\theta_S$$

all-or-none protection
against infection

Analytical final-size solution leads to escape pressure

Integrated escape pressure

$$P = \int_0^\infty (I_U + \theta_E I_V) dt = C_U + \theta_E C_V$$

Cumulative final-sizes

…similar to standard SIR final-size

$$P = (1 - c(1 - \theta_S \theta_E))(1 + R_e^{-1} W(-R_e e^{-R_e}))$$

Initial effective R-number

Lambert W function

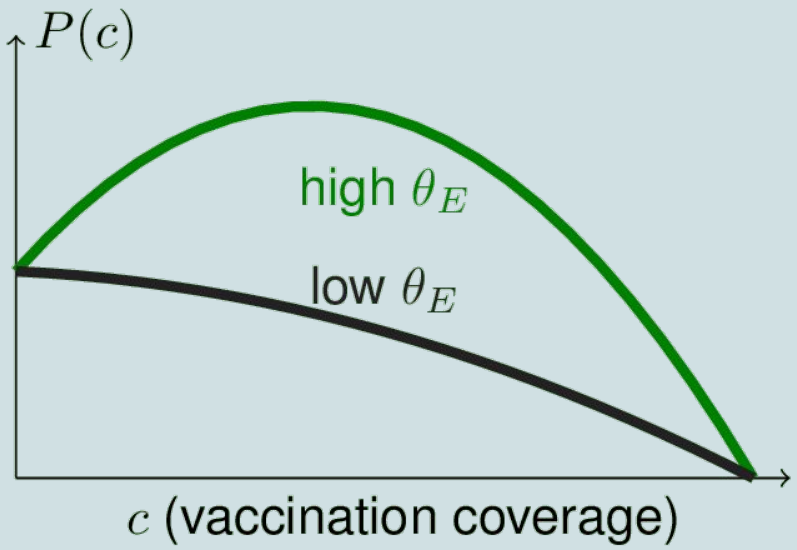
$$R_e = R_0 (1 - c(1 - \theta_S \theta_I))$$

Escape pressure *P* as a function of vaccination coverage *c*

$$P = C_U + \theta_E C_V$$

Behaviour of *P* depends on the relative escape contribution of vaccinees, θ_E

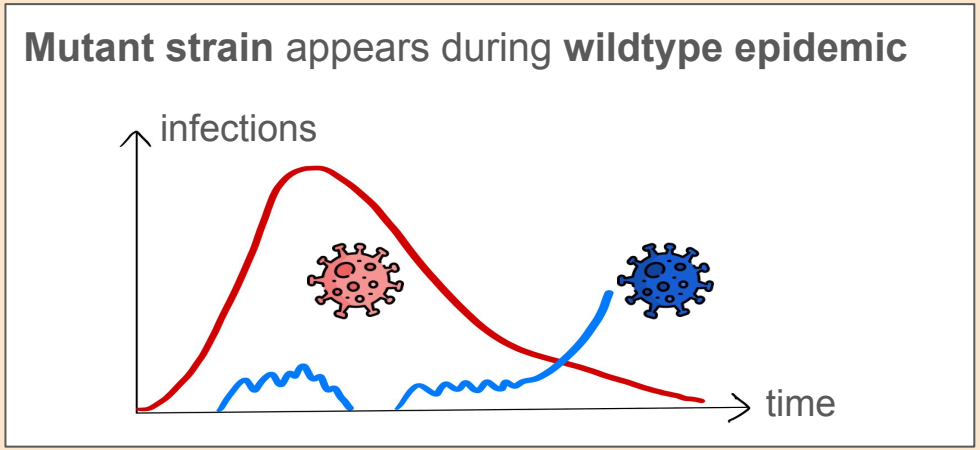
- Unimodal if θ_E above threshold
- Decreasing if θ_E below threshold



After an escape mutant *appears,* can it avoid extinction?

Stochastic dynamics for early mutant spread

Establishment probability p(t) changes with time:
Few hosts remain susceptible late in the epidemic

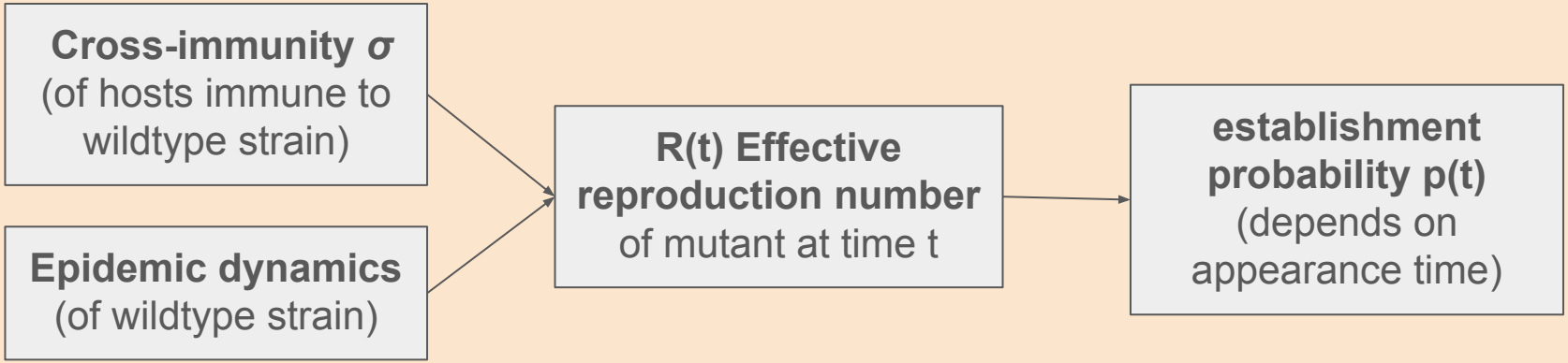


Net escape pressure rate
for appearance and establishment

Establishment probability
for mutants that appear at time t

$$P(t) = (I_U(t) + \theta_E I_V(t))p(t)$$

Cross-reactivity of immunity (from vaccines & WT infections)



Fully susceptible to WT

Fully immune to WT

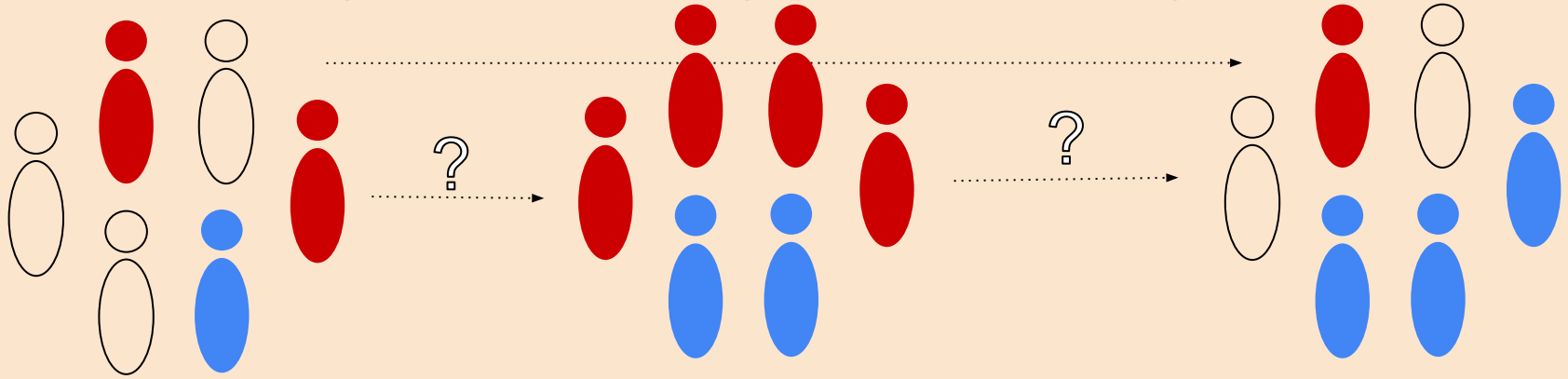
$$R(t) = R_0\left(S_U(t) + S_V(t) + (1-\sigma)\left(R_U(t) + R_V(t) + (c - S_V(0))\right)\right)$$

Cross-immunity reduces susceptibility

Recovered from WT

Full vaccine Immunity to WT

Time-inhomogeneous emergence branching process



Susceptible depletion (from wildtype strain)

→ traditional branching process (e.g., Whittle formula p=1-1/R) not valid

→ a **time-dependent transmission rate R(t)** in “birth-death” process

$$\dot{p} = p(1 - (1 - p)R(t))$$

Kendall formula solves for p(T)

If $R(\infty) > 1,$

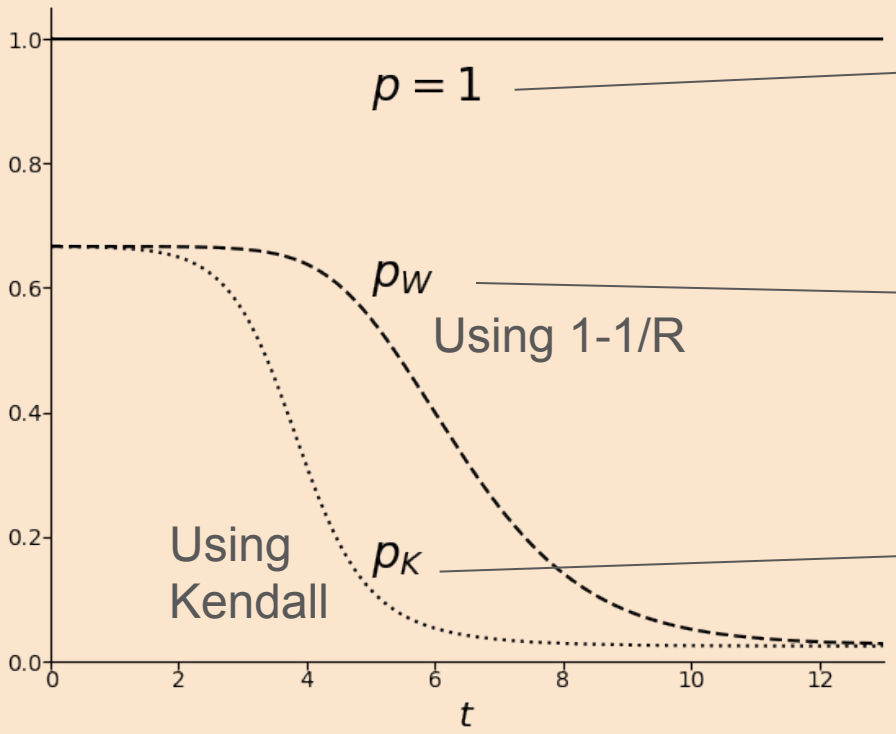
$$p(T) = \frac{1}{1+\int_T^\infty \exp\left[-\int_T^{\tau'}(R(\tau)-1)d\tau\right]d\tau'}$$

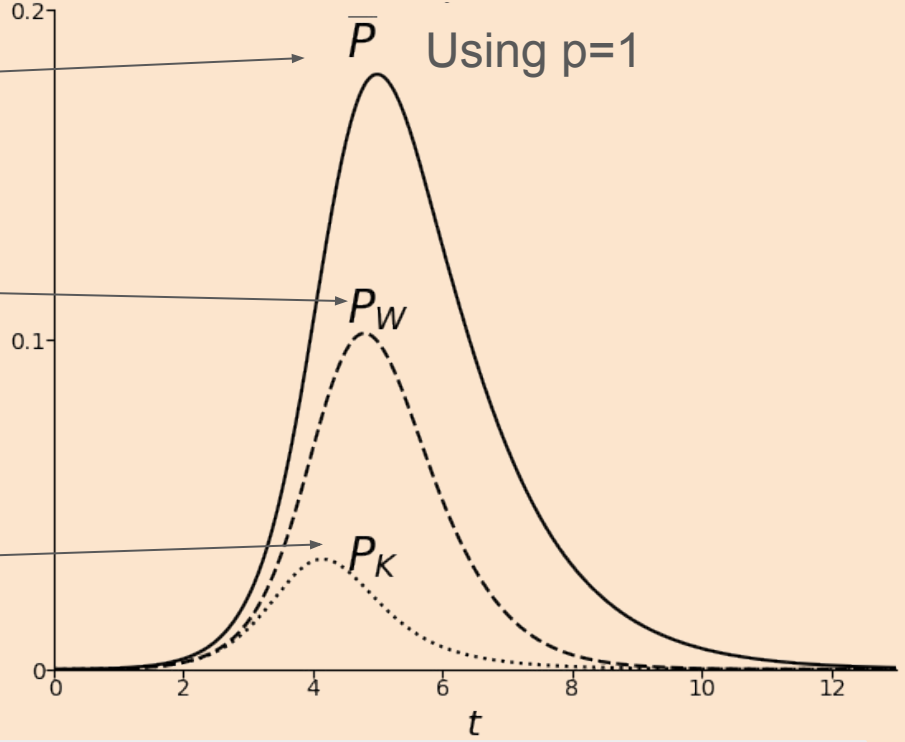
If $R(\infty) \leq 1, p(T) = 0$

Value of R(t) after the mutant appears (t>T) is important!

Establishment probability

Net escape pressure *rate*



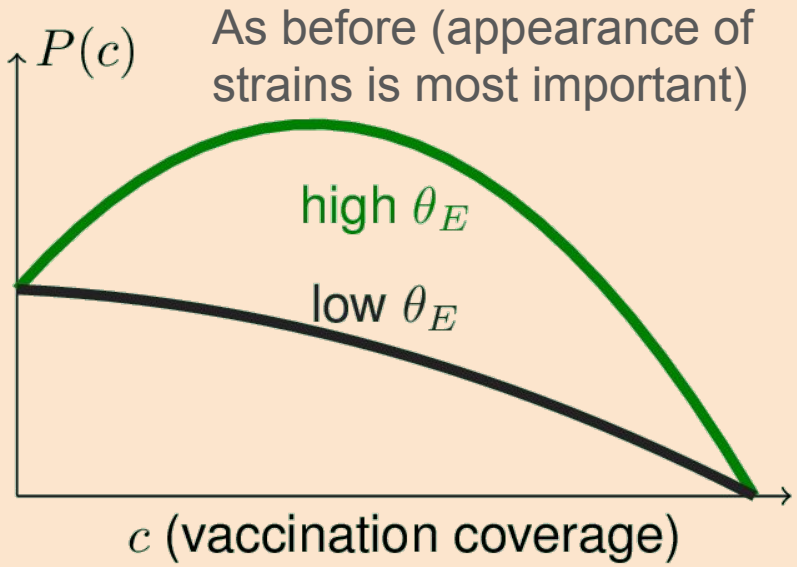


- Kendall formulation “foresees” the upcoming decreases in susceptibles.
- Maximum escape pressure is a bit earlier than the prevalence peak

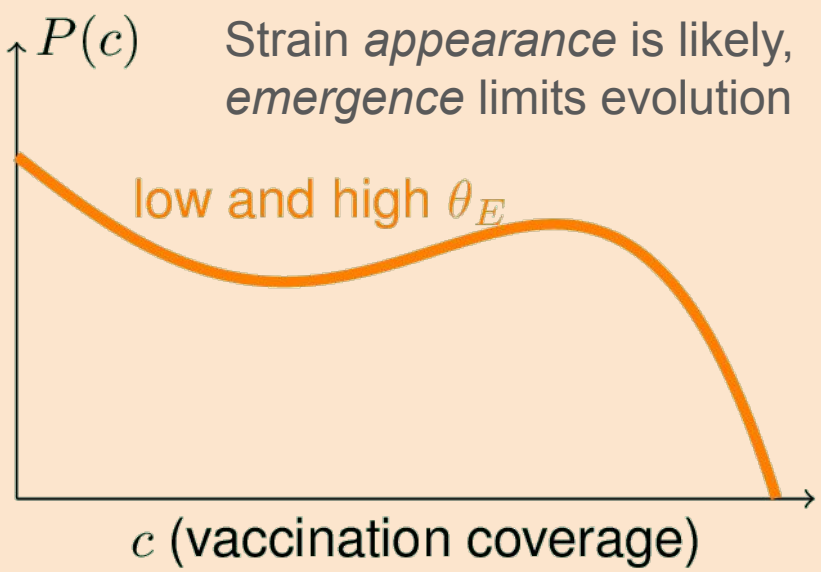
High cross-immunity leads to new behaviours

The shape of the **cumulative escape pressure P(c)** depends on the **cross-immunity σ** between the wildtype and mutant strains.

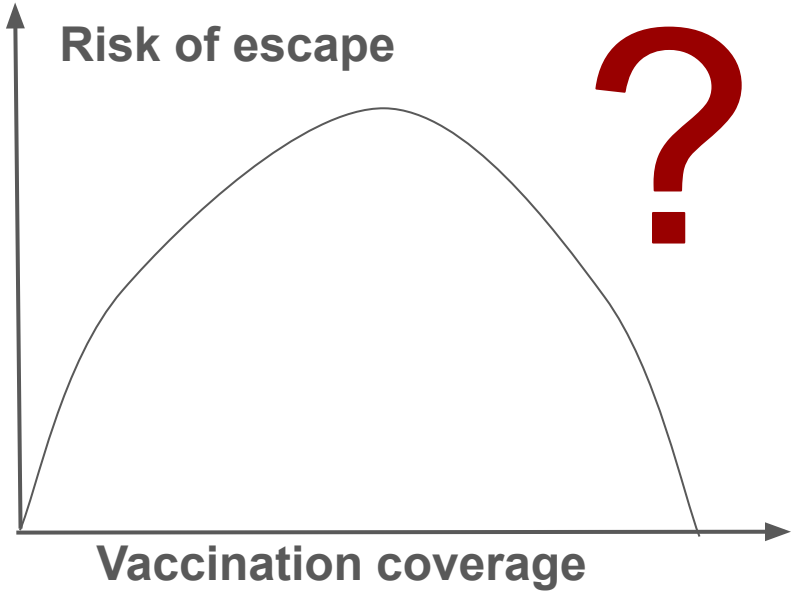
Low cross-immunity
(high emergence probability)



High cross-immunity
(low emergence probability)

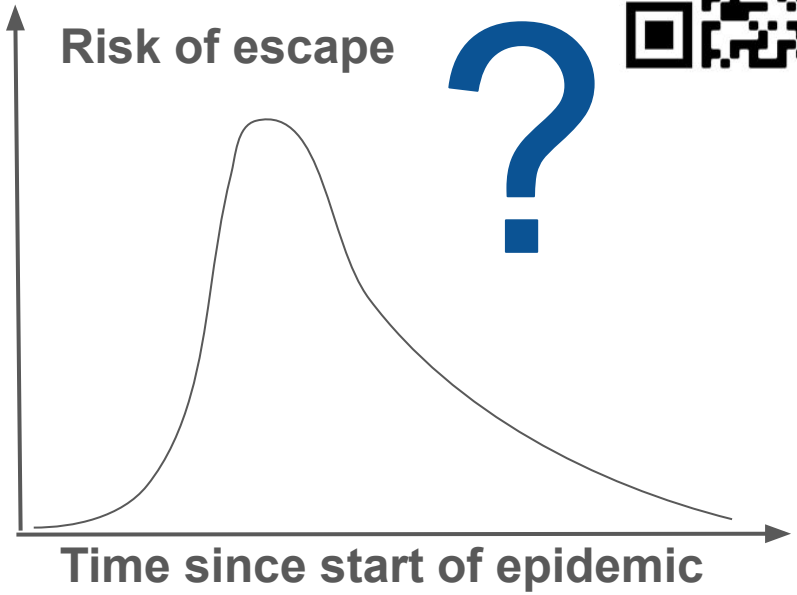


Question #1:



Intermediate vaccination coverages do not always maximise the risk of escape.

Question #2:



The peak escape pressure does not occur at the same time as the peak prevalence.