Modelling **vaccine escape** in a population

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Vaccination campaigns and antigenic escape strains

Might vaccination campaigns unintendedly select for pathogen strains that escape host immunity?

What's the balance between transmission-reduction and a potential selection increase?

Epidemiological and evolutionary considerations of SARS-CoV-2 vaccine dosing regimes

Chadi M. Saad-Roy[1]*, Sinead E. Morris[2], C. Jessica E. Metcalf[3,4], Michael J. Mina[5], Rachel E. Baker[3,
Jeremy Farrar[7], Edward C. Holmes[8], Oliver G. Pybus[9], Andrea L. Graham[3], Simon A. Levin[3],
Bryan T. Grenfell[3,4,10]*, Caroline E. Wagner[11]*

Rates of SARS-CoV-2 transmission and vaccination impact the fate of vaccine-resistant strains

Simon A. Rella[1], Yuliya A. Kulikova[2], Emmanouil T. Dermitzakis[3]✉ & Fyodor A. Kondrashov[1]✉

Vaccine escape in a heterogeneous population: insights for SARS-CoV-2 from a simple model

Julia R. Gog[1,2], Edward M. Hill[2,3,4,5], Leon Danon and Robin N. Thompson[2,3,4]

Approach and talk plan

1. Selection during an epidemic

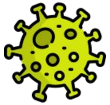
Paper

Gutierrez, M. A. and Gog, J. R.
The importance of vaccinated individuals to population-level evolution of pathogens. 2023, *Journal of Theoretical Biology.*

2. New epidemic: escape strain

Current work, unpublished

3. Discussion: applications & future work



Simplified scales of selection

not explicitly within-host,
but vaccination status matters!

generation of strains,
(emergence not yet)

Individual → **Population**

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

Escape pressure

infections in unvaccinated hosts

Relative selection in vaccinated hosts

infections in vaccinated hosts

Others use just I_V or I_U or a fixed linear combination.

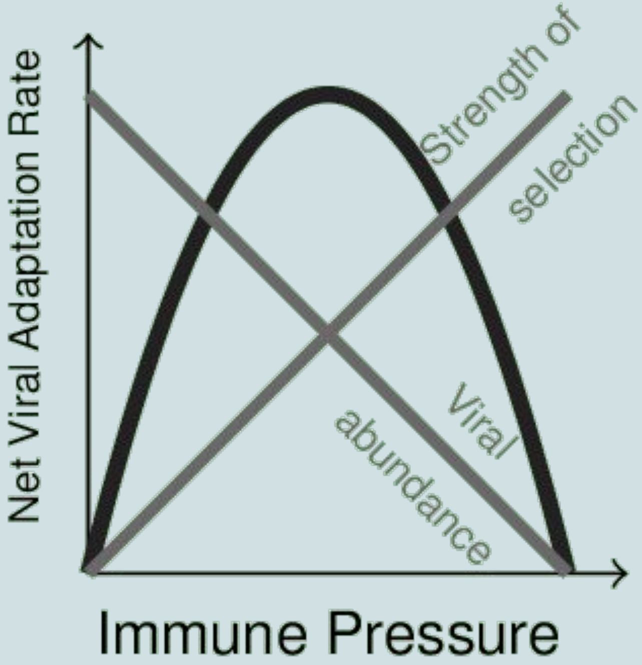
Gog et al 2021, Saad-Roy et al 2021, Thompson et al 2021, Rella et al 2021, Zhang et al 2022

Within-host selection by vaccination status

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

$\theta_E > 1?$

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

Initial conditions

$$S_U(0) = 1 - c$$

$$S_V(0) = c\theta_S$$

Polarised protection against infection

$$\dot{S}_U = -S_U\lambda$$

$$\dot{S}_V = -S_V\lambda$$

$$\dot{I}_U = S_U\lambda - I_U$$

$$\dot{I}_V = S_V\lambda - I_V$$

SIR dynamics

Force of infection

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

reduced transmissibility

<u>Further assumptions:</u>
well-mixing,
homogeneity,
no reinfections,
constant R0,
not time-since-infection,
same infectious period,
no births and deaths.

Analytical final-size solution leads to escape pressure

Initial effective R-number $R_e = R_0(1 - c(1 - \theta_S\theta_I))$

vaccine transmission-blocking

Same ratio vaccinated:unvaccinated through all compartments

$$(S_V, I_V, R_V) = \frac{c\theta_S}{1-c}(S_U, I_U, R_U)$$

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

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

“escape-blocking factor”

Lambert W function

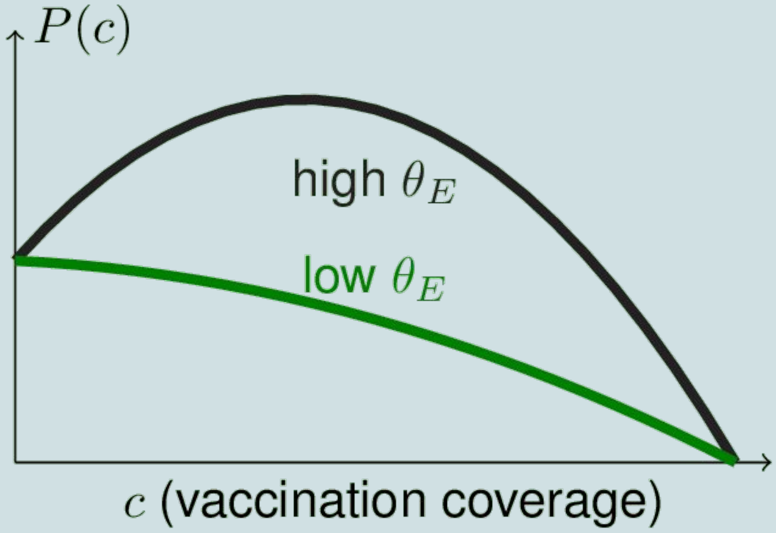
Escape pressure *P* as a function of vaccination coverage *c*

$$P = C_U + \theta_E C_V$$

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

P always decreases to zero if vaccination coverage is near herd immunity threshold



Gutierrez and Gog, 2023, *JTB*

What are the consequences of a high escape pressure?

After the first epidemic wave, a new escape strain generates a 2nd epidemic wave

antigenic distance
between strains

$$d = \delta + bP$$

The antigenic distance is linear on the escape pressure, $P = C_U + \theta_E C_V$ so includes infections in both vaccinated and unvaccinated, weighted by θ_E

Adapted to include vaccination from Boni et al 2004 ($d = \delta + bC$ using total infections *C*)

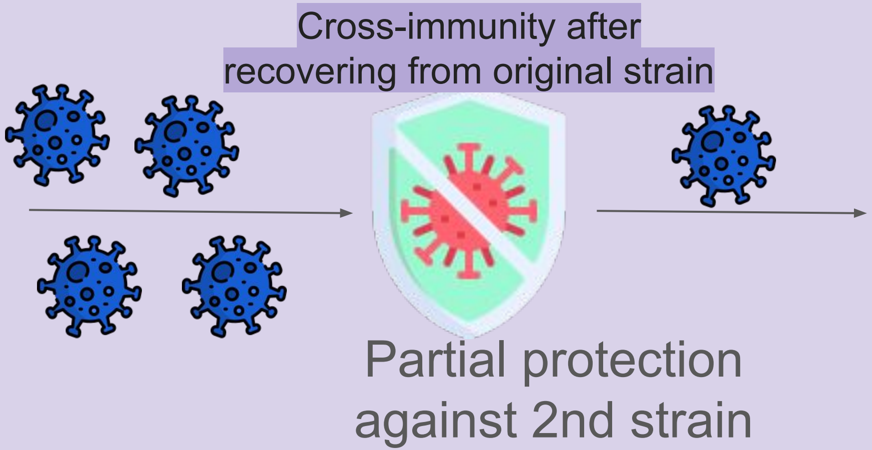
Unpublished work, in preparation for PhD thesis

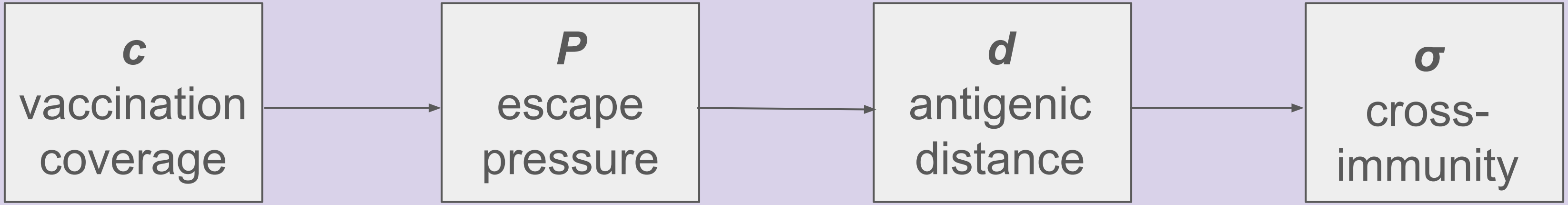
The antigenic distance determines the cross-immunity

Cross-immunity between strains decays exponentially with the antigenic distance

$$\sigma = \exp\left(-ad\right)$$

Boni et al 2004





Total infections *C* as a function of vaccination coverage *c*

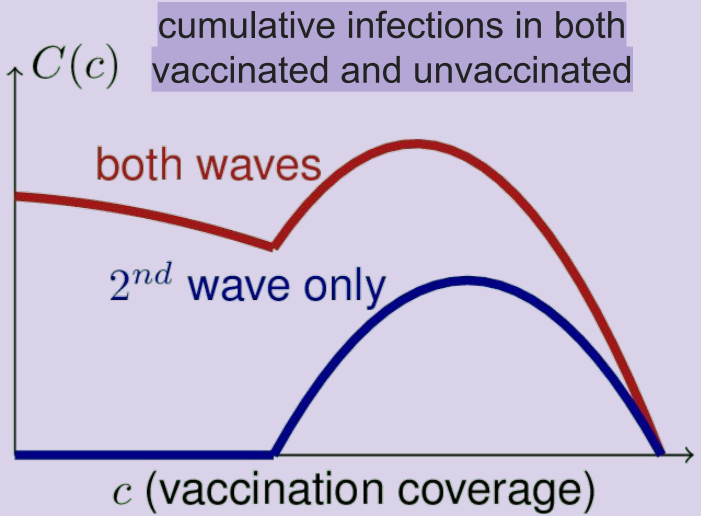
1st wave:
decreasing

+

2nd wave:
unimodal
(large θ_E)

Total infections (both waves):

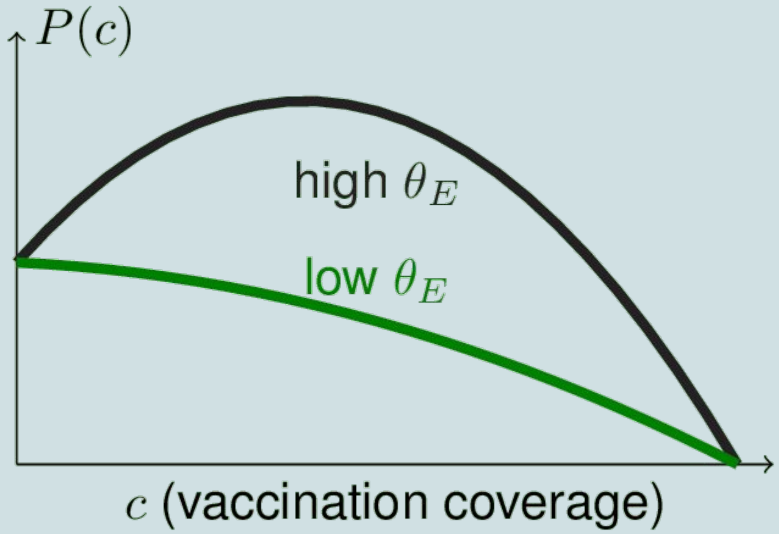
1. initially decreasing (no 2nd wave)
2. increasing as 2nd wave becomes possible
3. local maximum at intermediate vaccination
4. decreases for large vaccination coverages



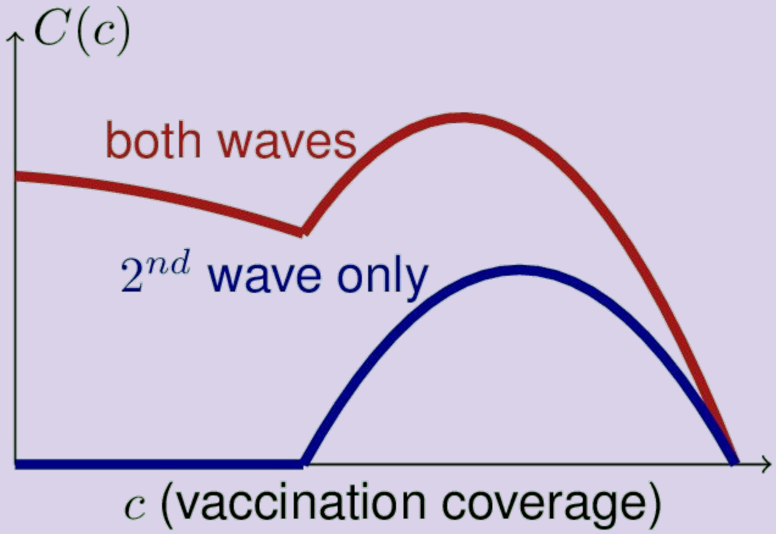
Caveat: slightly different overall balance depending on the drift rate *a* for the cross-immunity $\sigma = \exp(-ad)$

Summary

Total **escape pressure** from a single epidemic wave, without escape strain.



Total **infections** including a second epidemic wave with an escape strain.



Escape risk and total infections may be highest at intermediate vaccination.

Applications and work in progress

Vaccination strategies & surveillance…

eg, saving some vaccine doses for the second wave

Heterogeneous population & immunocompromised hosts

Reinfections during the first wave & infection-acquired immunity versus vaccines

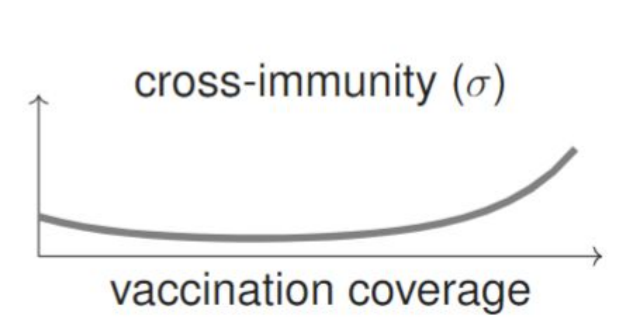
Stochastic invasion dynamics of the escape strain

Further epidemic evolution?

What is the value of θ_E and the drift rate *a* (eg, for SARS-CoV-2, Influenza)?

Extras

Immunity assumptions for second strain



Cross-immunity protects (partially) against *infection*

in vaccinees and hosts recovered from the first strain

Conserved vaccine efficacy (VE) against *transmission*

Increasing the vaccination coverage…

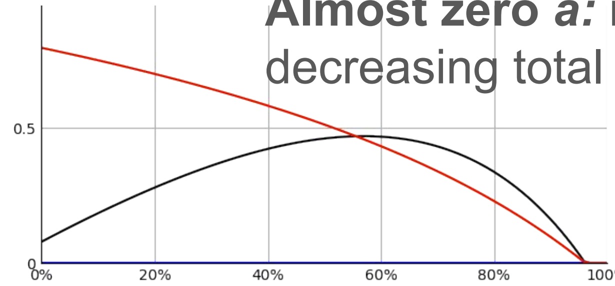
- Fewer hosts infected with the first strain, so now more susceptible hosts
- Non-monotonic effects on the cross-immunity ("U-shaped")
- Reduces transmission through the VE against transmission

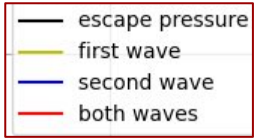
Overall balance of vaccination effects for 2nd wave: a priori unclear

The drift rate *a* matters

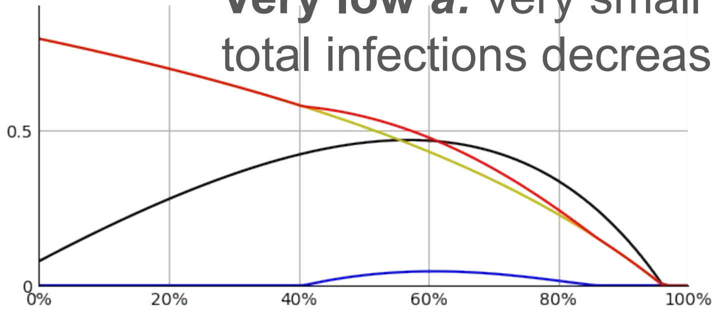
$$\sigma = \exp(-ad)$$

Almost zero *a*: no 2nd wave, so decreasing total infections

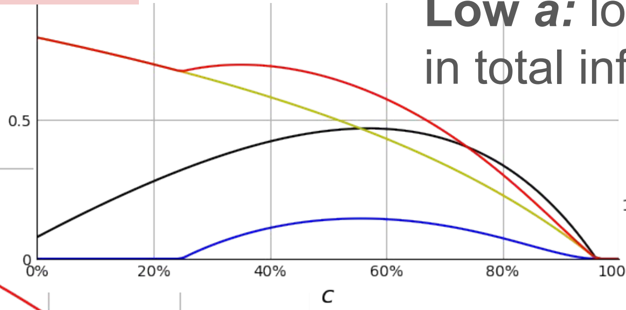




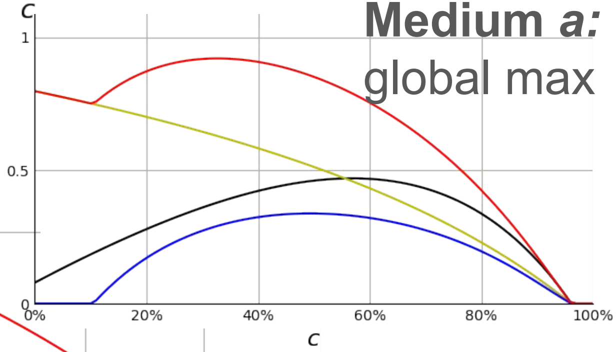
Very low *a*: very small 2nd wave, total infections decreasing



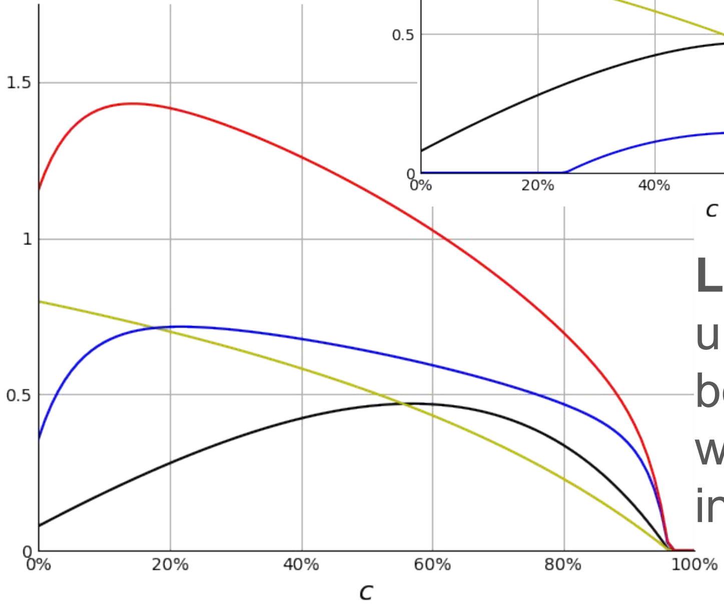
Low *a*: local maximum in total infections



Medium *a*: global max



Large *a*: unimodal both 2nd wave & total infections



Very large *a*: decreasing both 2nd wave & total infections