

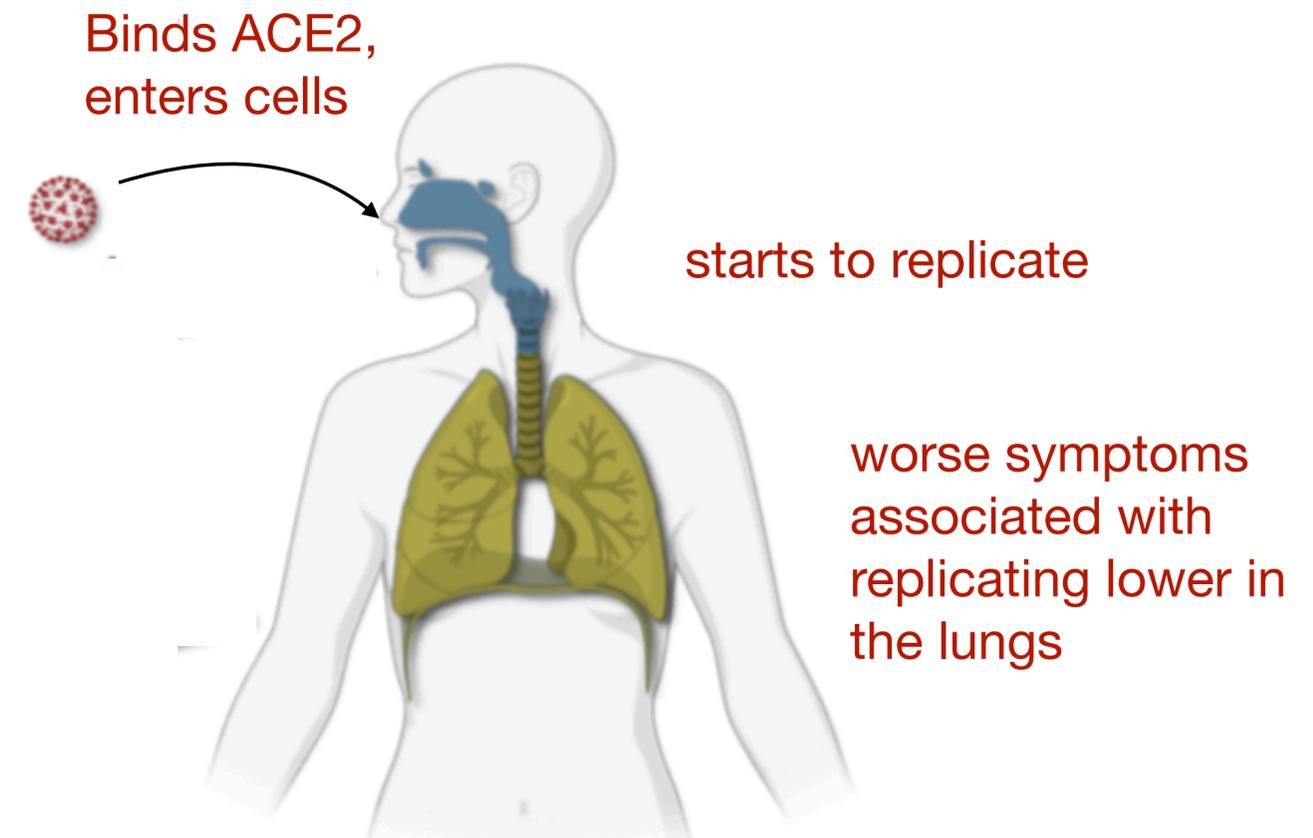
SARS-CoV-2 evolution & vaccination

C. Jessica E. Metcalf

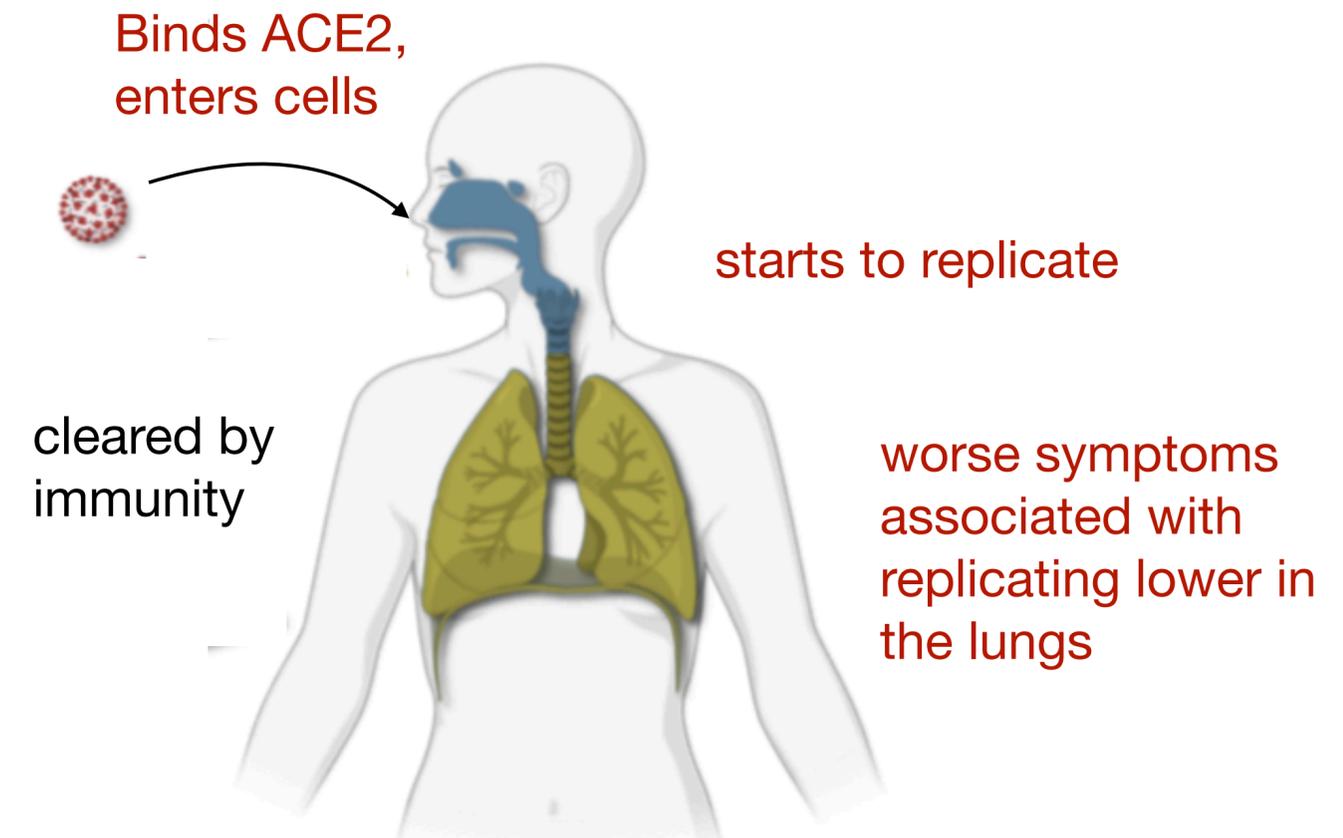
cmetcalf@princeton.edu



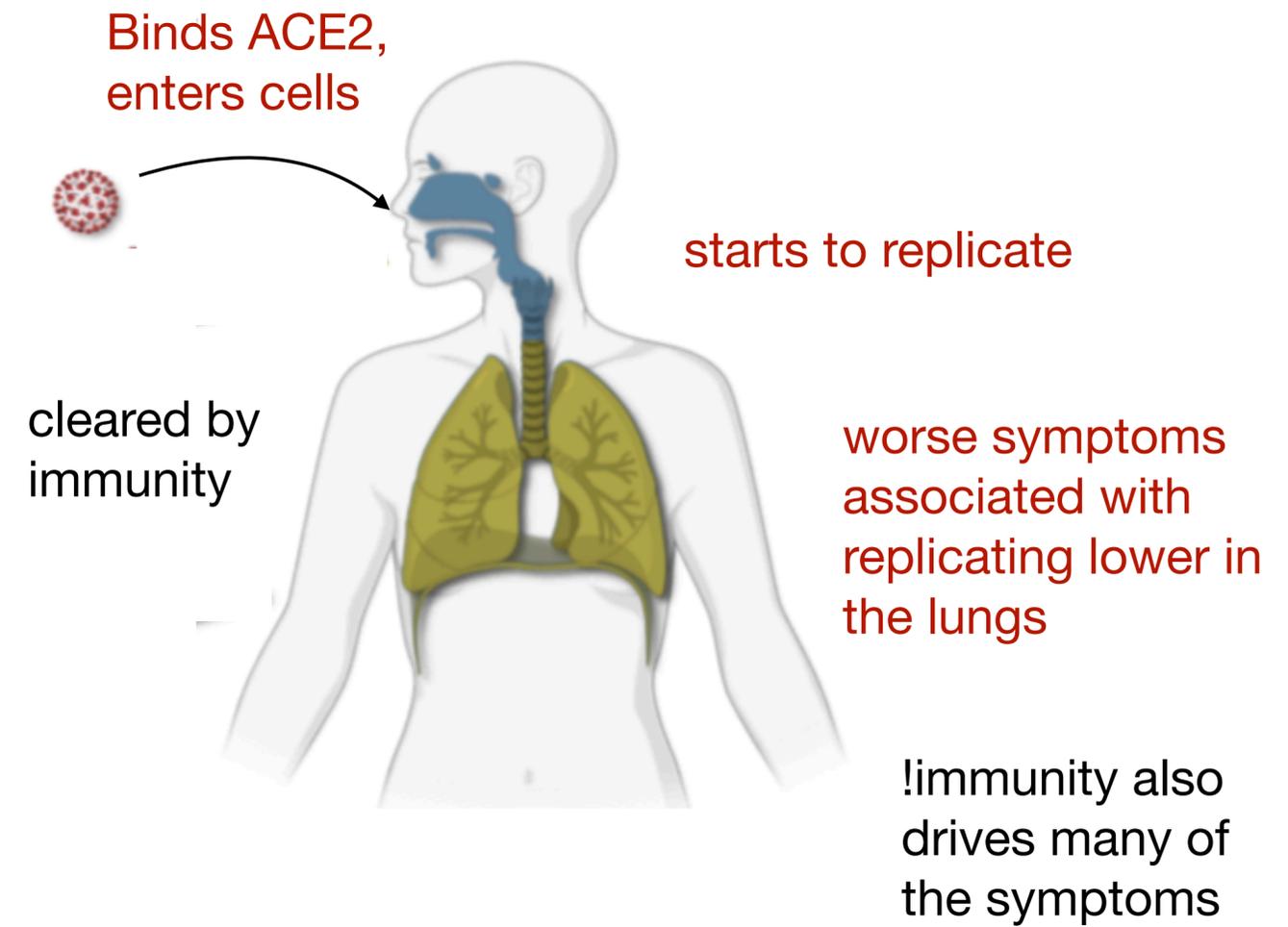
Biological underpinnings



Biological underpinnings



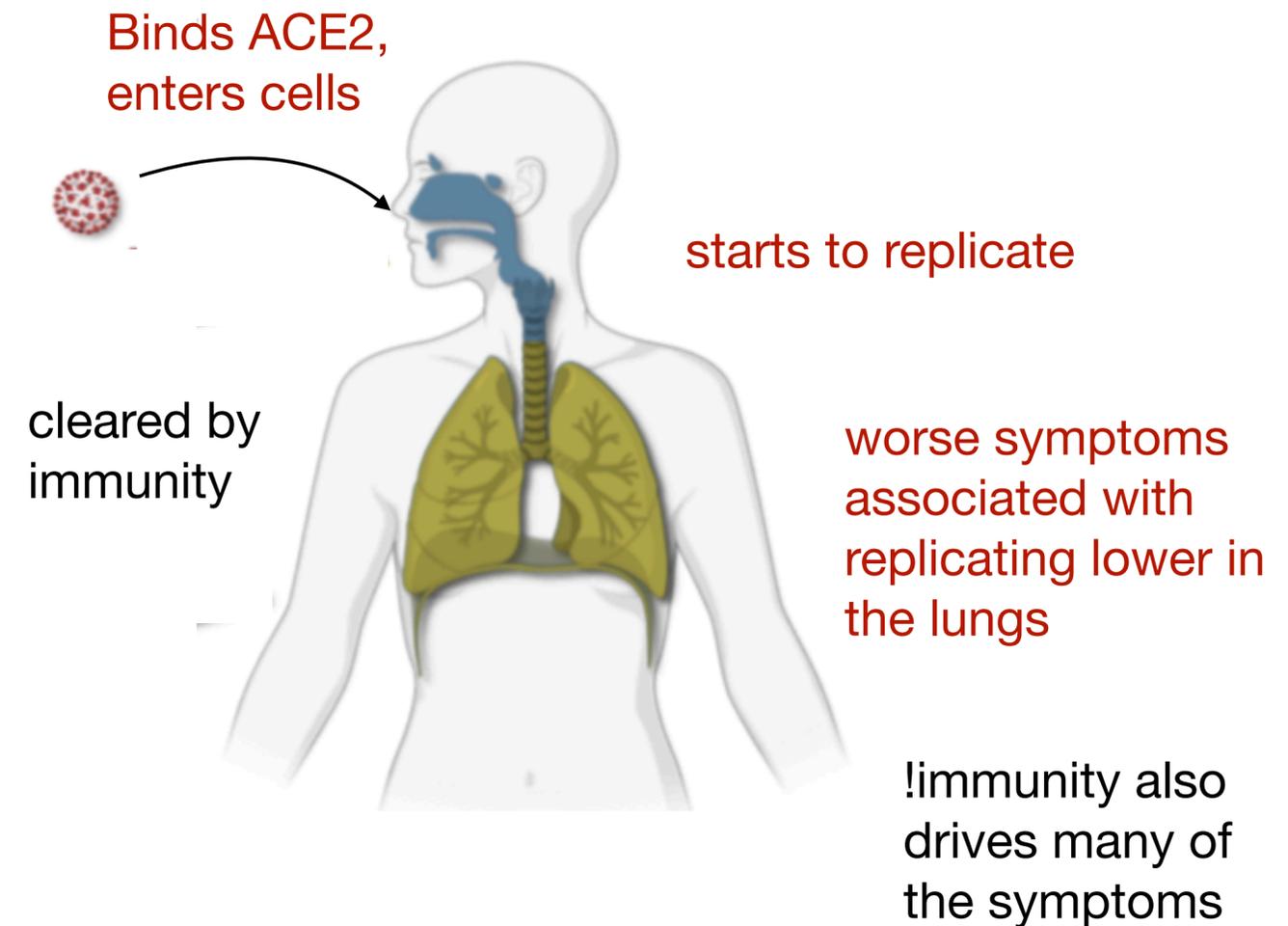
Biological underpinnings



Biological underpinnings

New phenotypes from new variants

- increased **avidity** for ACE2
- increased **transmissibility**
- increased capacity to **overcome natural or vaccinal immunity**
- increased **virulence**

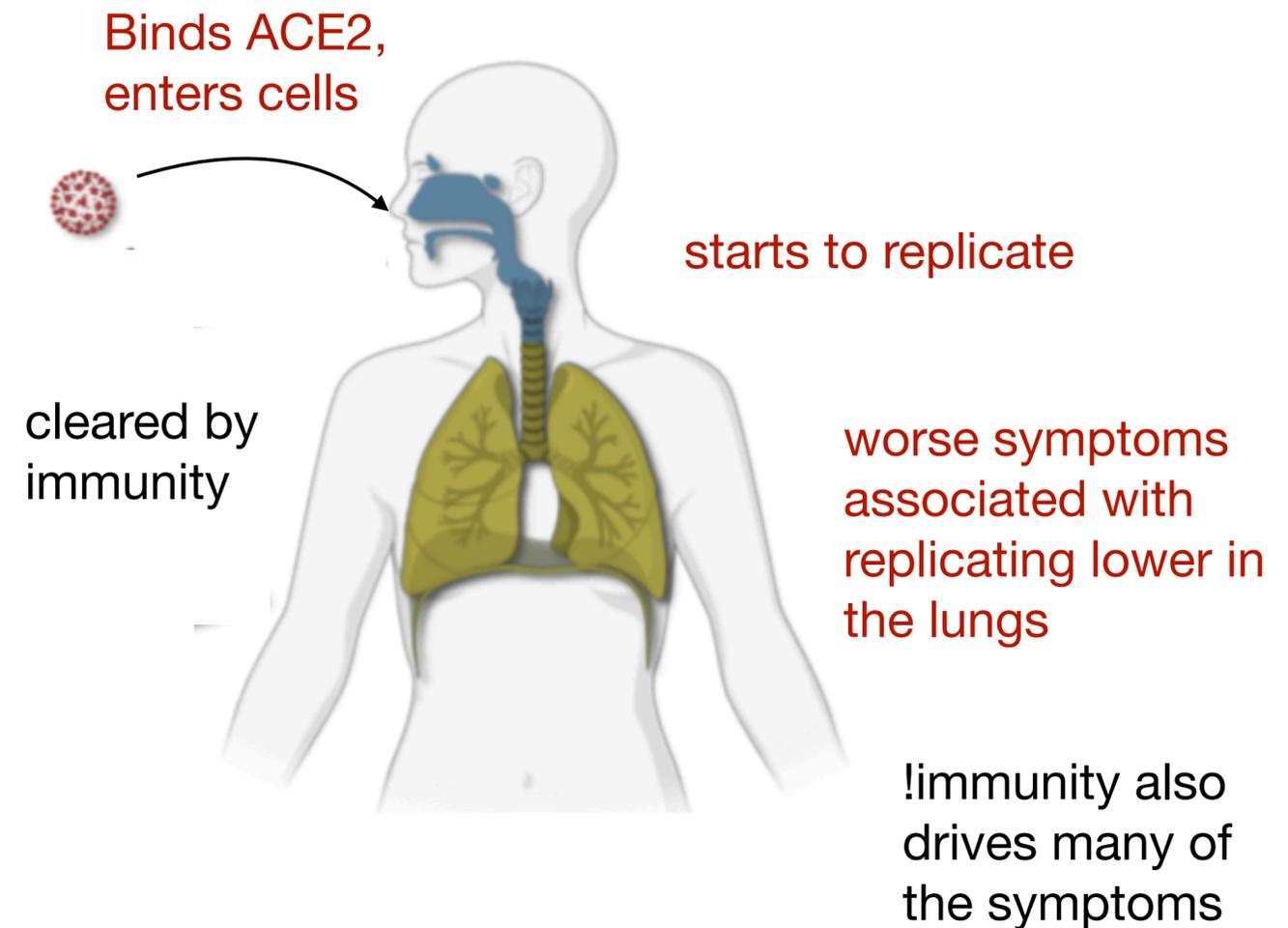


Biological underpinnings

New phenotypes from new variants

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B.1.1.7

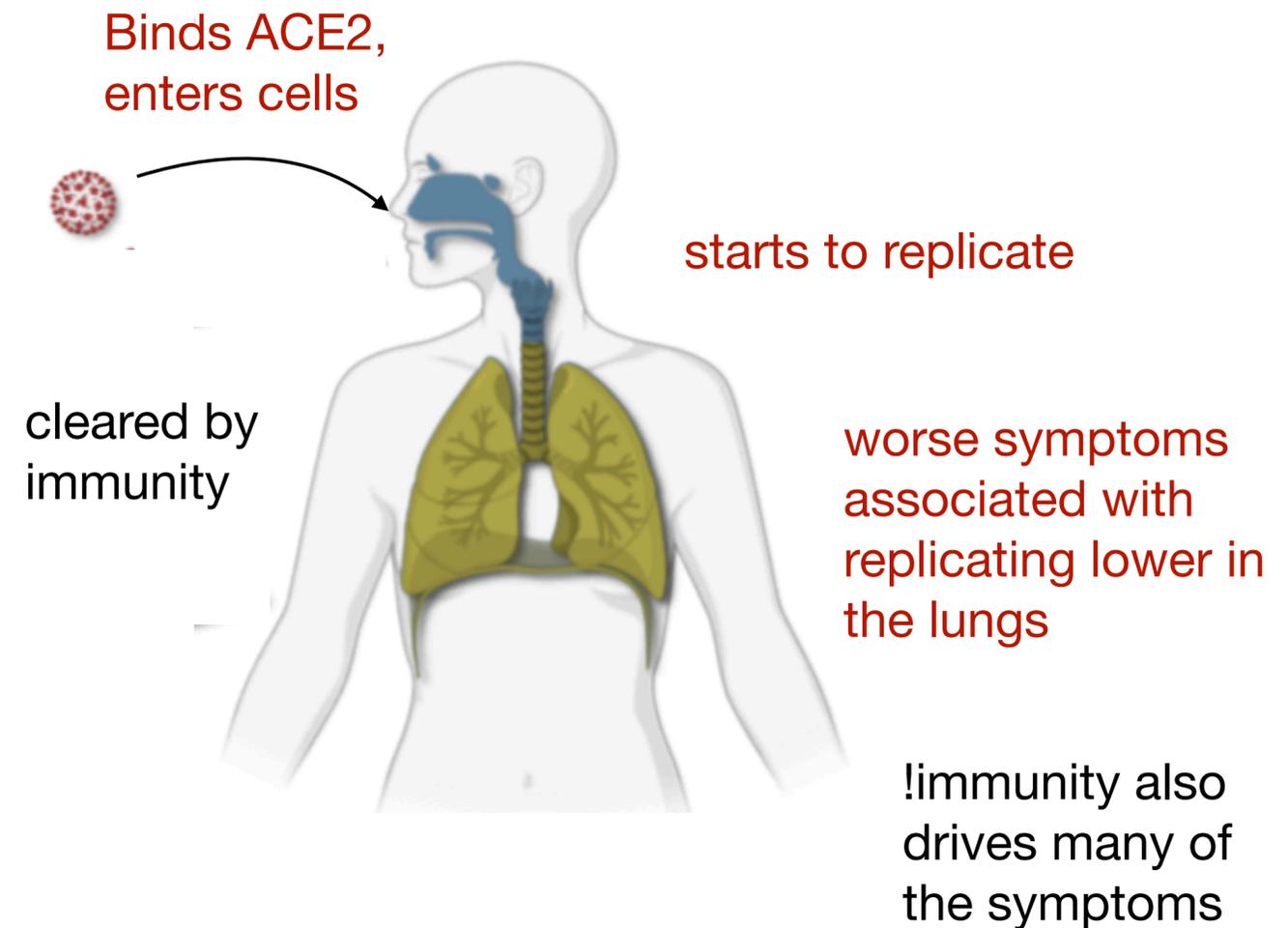


Biological underpinnings

New phenotypes from new variants

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P1

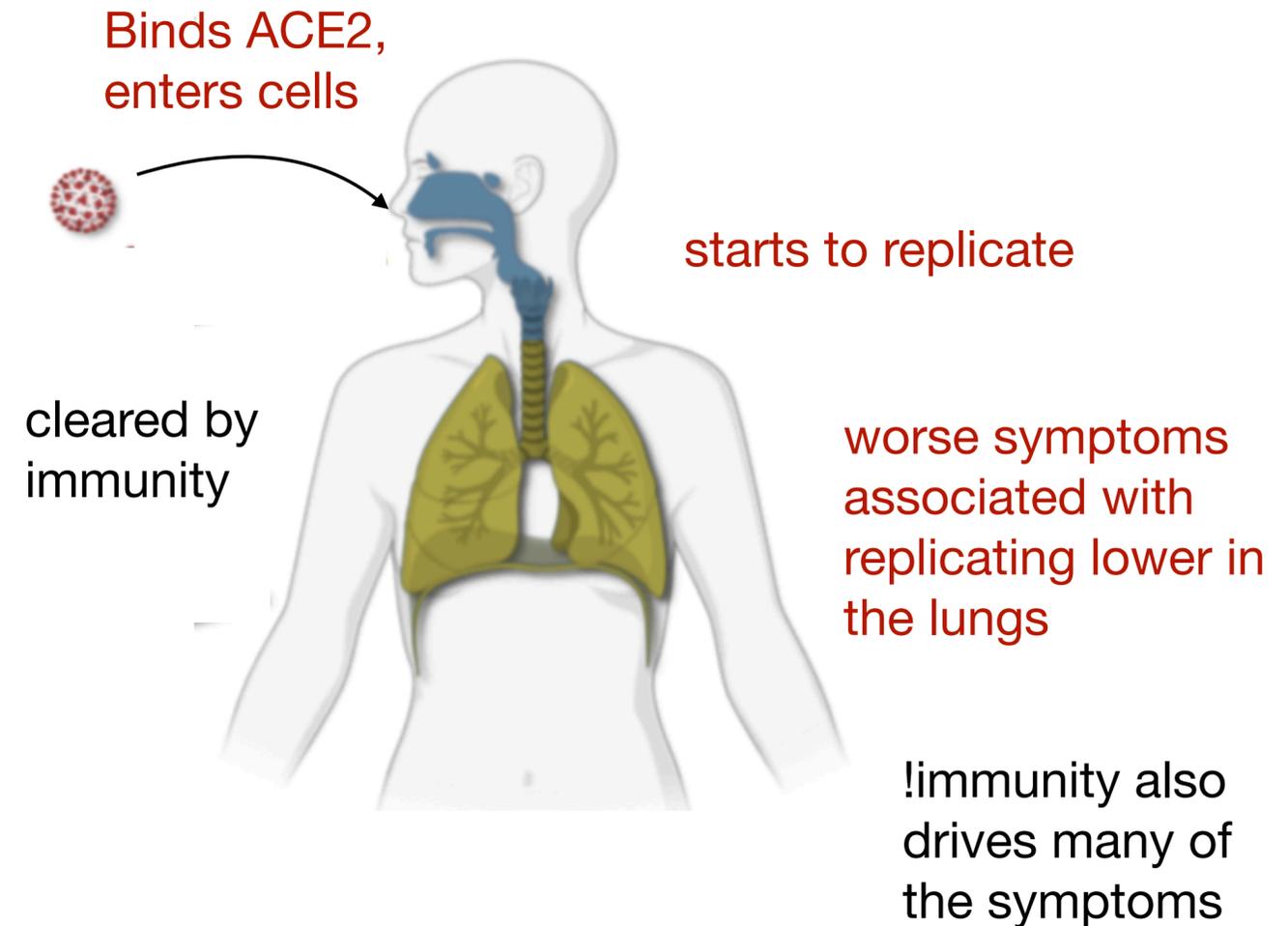


What do we know about the variants?

New phenotypes from new variants

- increased **avidity** for ACE2
- increased **transmissibility**
- increased capacity to **overcome natural or vaccinal immunity**
- increased **virulence**

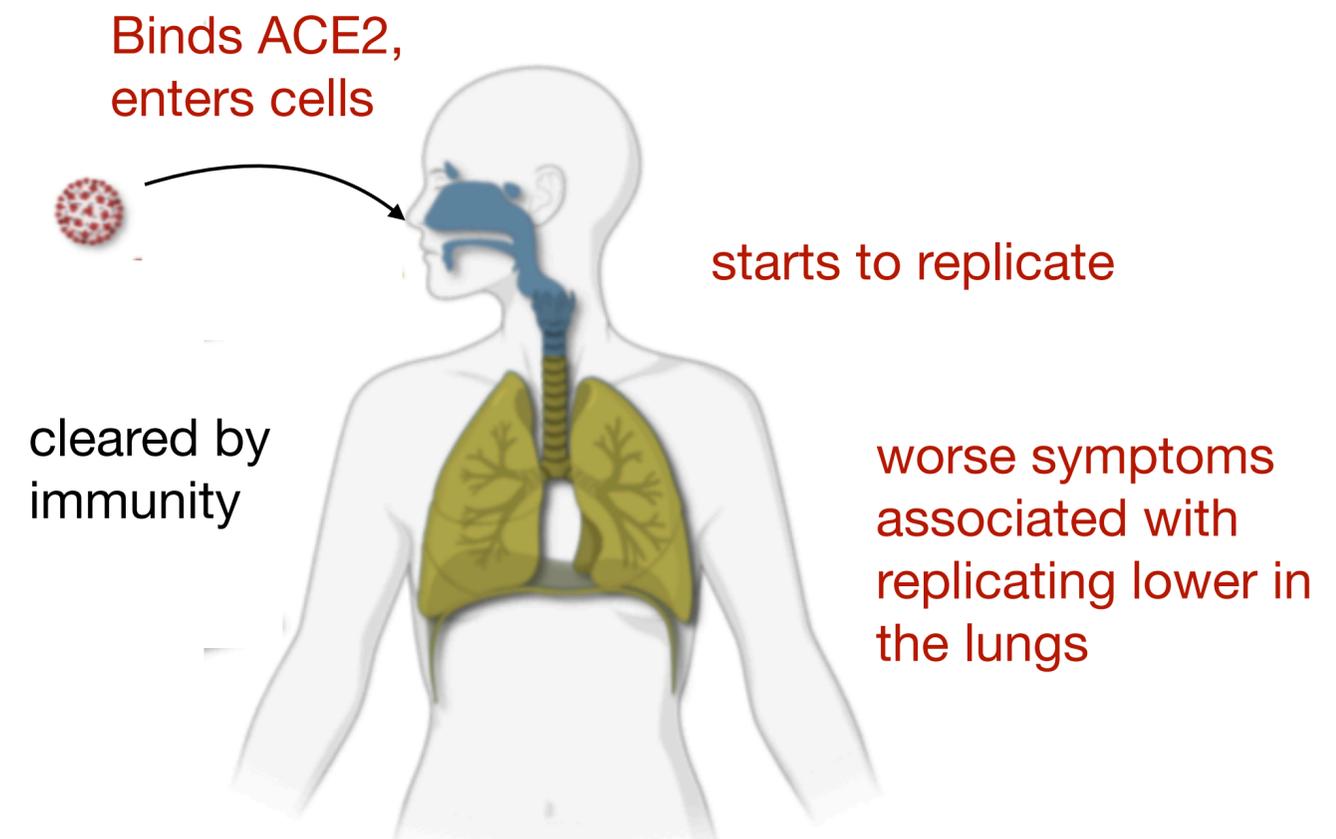
B.1.351



Biological underpinnings

New phenotypes from new variants

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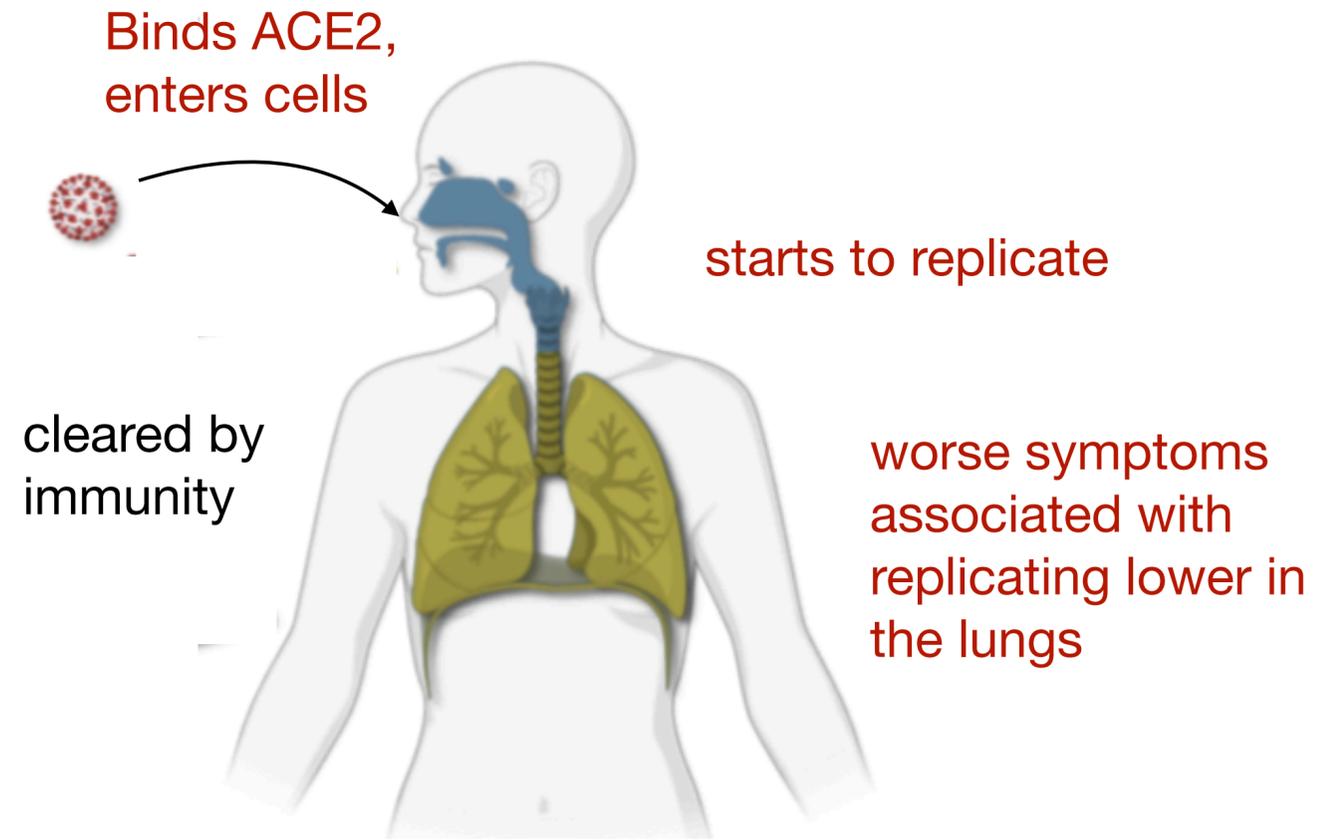
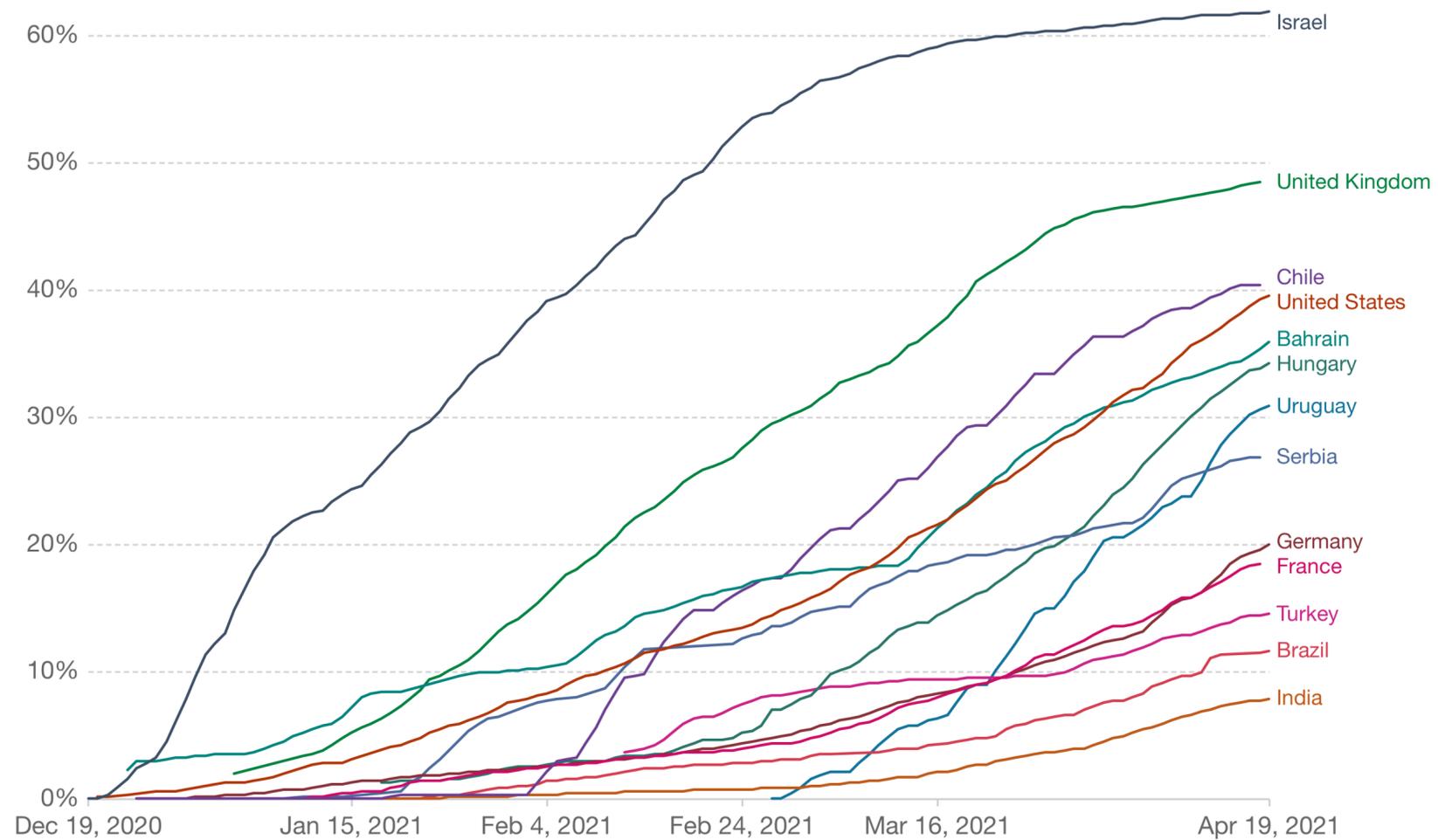


Why the **sudden surge in variants** at the end of 2020?

Vaccine driven evolution



Percent vaccinated

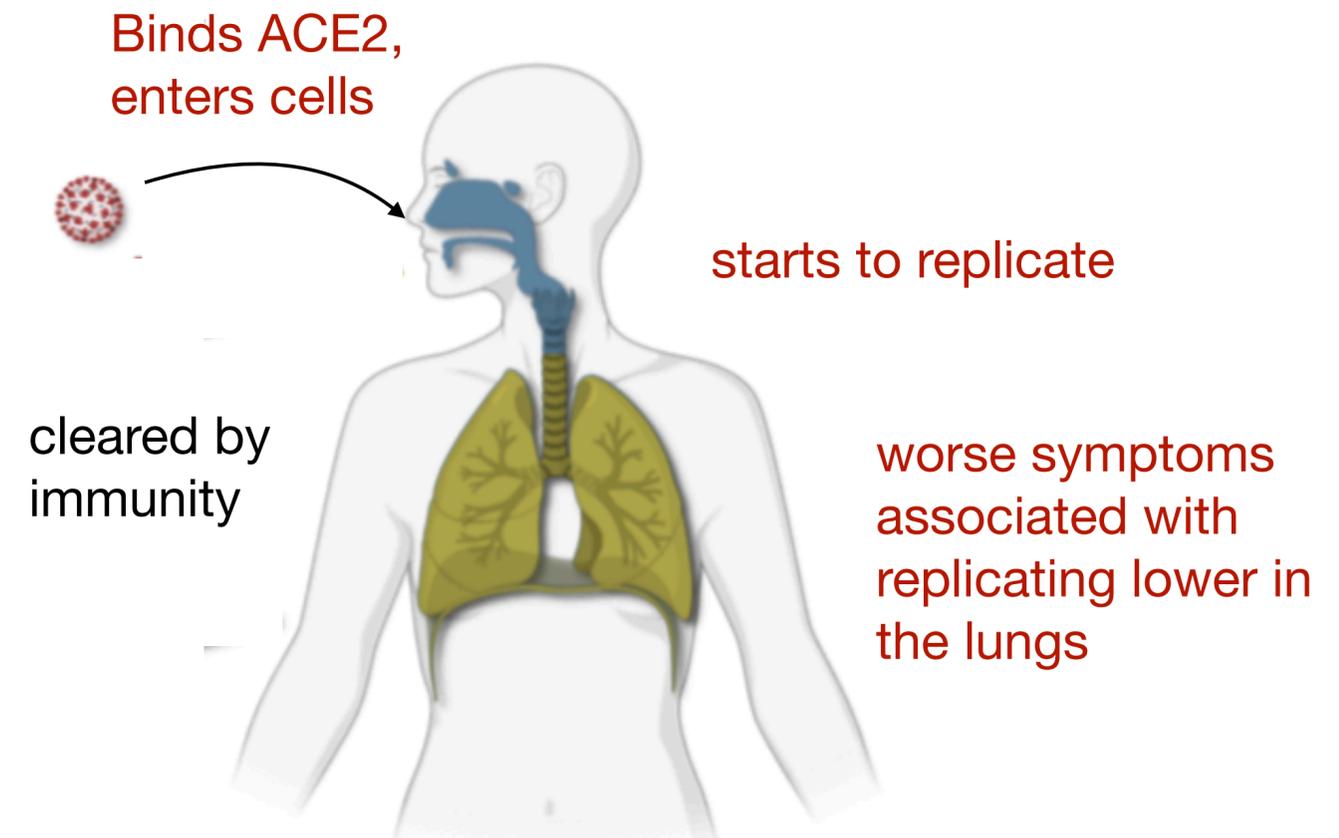
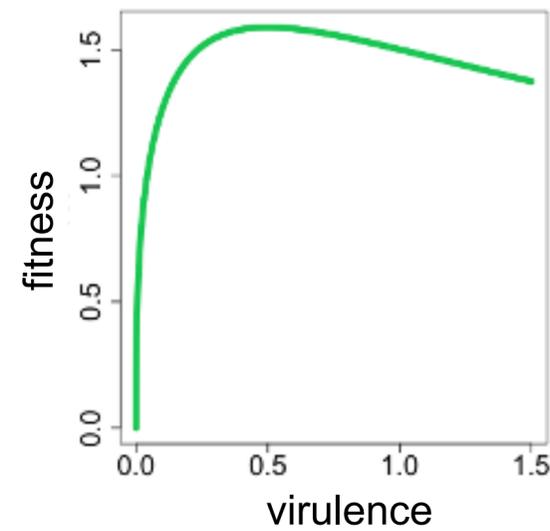
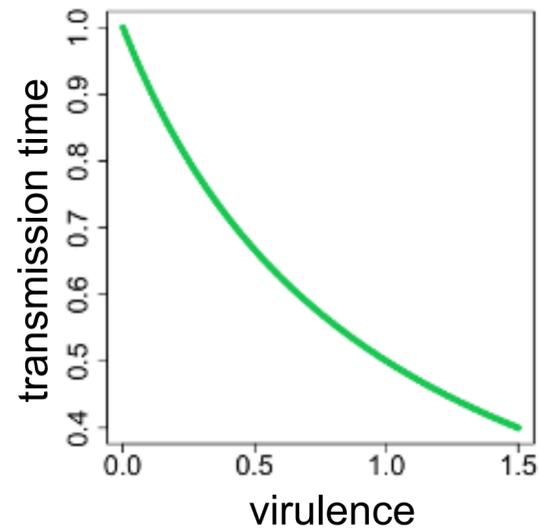
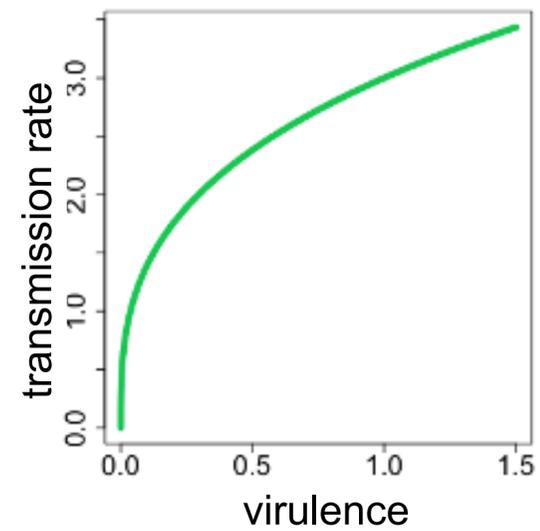


Dramatic change in the selection landscape

Vaccine driven evolution: virulence?



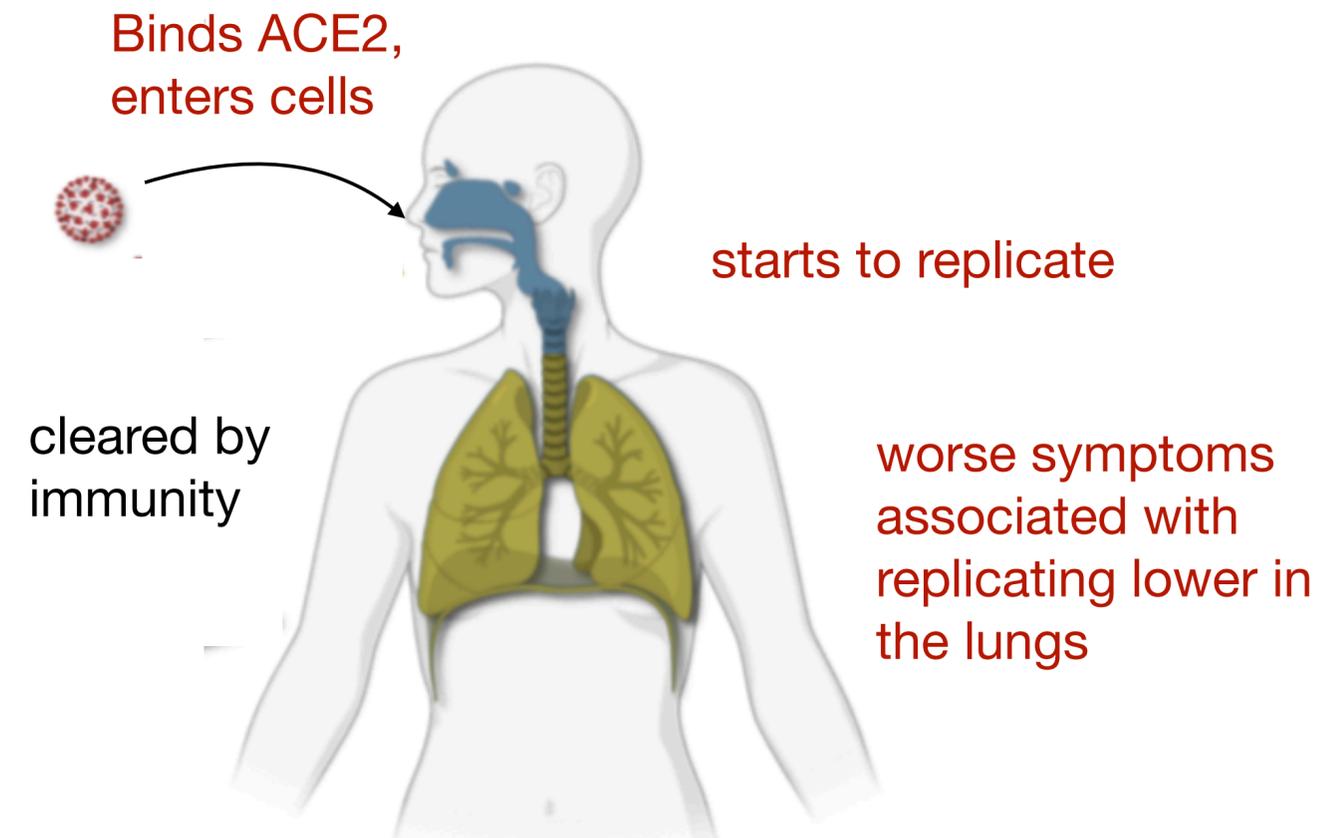
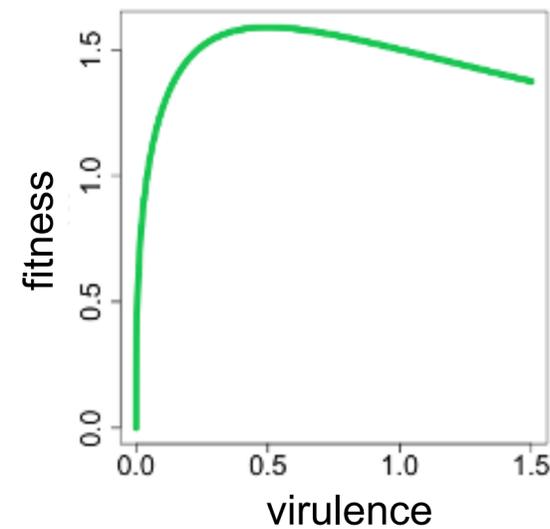
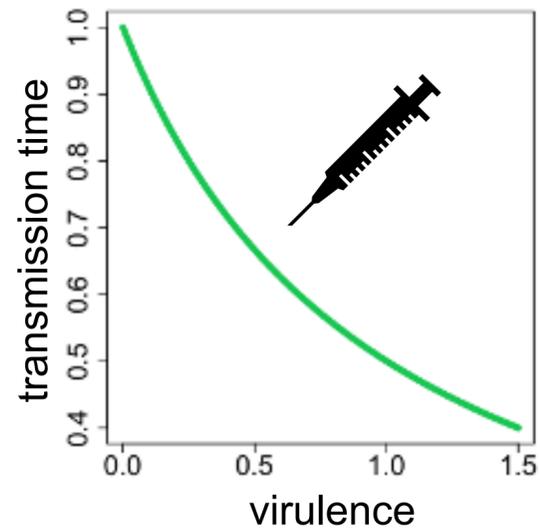
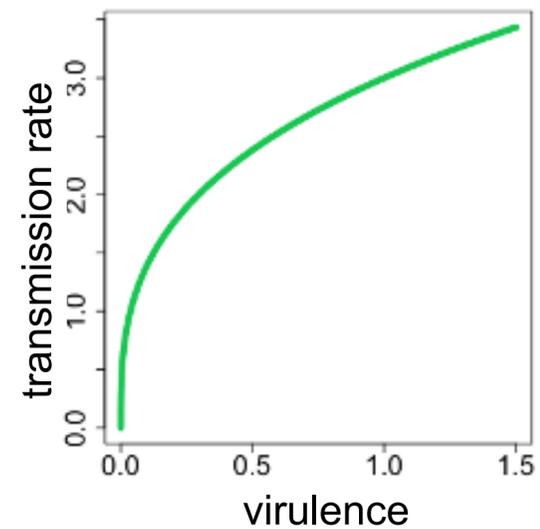
Evolution of virulence



Vaccine driven evolution: virulence?



Evolution of virulence



Vaccine driven evolution: virulence?

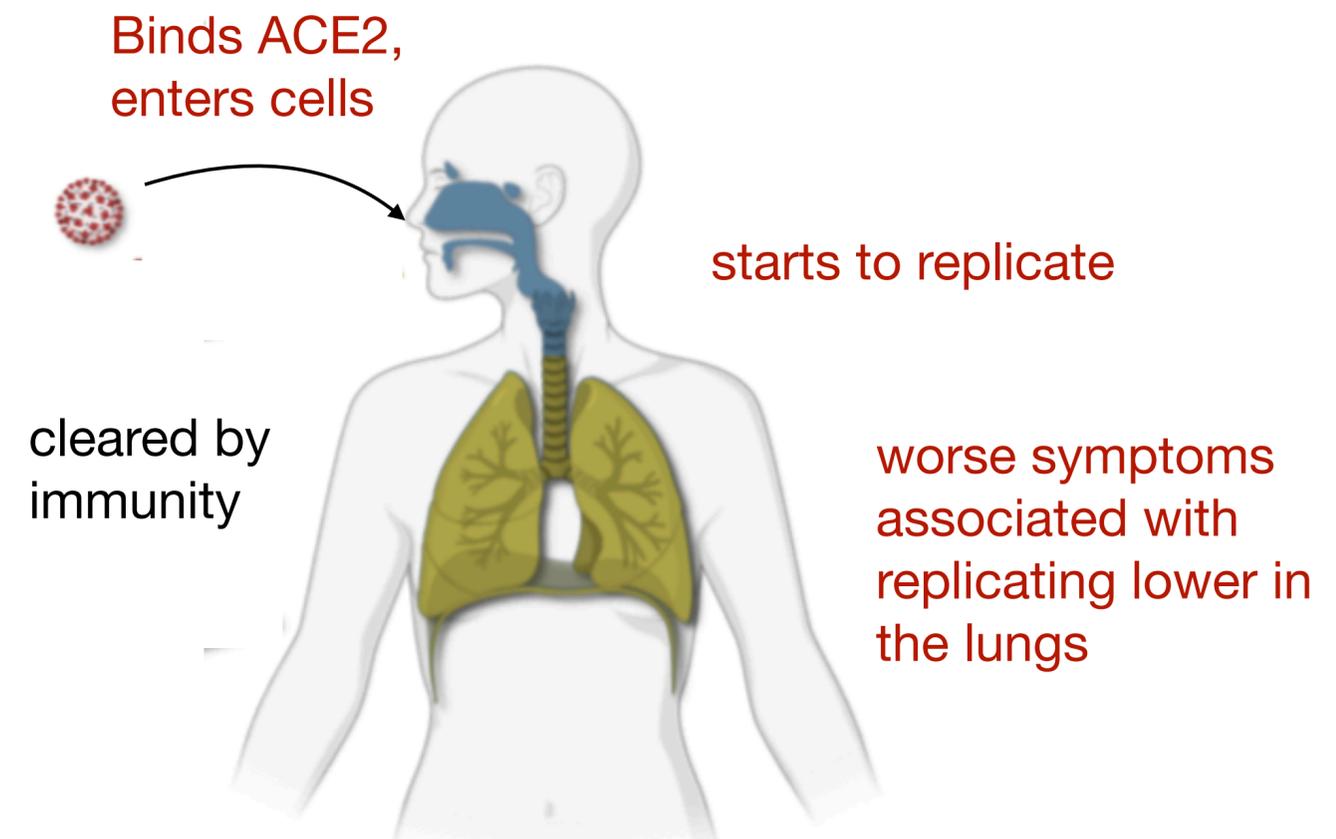


Evolution of virulence

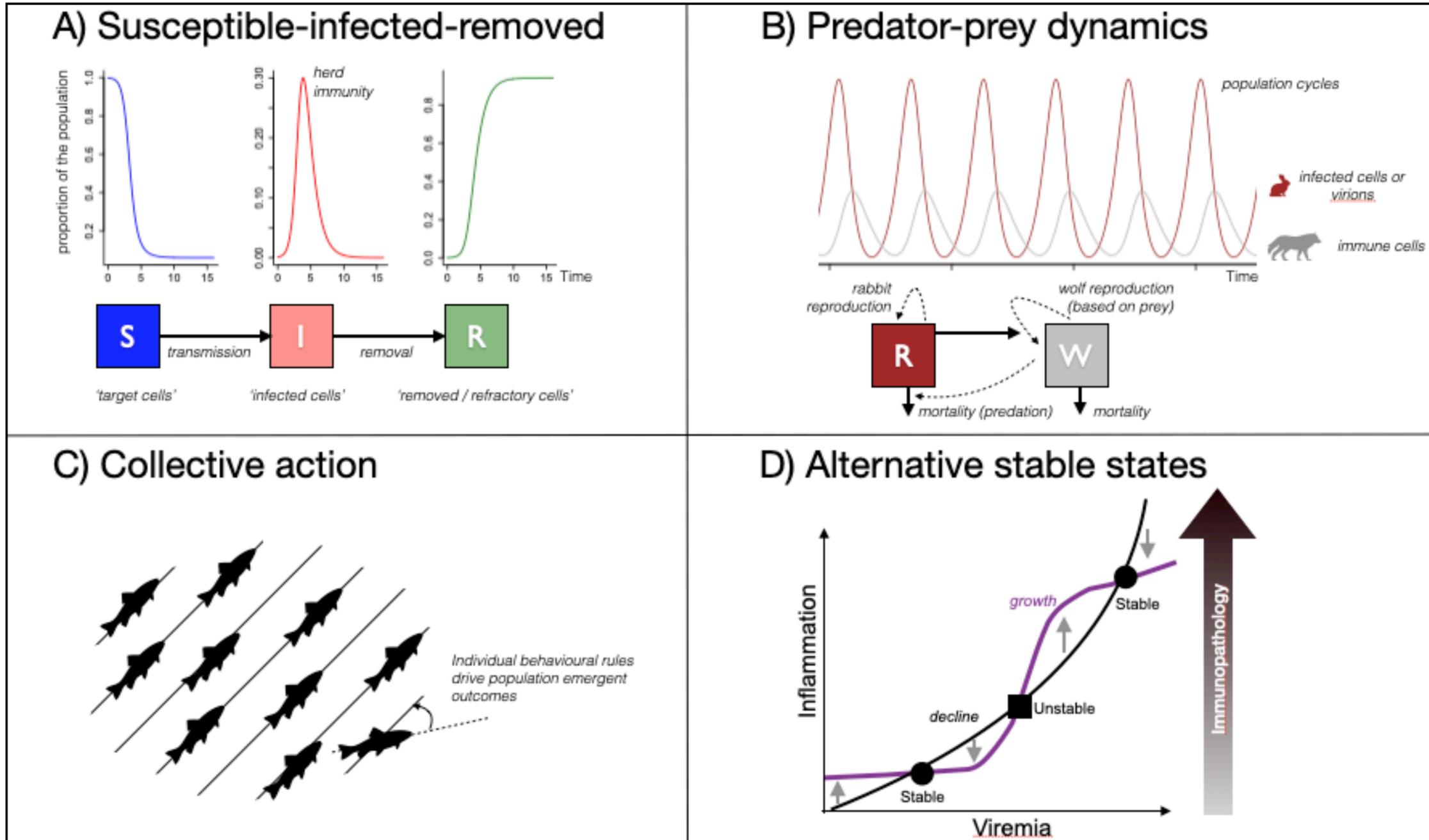
Is the evolution of increased transmission possible? **Yes**

Is increased transmission linked to increased virulence? **Yes, but not always**

Can vaccines alter selection for virulence? **Potentially**



Within host dynamics



Vaccine driven evolution: virulence?

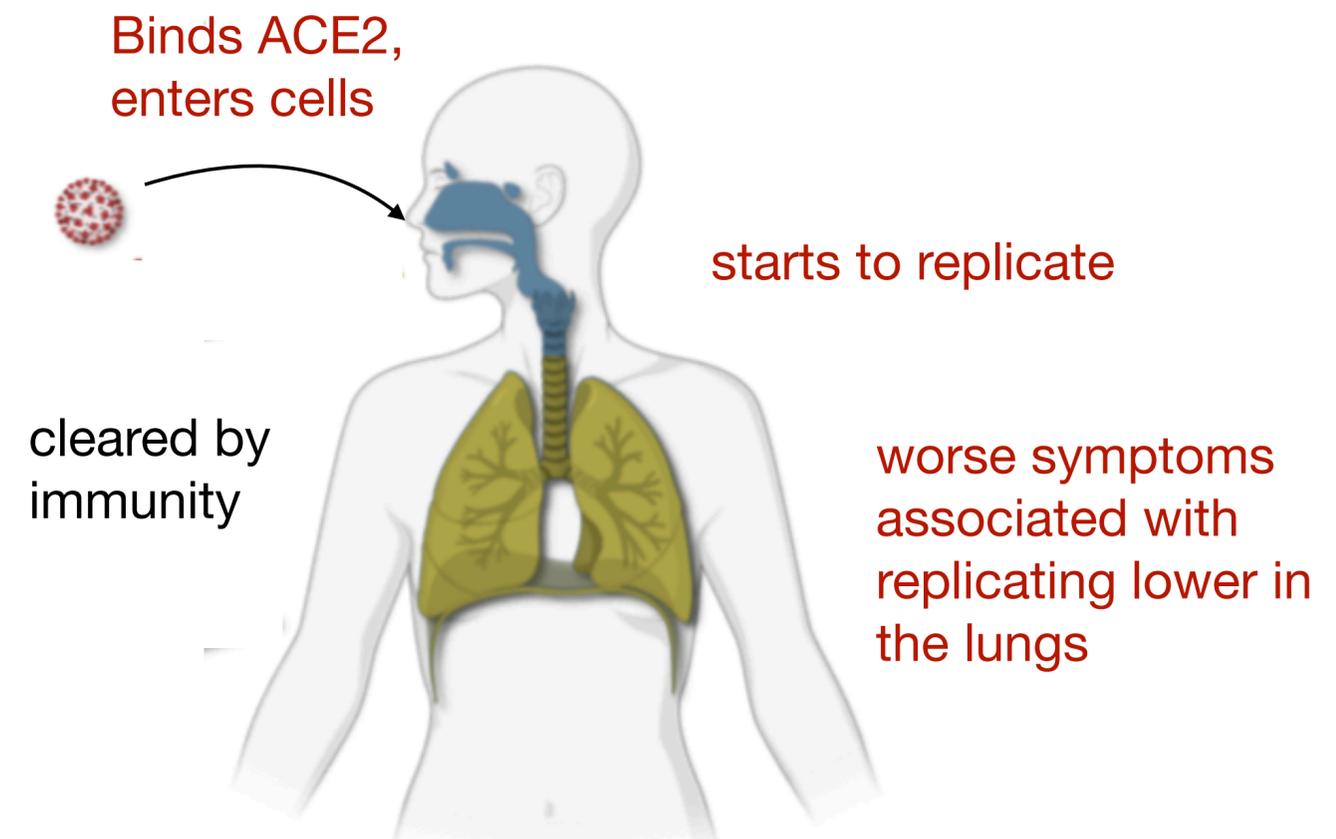


Evolution of virulence

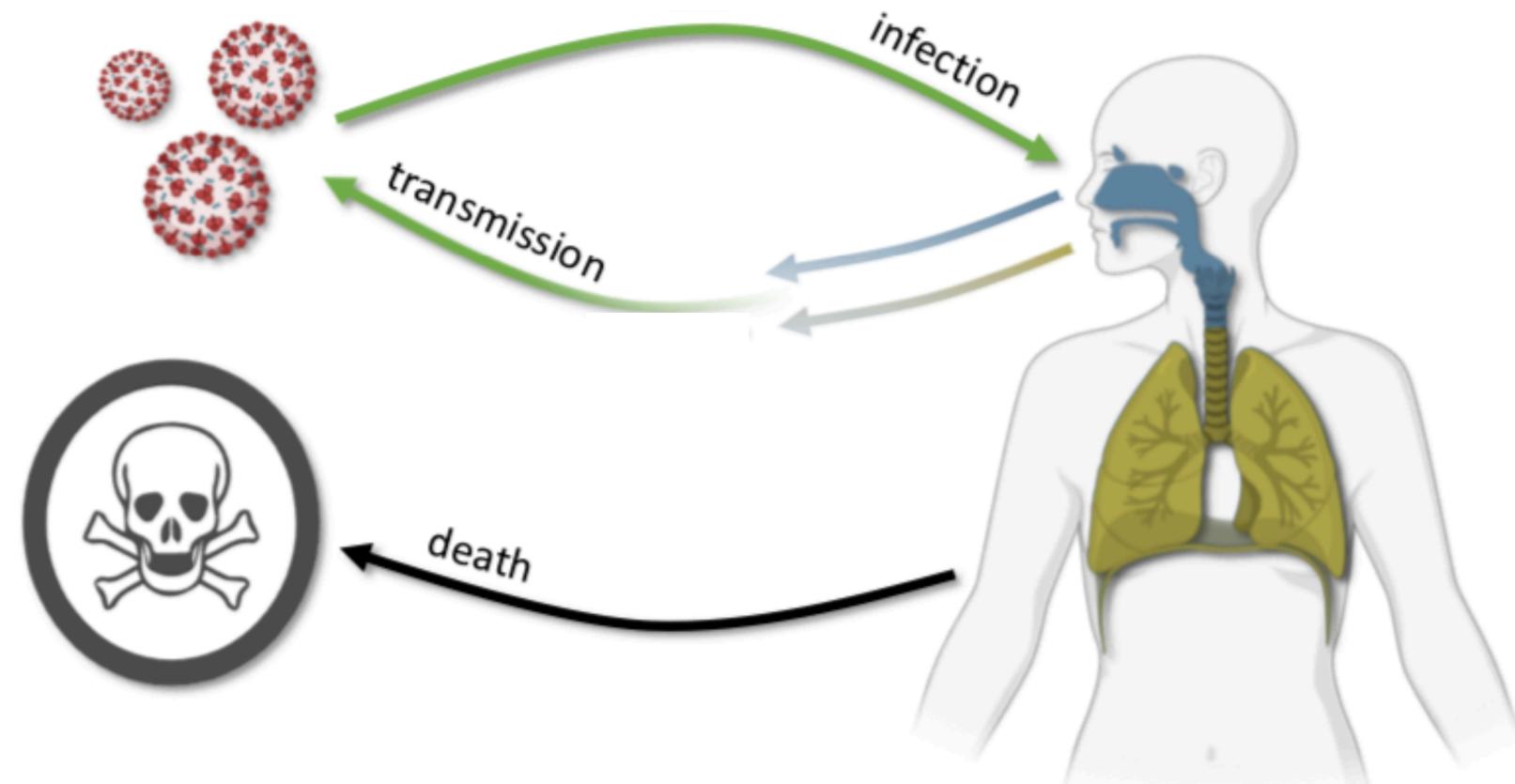
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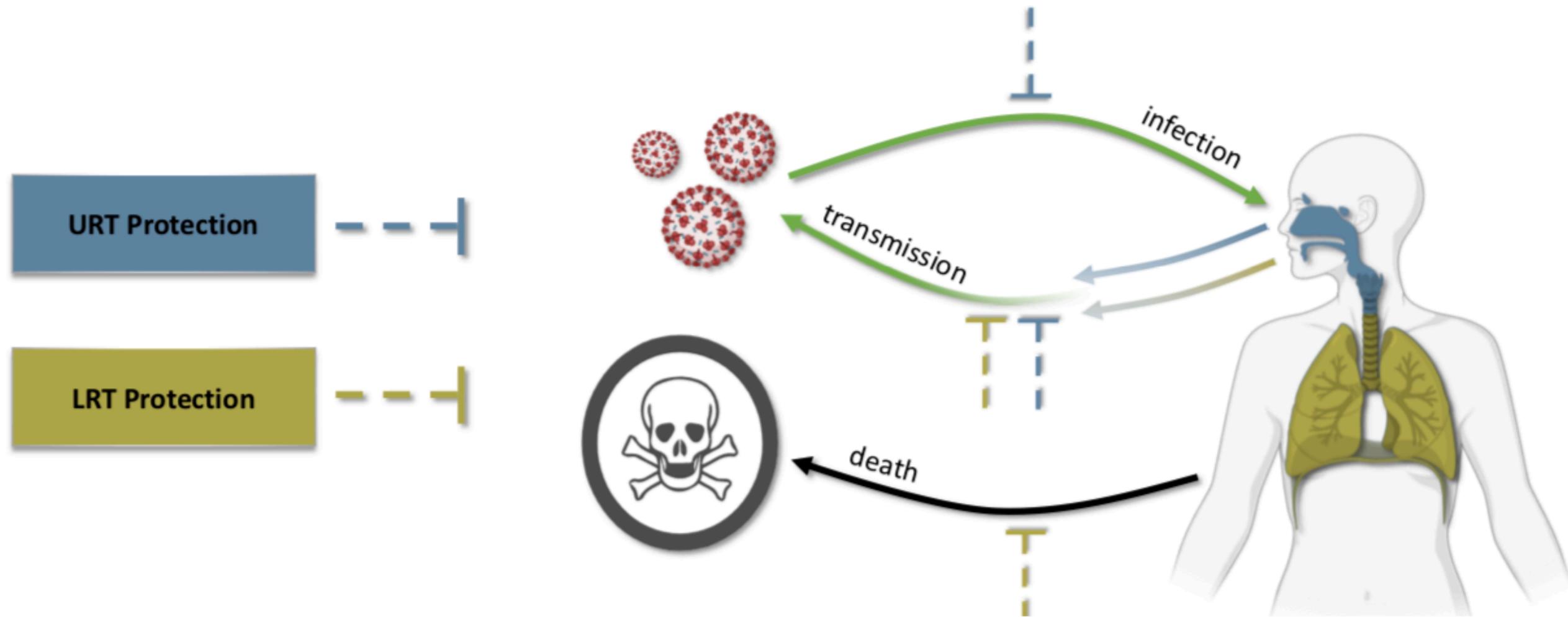
Can vaccines alter selection for virulence? **Potentially**



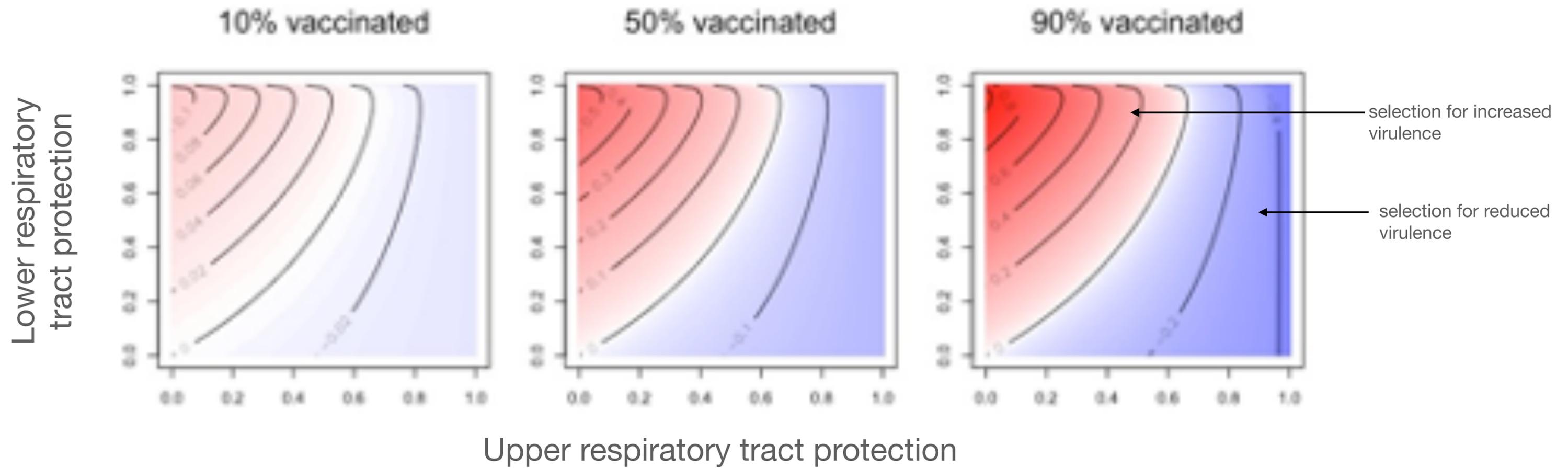
Vaccine driven evolution: virulence?



Vaccine driven evolution: virulence?



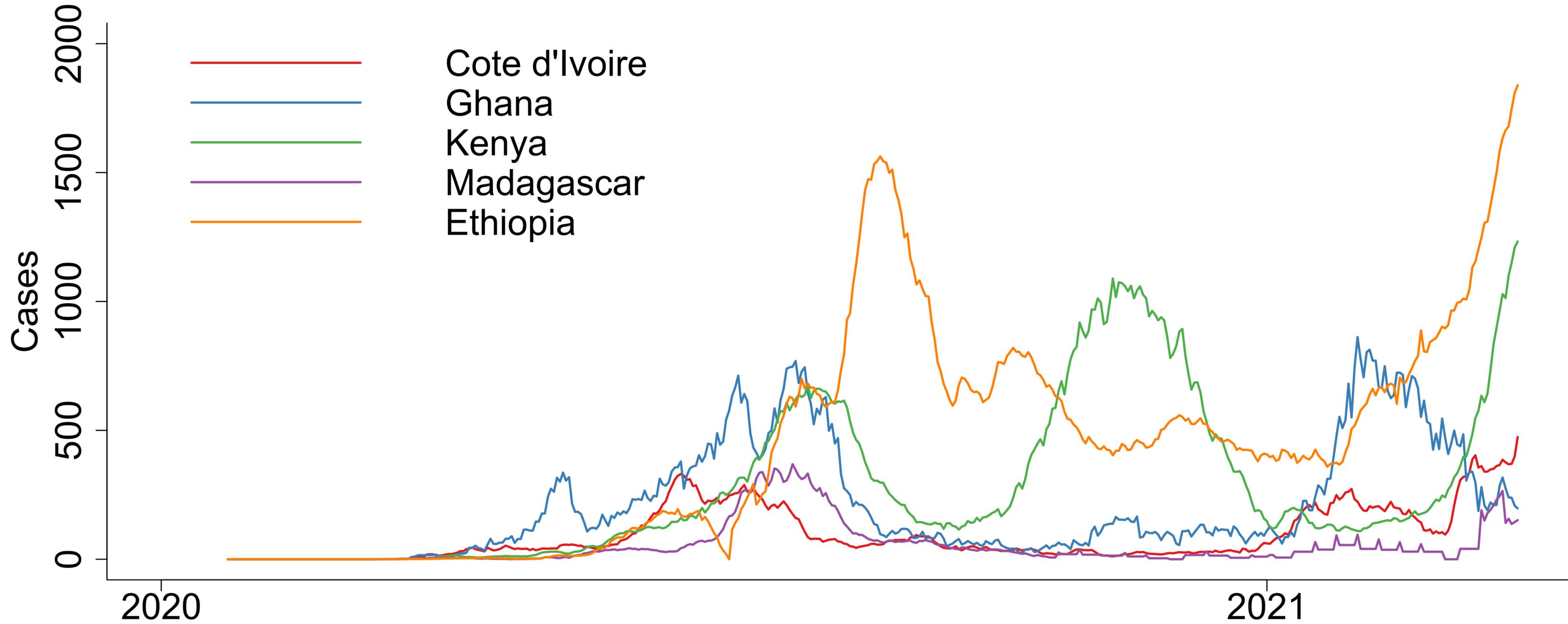
Vaccine driven evolution: virulence?



Vaccine driven evolution: virulence?



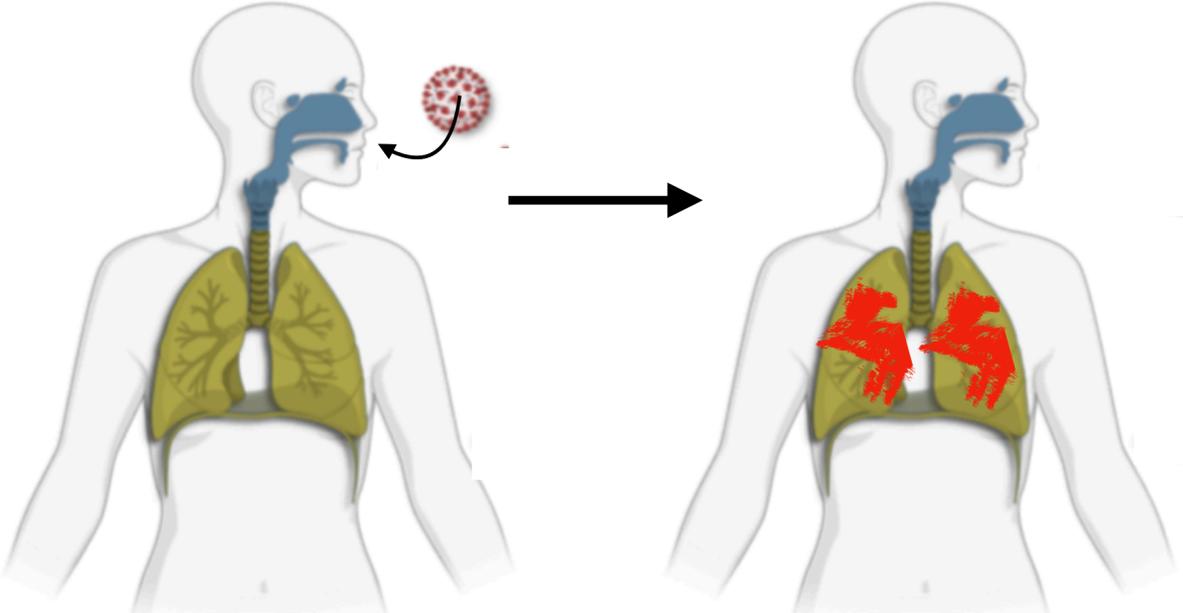
- Prospects for SARS-CoV-2 virulence evolution remain **uncertain**
- Vaccines have **theoretical potential** to select for increased virulence if they **fail to provide URT protection**
- Clear benefits of vaccines vastly outweigh risks
- Virulence evolution should be monitored
- Costs of virulence evolution would likely **fall on those without access to vaccines**



Secondary infections?

Infection

Symptoms

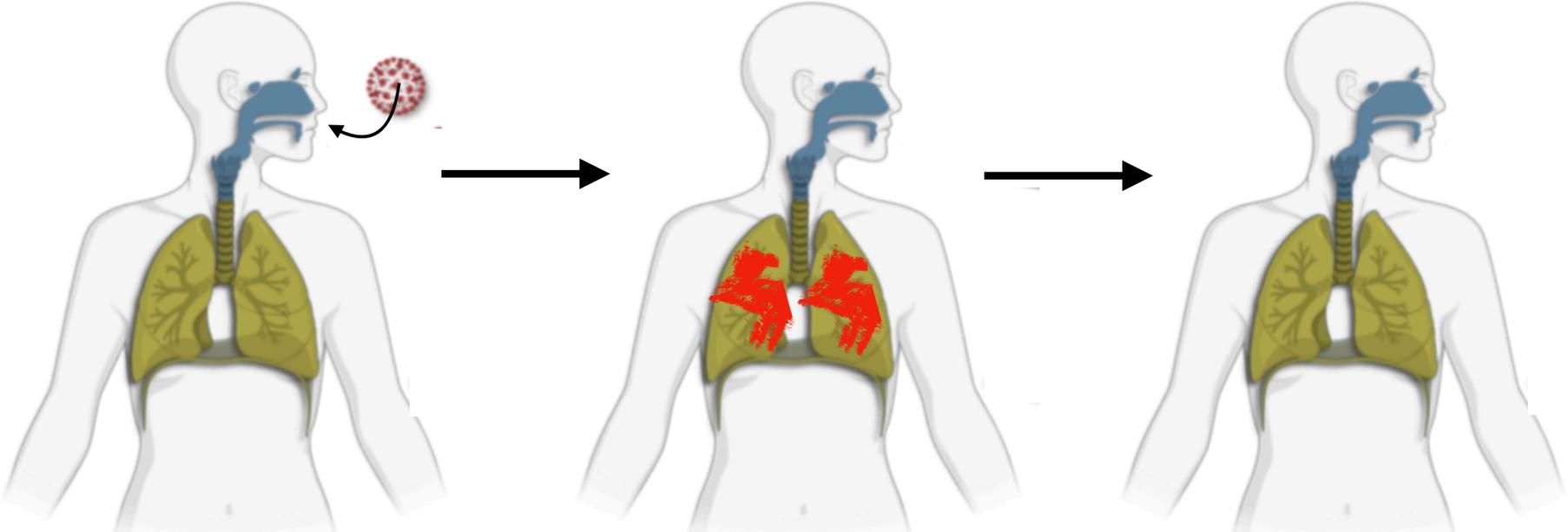


Secondary infections?

Infection

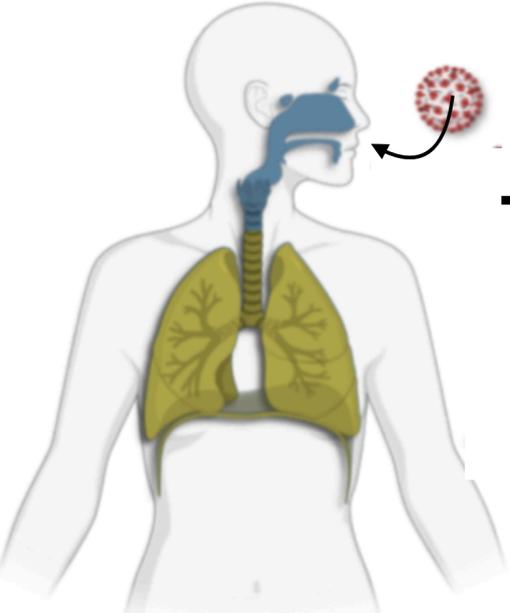
Symptoms

Recovery

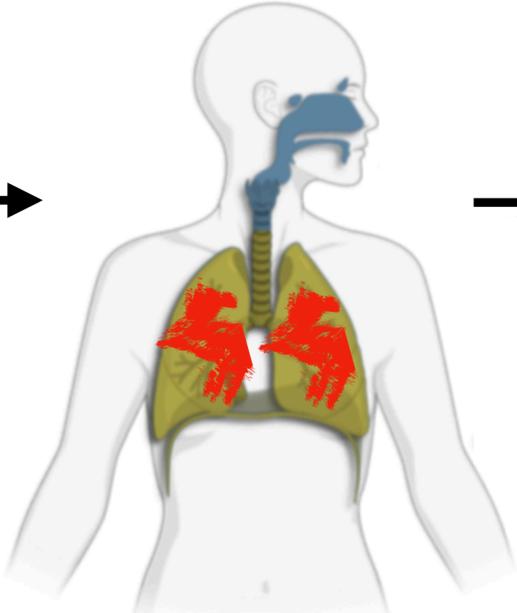


Secondary infections?

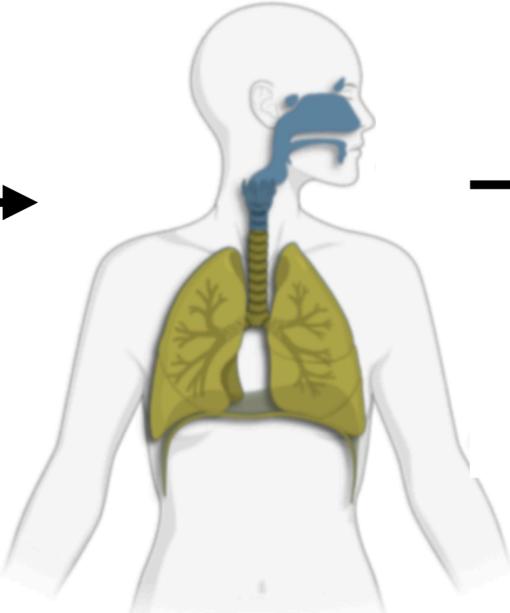
Infection



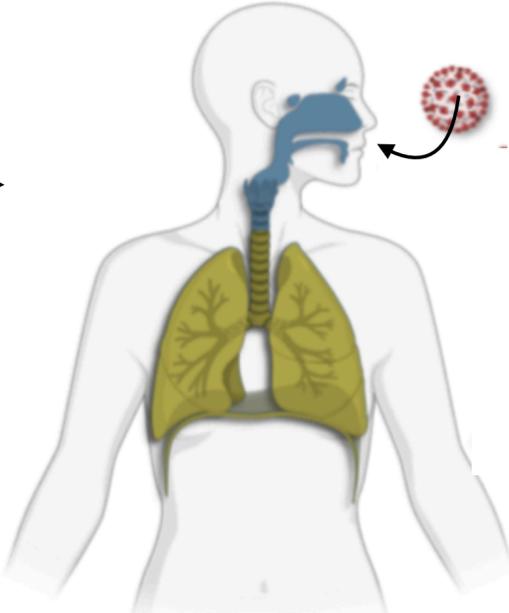
Symptoms



Recovery

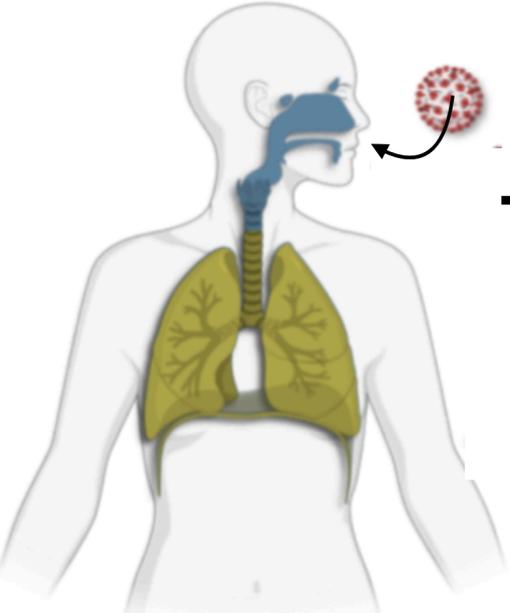


Exposure

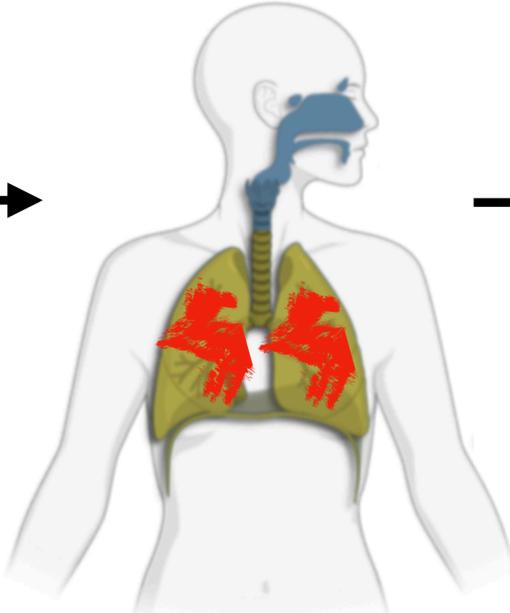


Secondary infections?

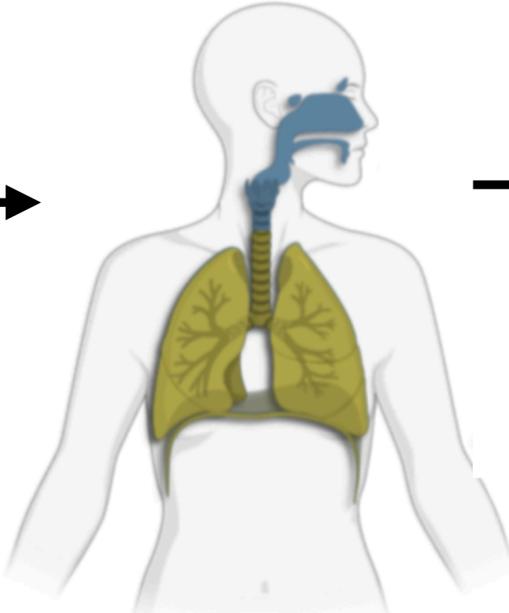
Infection



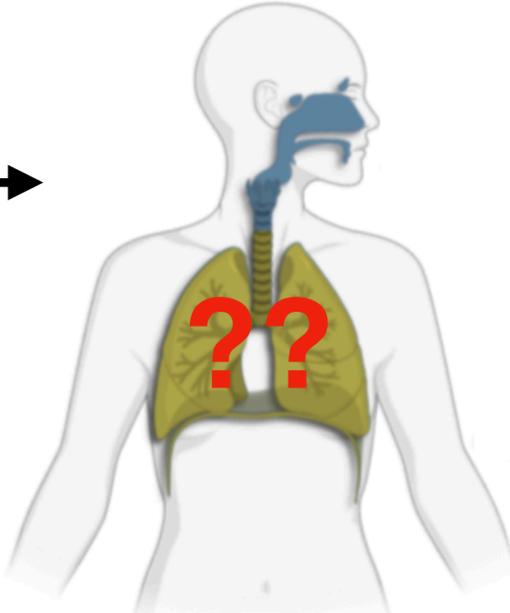
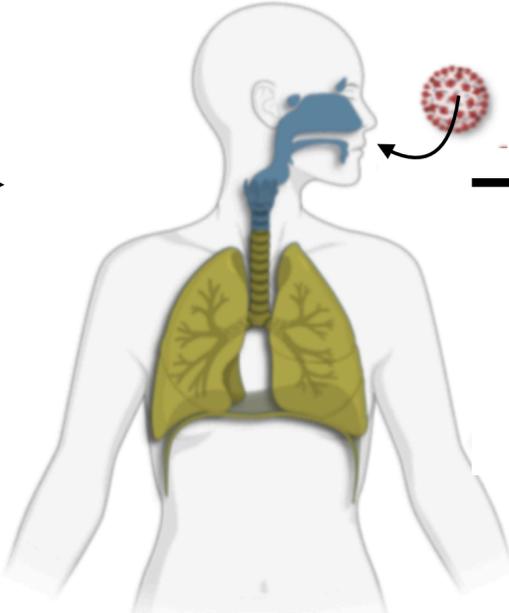
Symptoms



Recovery

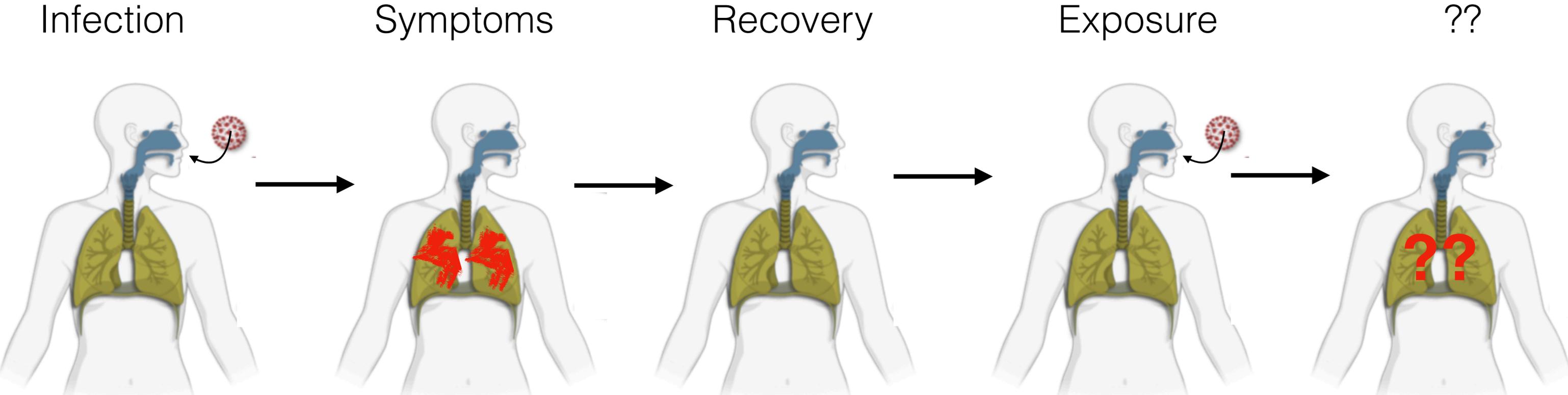


Exposure



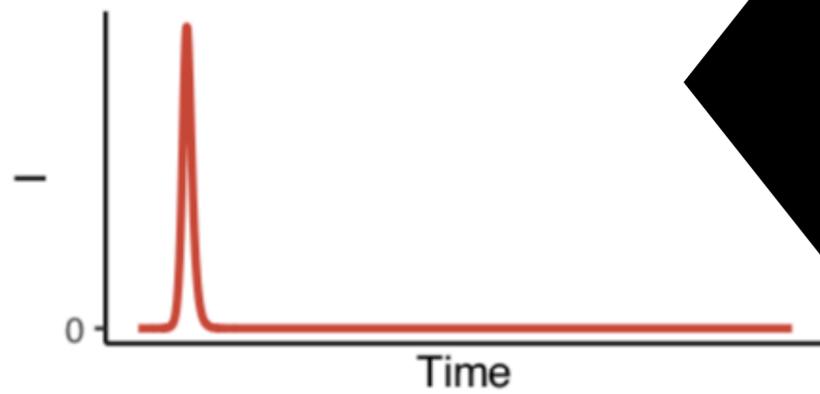
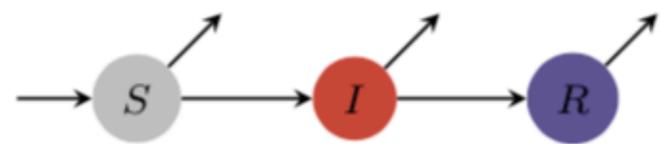
Re-infection?
Symptoms?

Secondary infections?

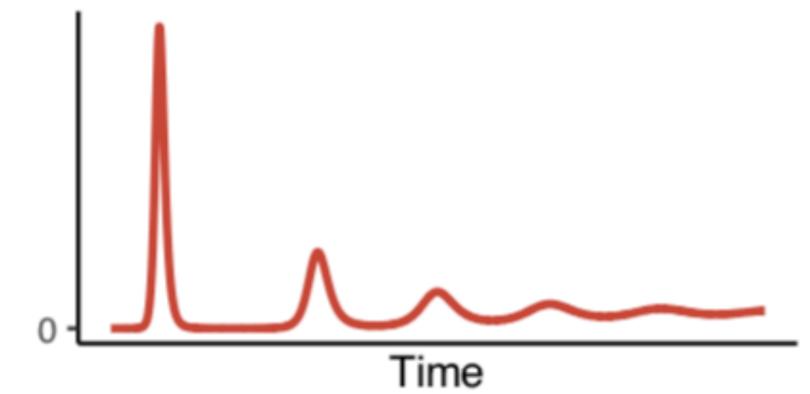
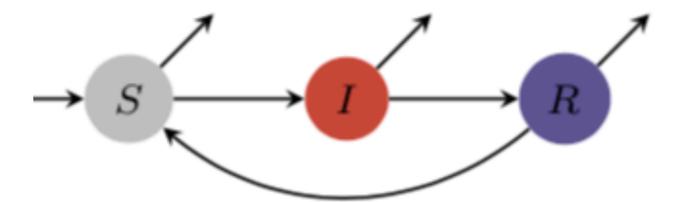


Re-infection?
Symptoms?

For endemic coronaviruses, Callow et al. (1990) suggest that reinfection can occur within a year, but symptoms are **mild**, and the virus is **cleared more quickly**.

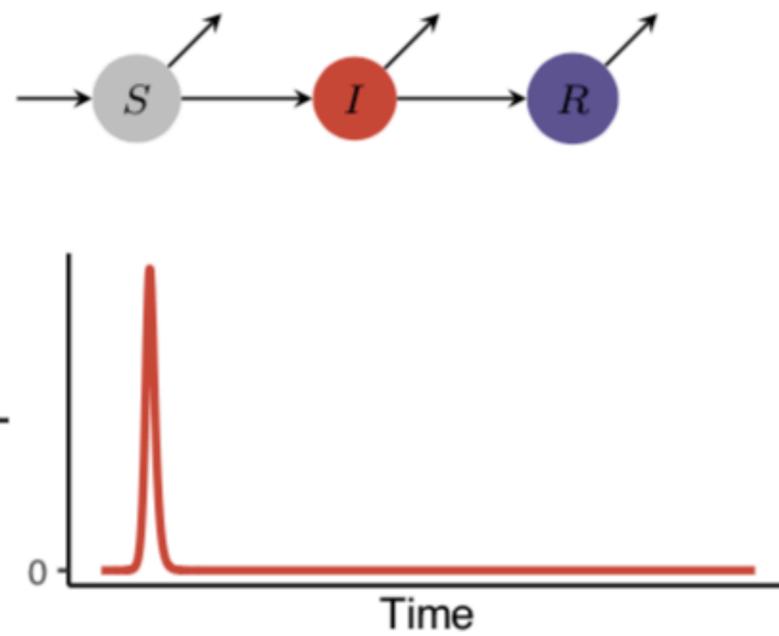


‘Susceptible-Infected-Recovered’

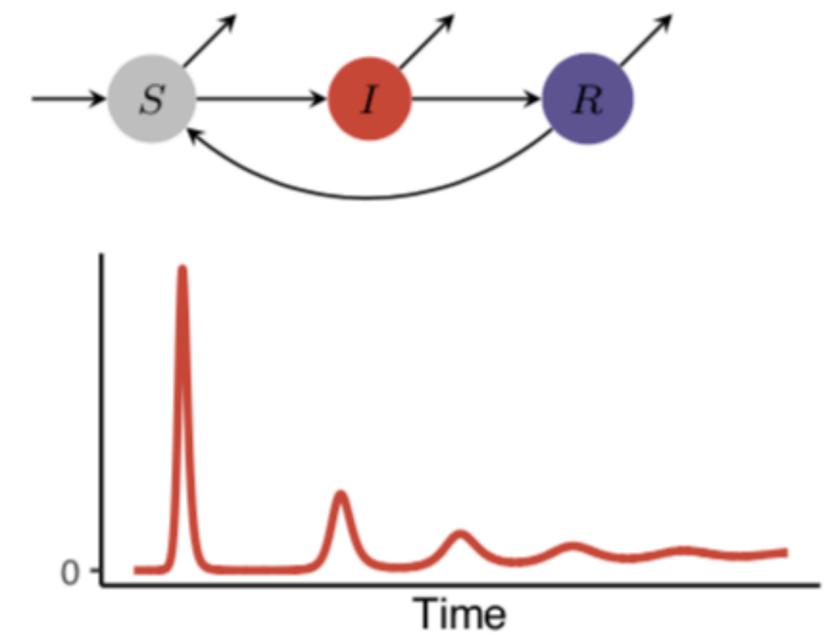
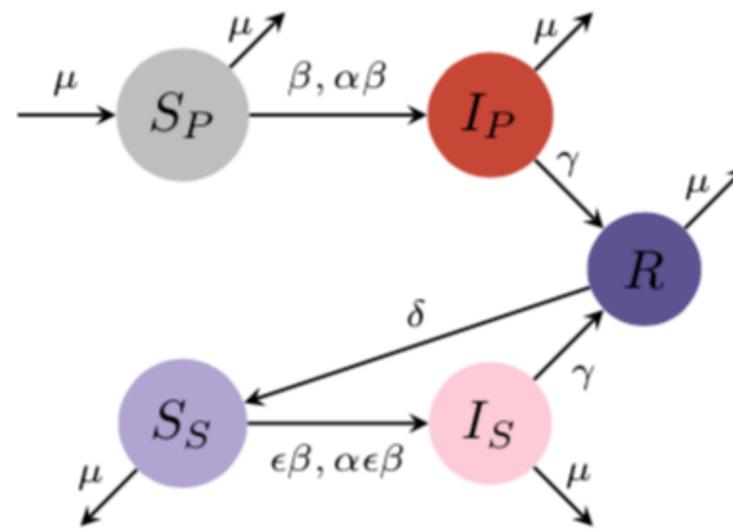


‘Susceptible-Infected-Recovered-Susceptible’

An intermediate model

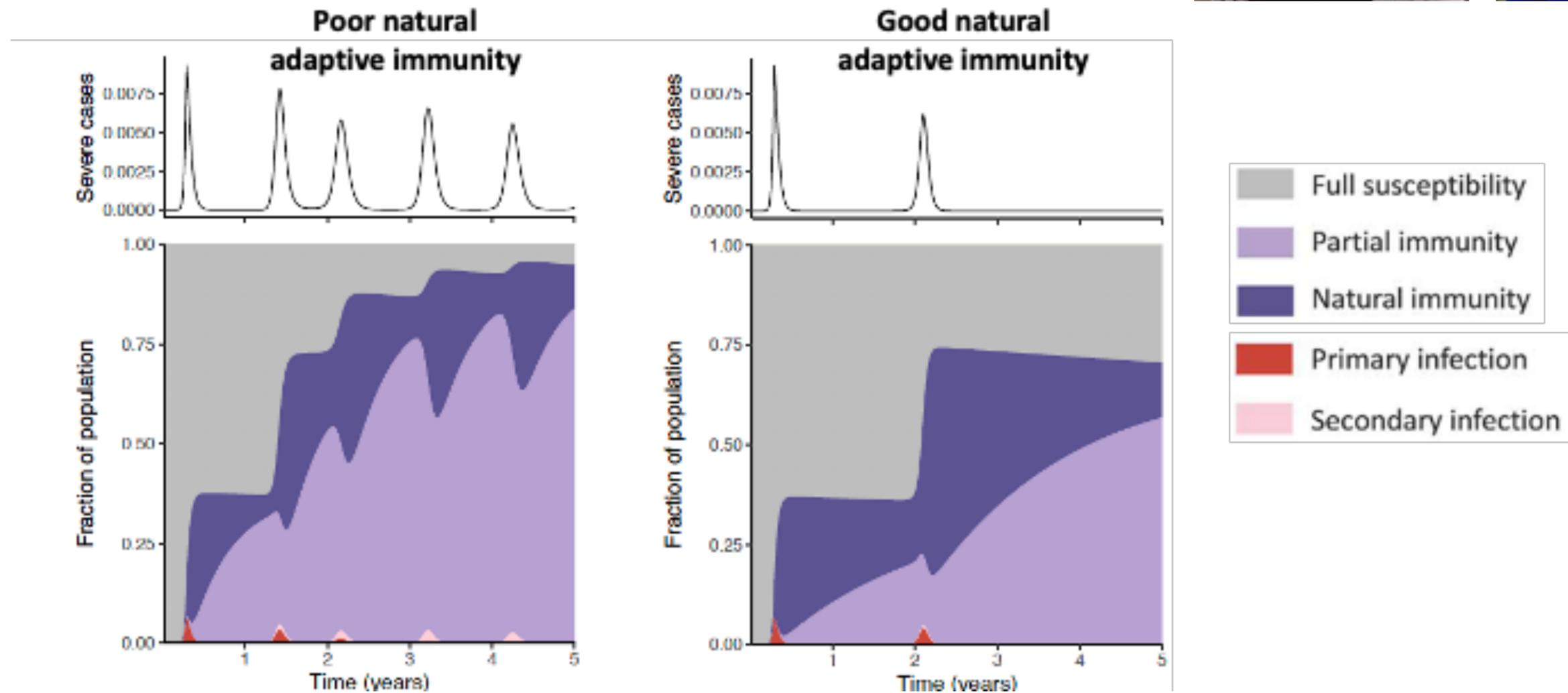


‘Susceptible-Infected-Recovered’



‘Susceptible-Infected-Recovered-Susceptible’

Secondary infections?



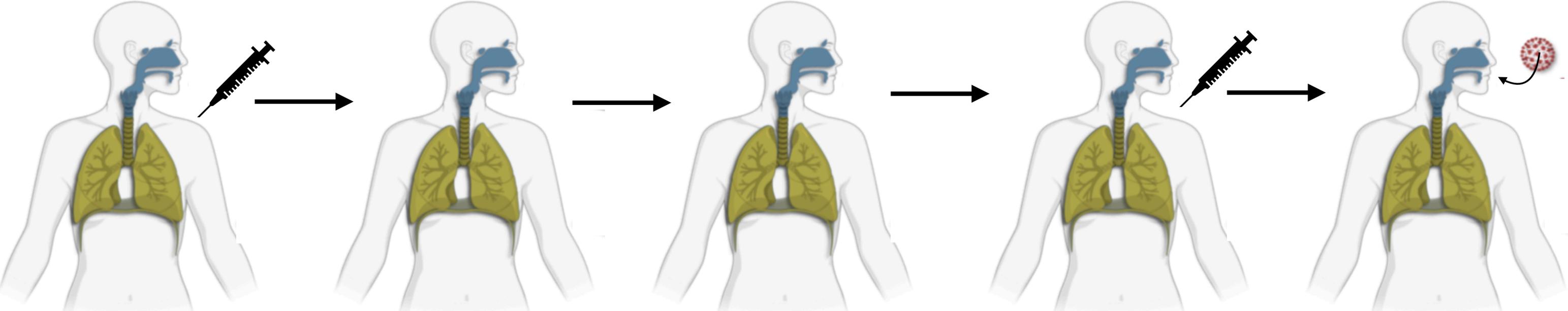
Range of epidemiological outcomes depending on assumptions related to strength and duration of adaptive immune responses following primary and secondary infections.

Add vaccination?

Vaccination

Immunity develops

Booster



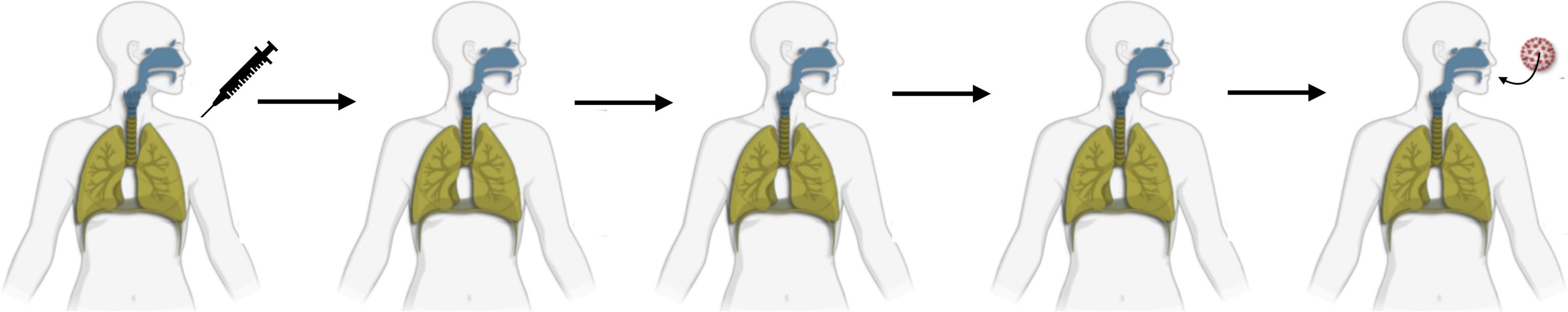
Very low risk of symptoms

Add vaccination?

Vaccination

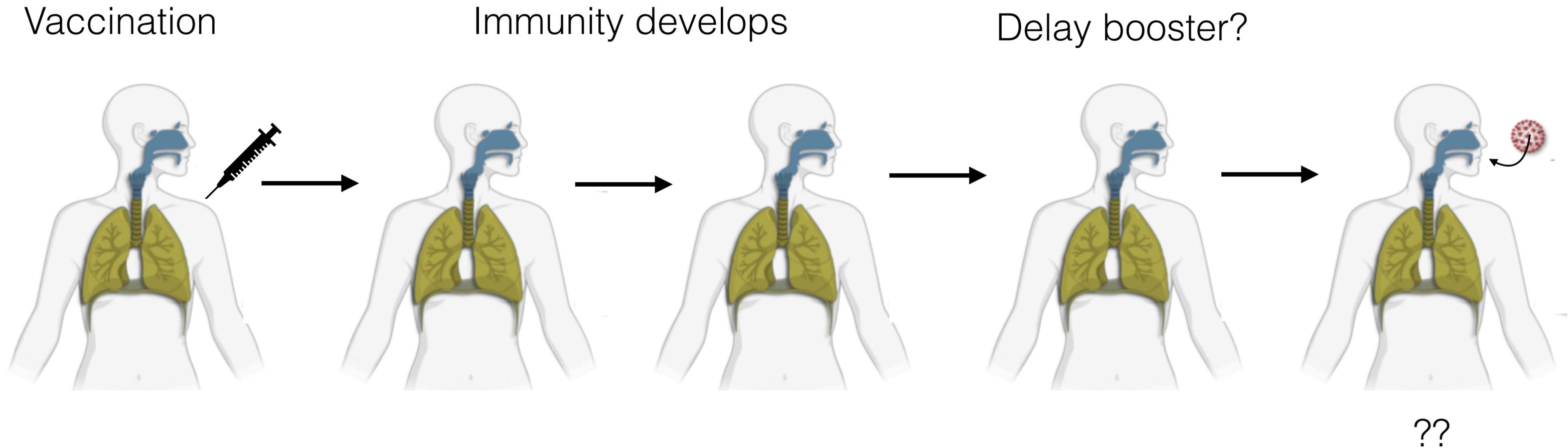
Immunity develops

Delay booster?



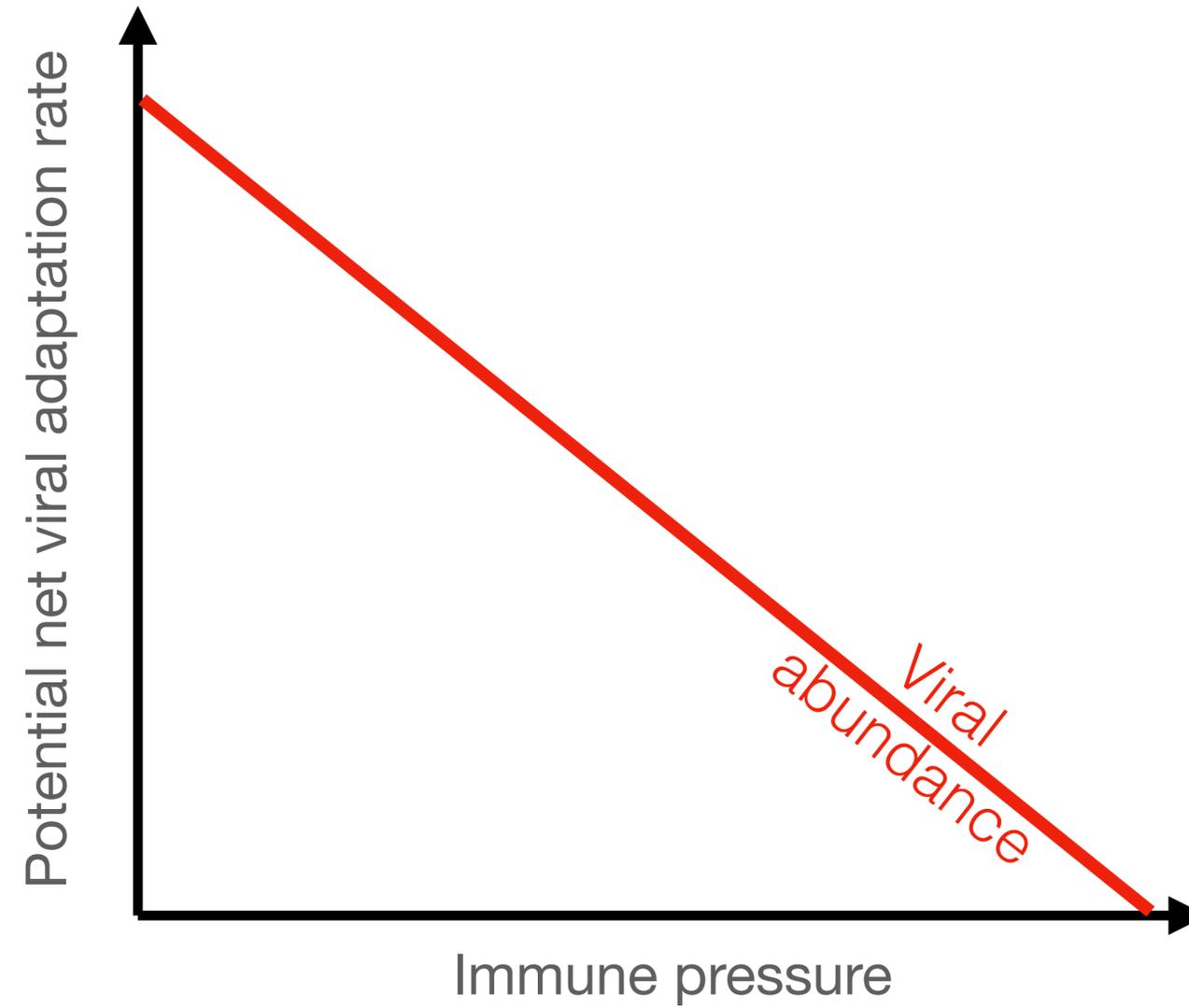
??

Add vaccination?

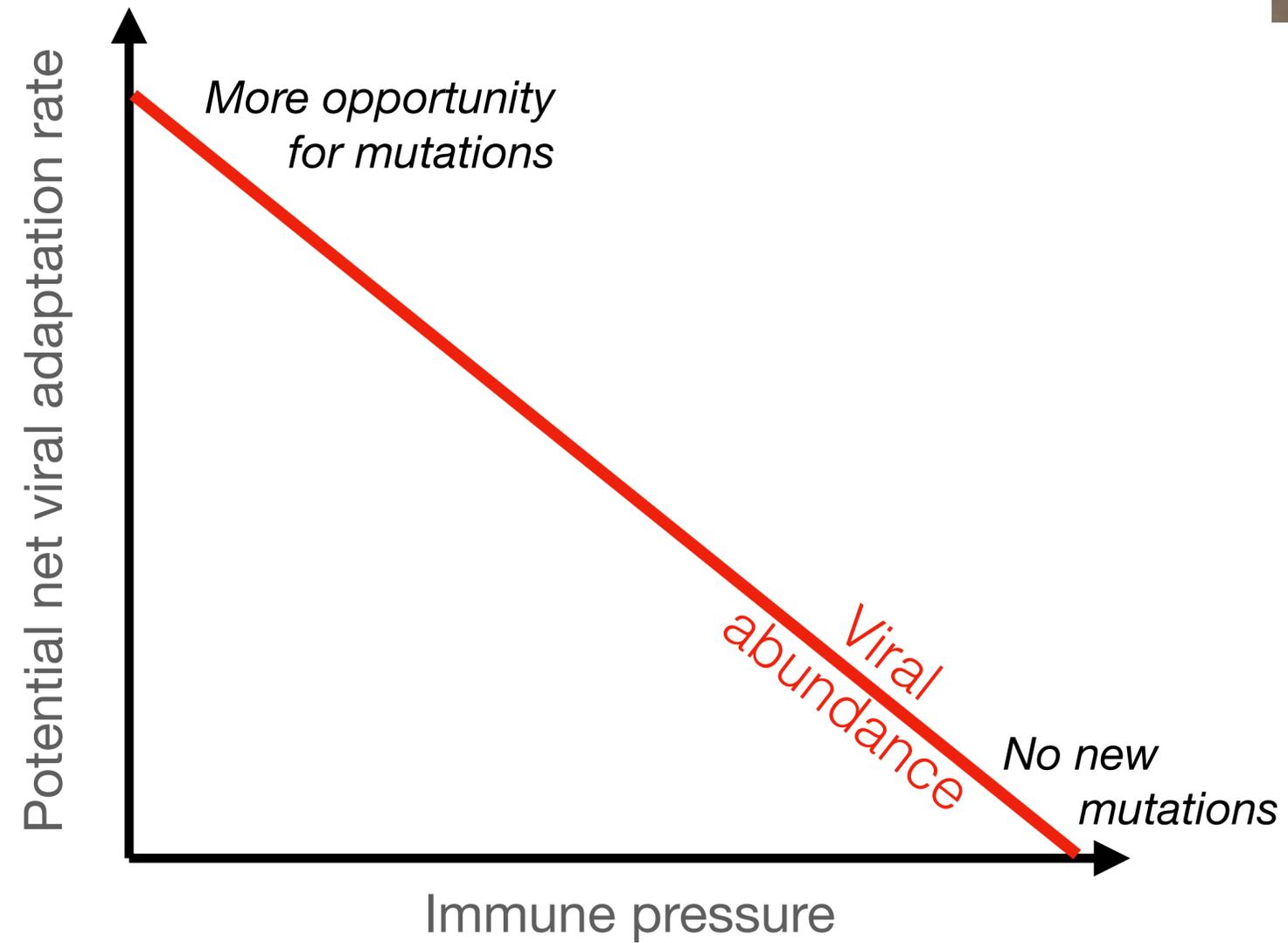


Epidemiological issue (potential burden of symptomatic disease) but also an **evolutionary** one (evolution of immune escape).

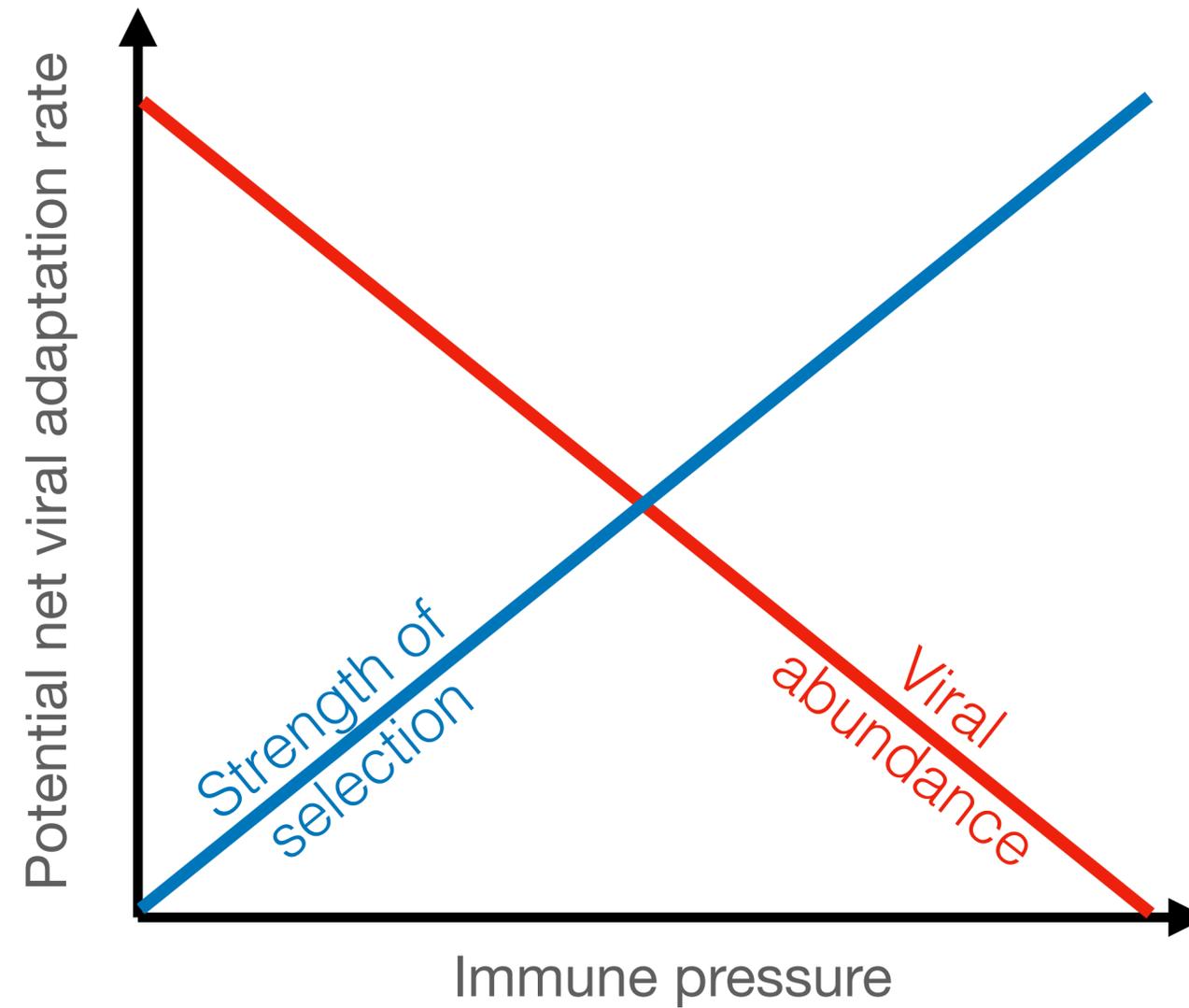
Selection for immune escape?



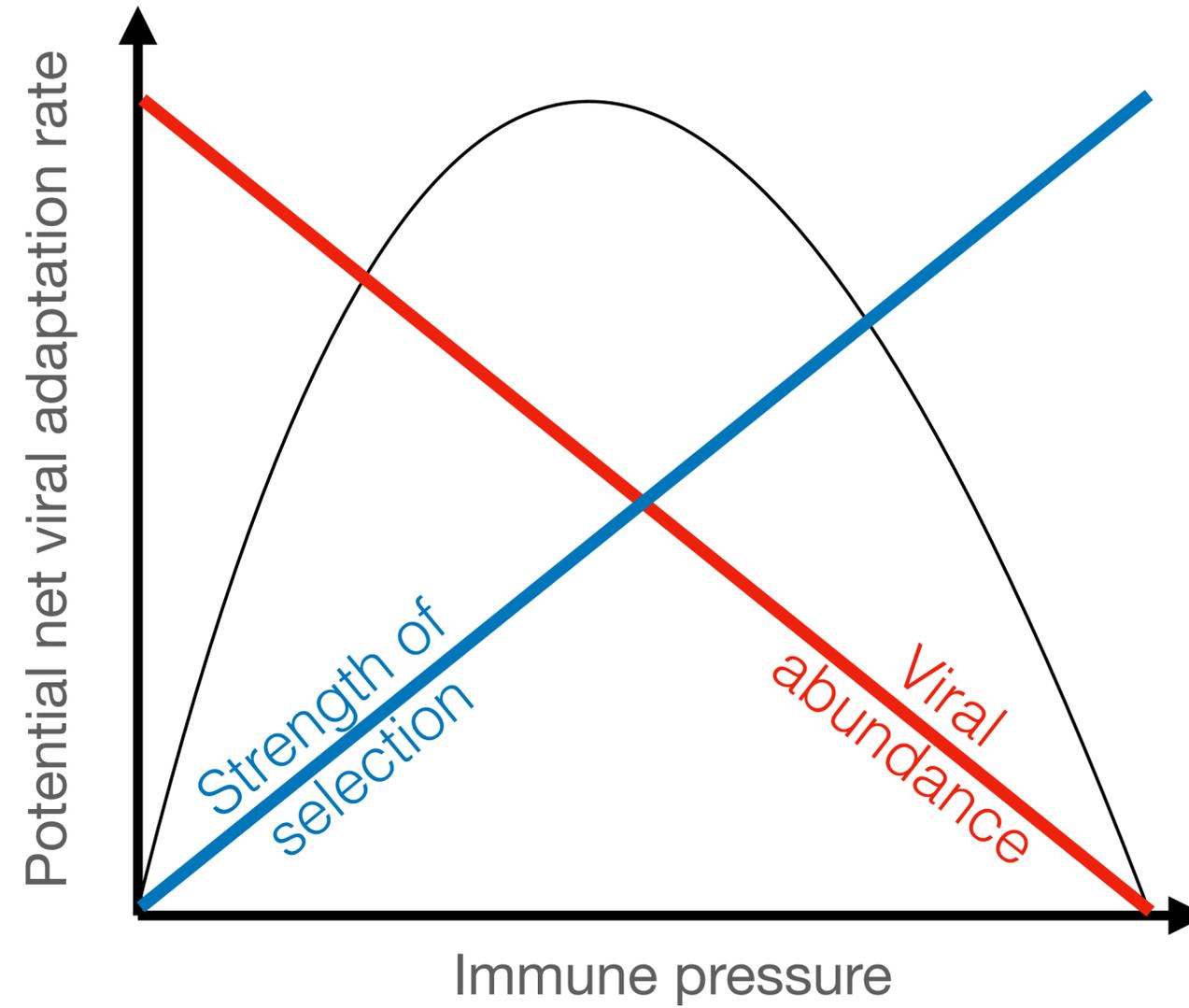
Selection for immune escape?



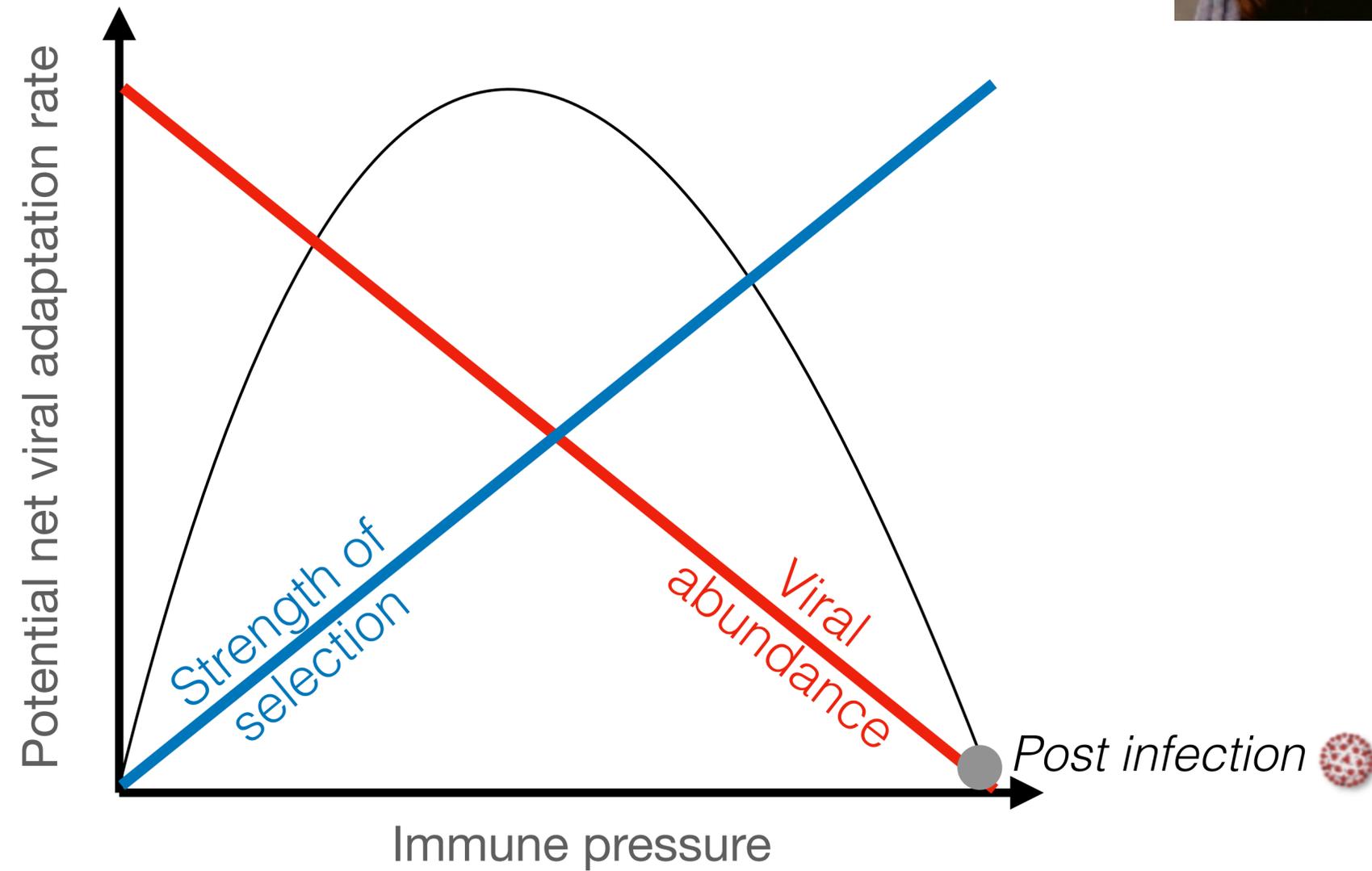
Selection for immune escape?



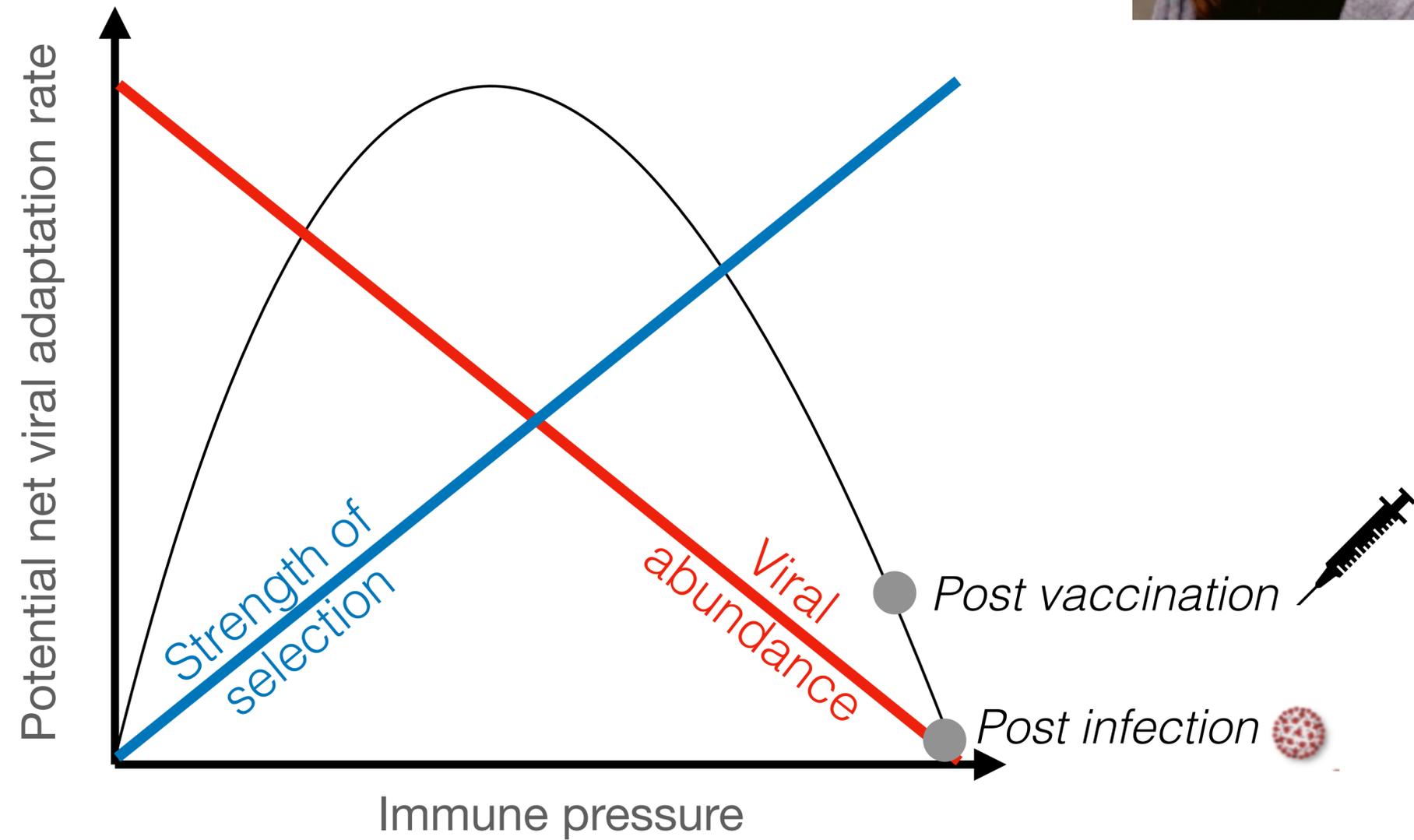
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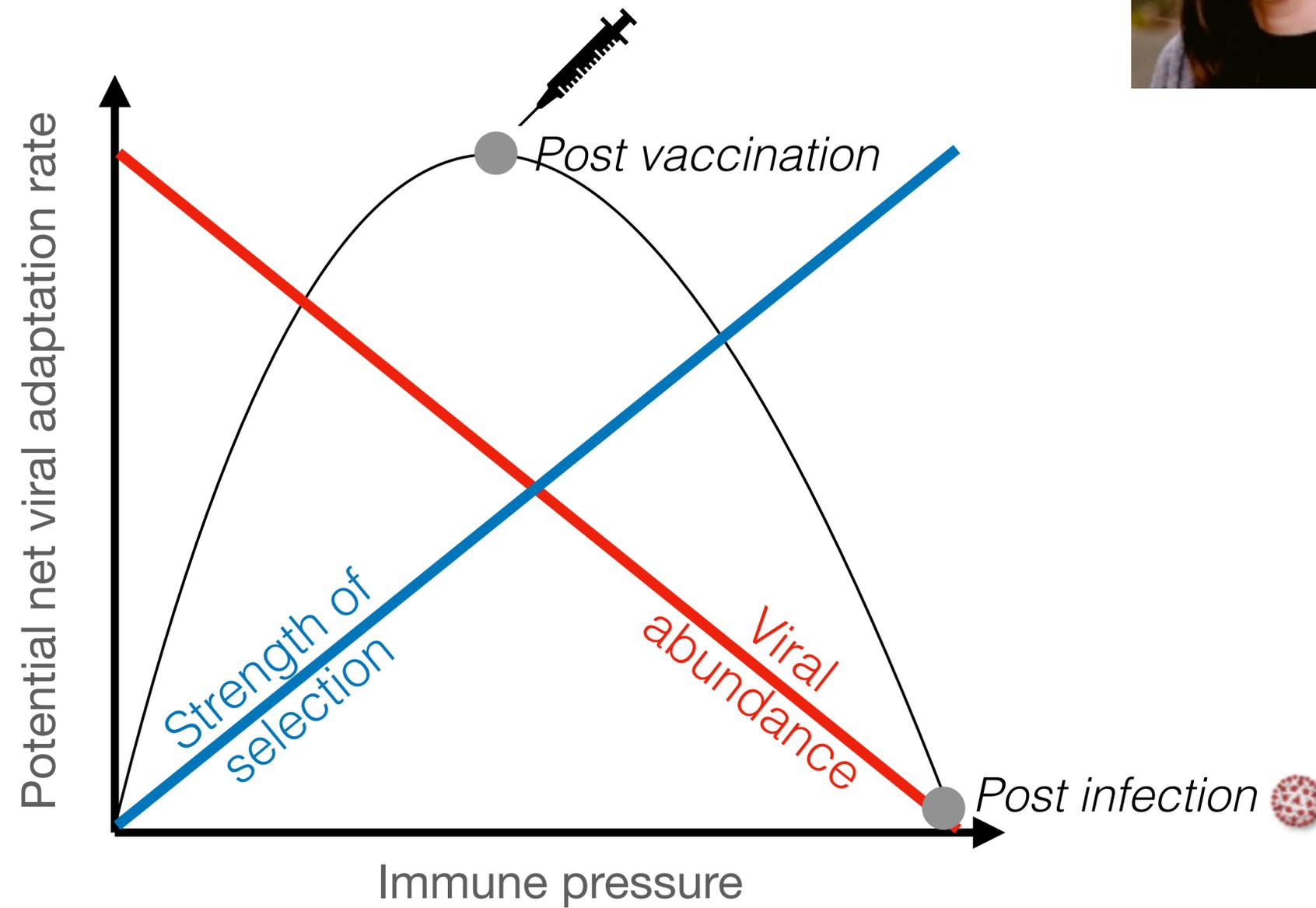
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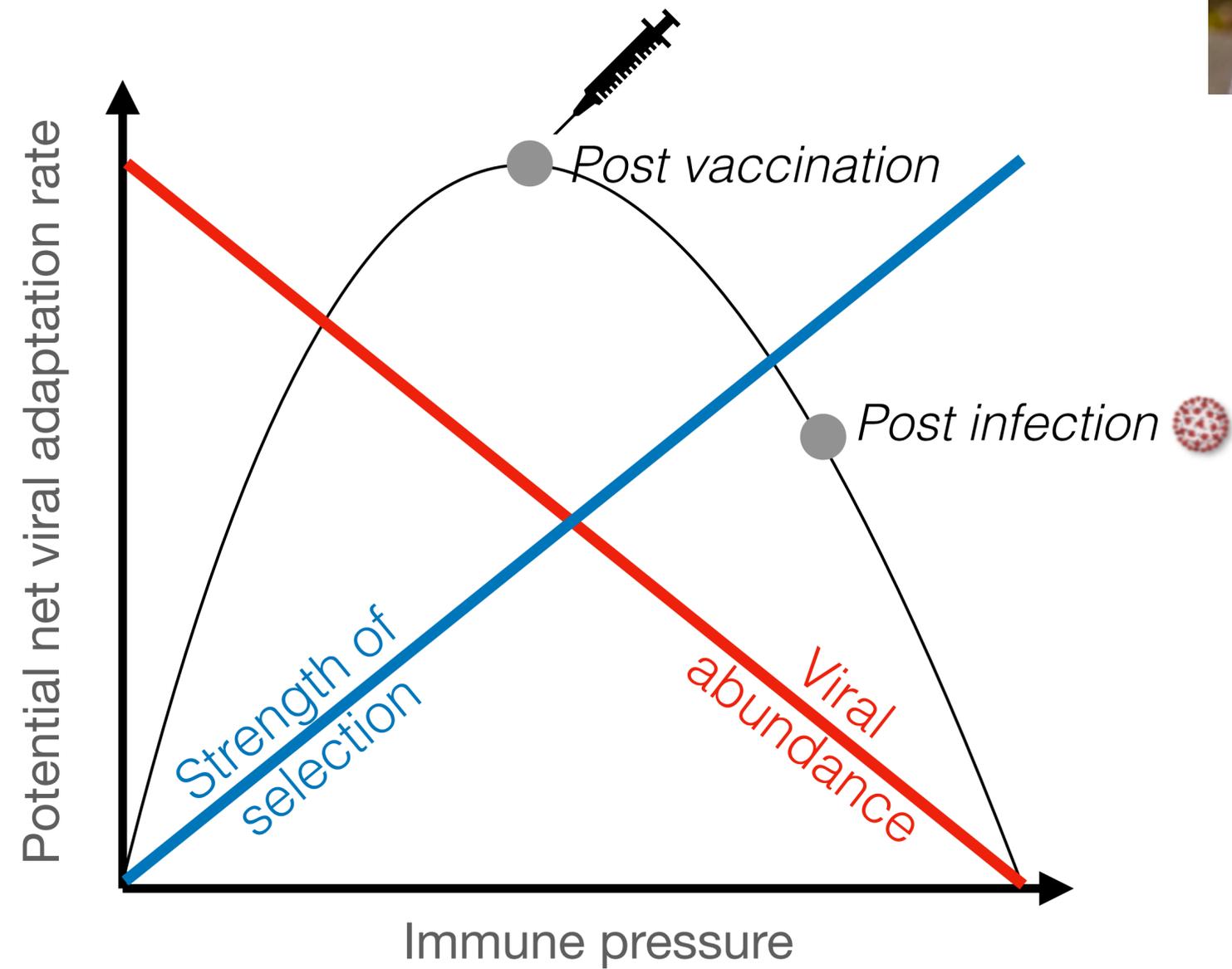
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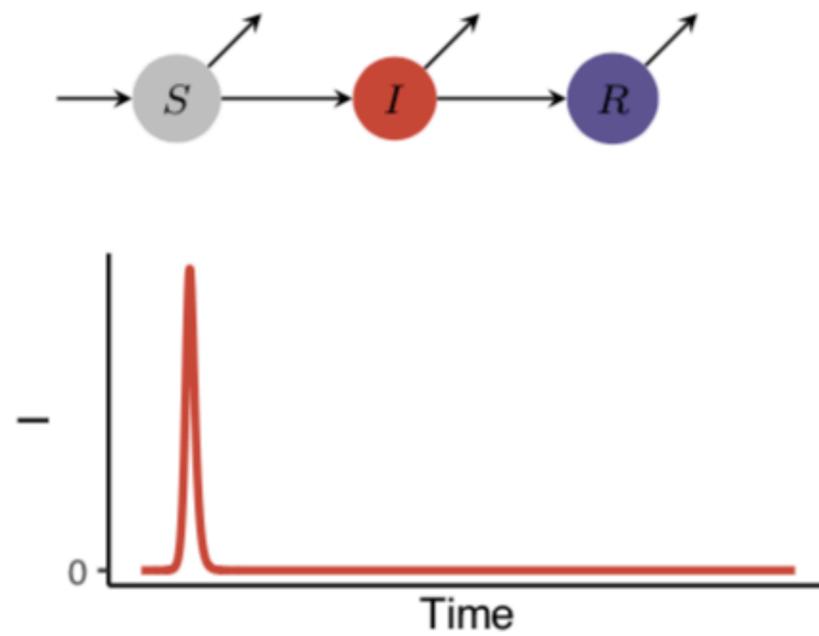
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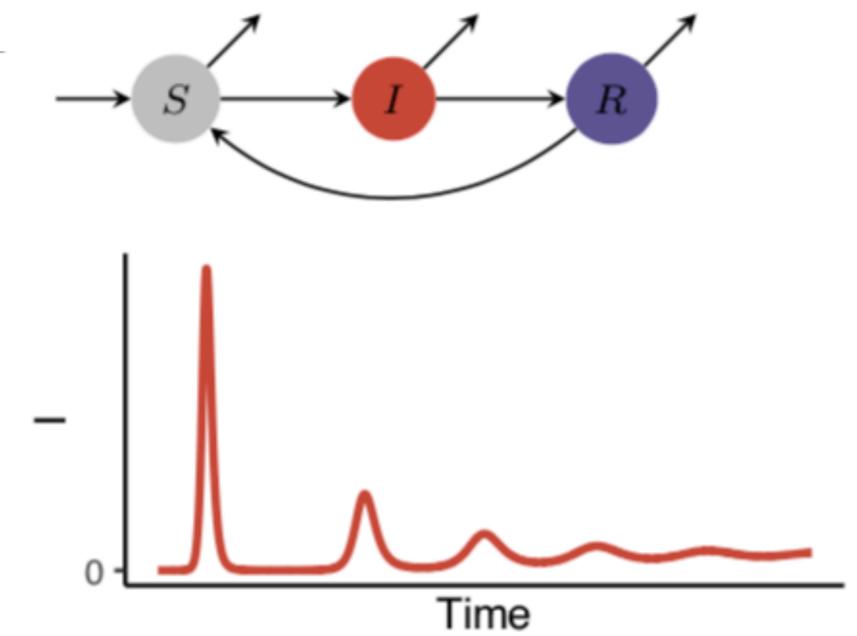
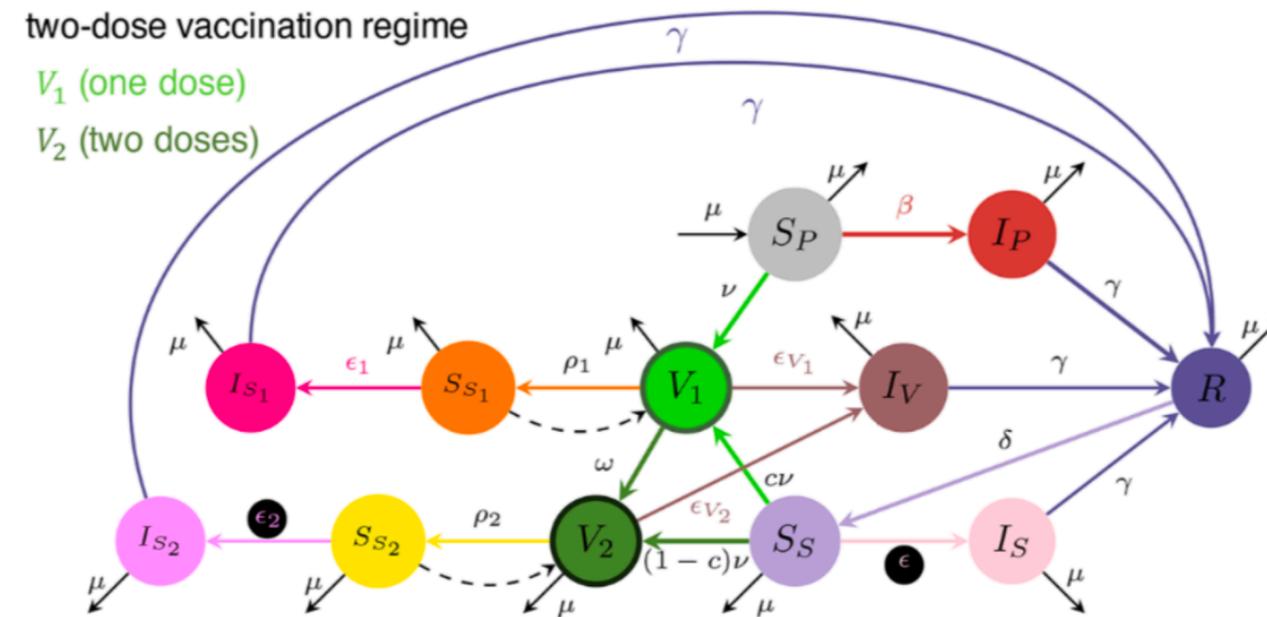
Selection for immune escape?



An intermediate model with vaccination



‘Susceptible-Infected-
Recovered’



‘Susceptible-Infected-
Recovered-Susceptible’

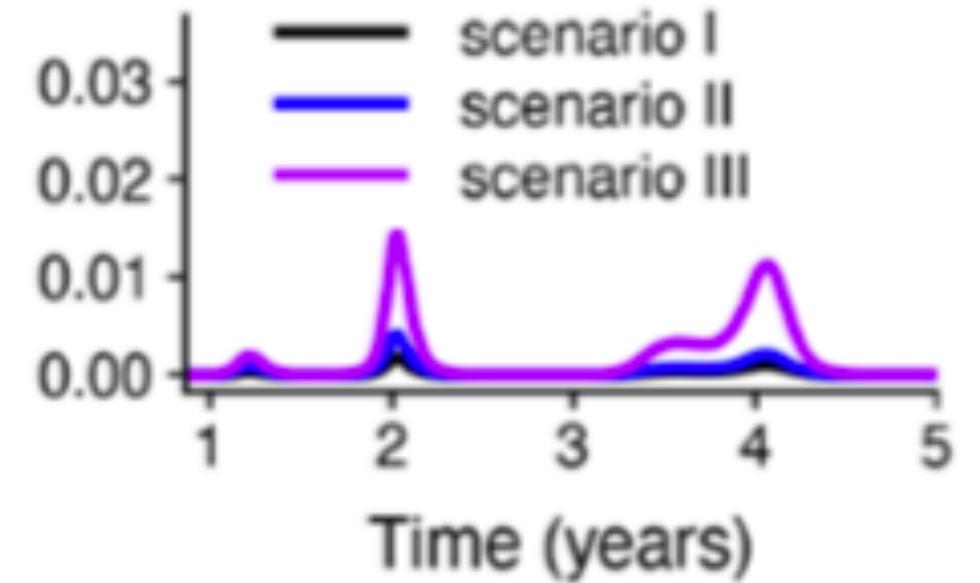
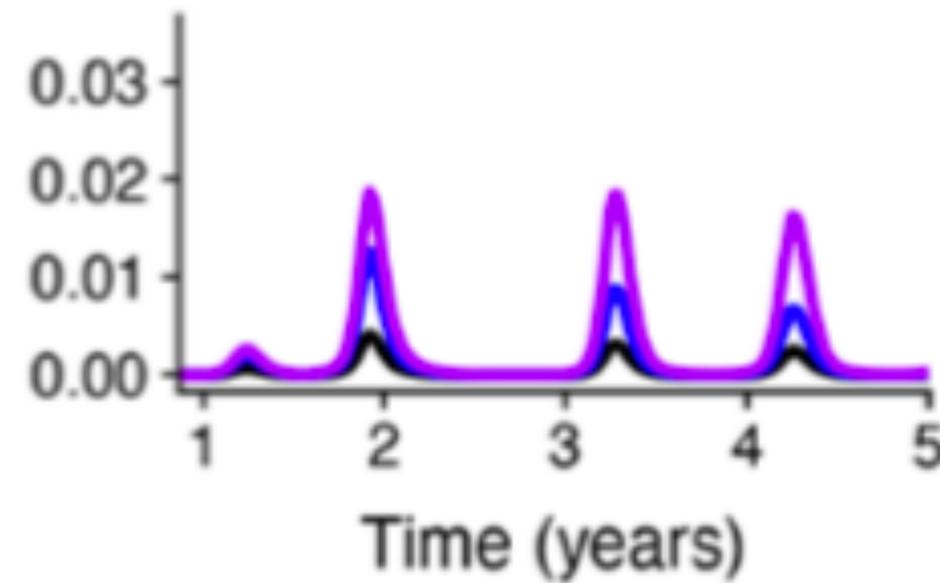
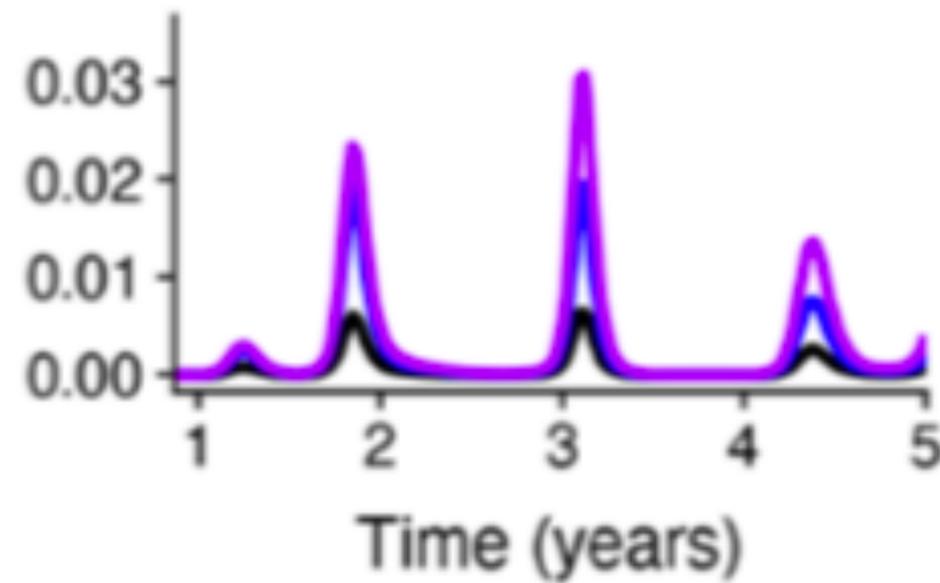
Relative rate of net adaptation



One dose strategy

24 week inter-dose period

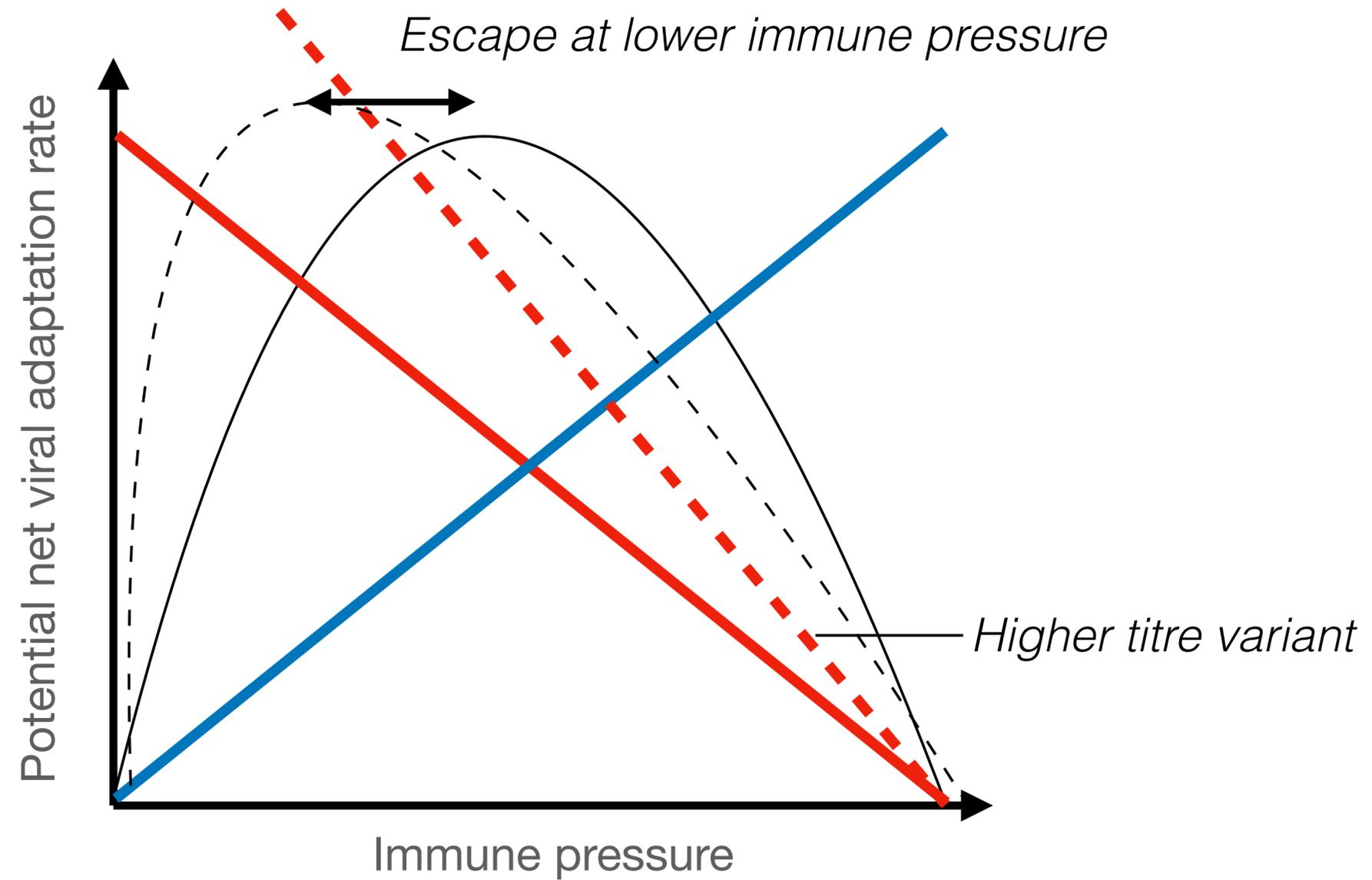
Recommended 2 dose



Selection for immune escape?

- **Burden and timing of SARS-CoV-2 infections** and potential for **viral adaptation** are shaped by **immune responses** following natural infection and one or two vaccine doses in the short and longer term
- A **one dose strategy may be good in short term** to increase the number of people immunized and reduce infections, but in the longer term the **recommended two doses should be given to mitigate the potential for antigenic evolution or later epidemics due to immune waning**
- **Vaccines must be distributed rapidly and equitably globally – antigenic evolution in one location will rapidly spread**

Selection for immune escape?



Getting Vaccines

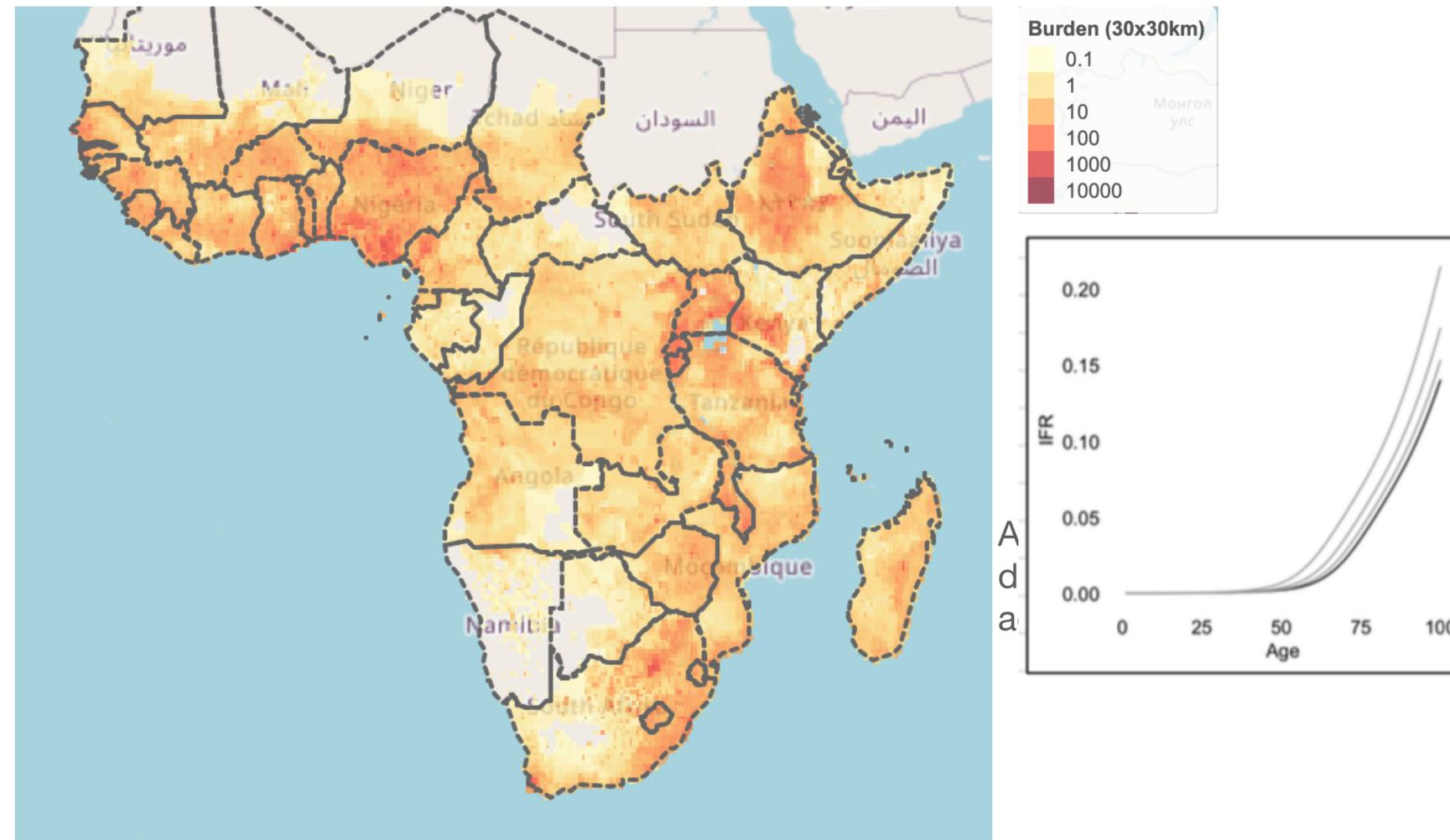
“Africa will need about **1.5 billion doses of vaccine**. (Its population is 1.2 billion, and most vaccine candidates require two doses.) The cost of the vaccine and of building systems and structures required for delivery is estimated at between **\$7 billion and \$10 billion, according to Africa CDC**. For comparison, the **2020 US PEPFAR budget was \$6.9 billion.**”

John N. Nkengasong (director of Africa CDC), Nicaise Ndembi (senior science adviser at Africa CDC), Akhona Tshangela (programme manager for mortality surveillance at Africa CDC), Tajudeen Raji (head of the division of public-health institutes and research at Africa CDC).



A volunteer nurse assesses a visitor to a health centre in Nairobi that trains the public on infection prevention.

Limits of surveillance



Reporting of **cases**, and even of **deaths** may be extremely low, yielding a very **incomplete picture of the state of the pandemic** in much of the world.



A Global Immunological Observatory

Data

Convenience samples
Longitudinal age serology

Methods

Laboratory techniques
Statistical approaches

Use of serological surveys to generate key insights into the changing global landscape of infectious disease



C Jessica E Metcalf, Jeremy Farrar, Felicity T Cutts, Nicole E Basta, Andrea L Graham, Justin Lessler, Neil M Ferguson, Donald S Burke, Bryan T Grenfell

SCIENCE FORUM

**A Global Immunological
Observatory to meet a time of
pandemics**

**MICHAEL J MINA^{†*}, C JESSICA E METCALF^{†*}, ADRIAN B MCDERMOTT,
DANIEL C DOUEK, JEREMY FARRAR AND BRYAN T GRENFELL**



Ian Miller

Thank you!

Within host dynamics: <https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1009105>

The next five years: <https://science.sciencemag.org/content/370/6518/811.abstract>

Selection for immune escape: <https://science.sciencemag.org/content/370/6518/811>

A Global Immunological Observatory: <https://elifesciences.org/articles/58989v1>

SARS-CoV-2 in SSA: <https://www.nature.com/articles/s41591-021-01234-8>

Mortality registration in Madagascar: <https://www.sciencedirect.com/science/article/pii/S1201971220324954>

Bryan Grenfell

Caroline Wagner

Chadi Saad-Roy

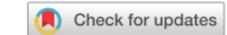


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PRINCETON
UNIVERSITY



Variation in SARS-CoV-2 outbreaks across sub-Saharan Africa

Benjamin L. Rice ^{1,2} , Akshaya Annapragada ³, Rachel E. Baker ^{1,4}, Marjolein Bruijning¹, Winfred Dotse-Gborgbortsii ⁵, Keitly Mensah ⁶, Ian F. Miller ¹, Nkengafac Villyen Motaze^{7,8}, Antso Raherinandrasana^{9,10}, Malavika Rajeev¹, Julio Rakotonirina^{9,10}, Tanjona Ramiadantsoa^{11,12,13}, Fidisoa Rasambainarivo^{1,14}, Weiyu Yu ¹⁵, Bryan T. Grenfell^{1,16}, Andrew J. Tatem ⁵ and C. Jessica E. Metcalf ^{1,16}



Benjamin Rice



Rachel Baker



Marjolein
Bruijning



Keitly Mensah



Ian Miller



Villyen Motaze



Antso
Raherinandrasana



Malavika Rajeev



Tanjona
Ramiadantsoa



Fidisoa
Rasambainarivo