

# **International vaccination**

# **Potential impacts on viral evolution**

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# Future variants of concern

Transmissibility

Severity

Immune escape

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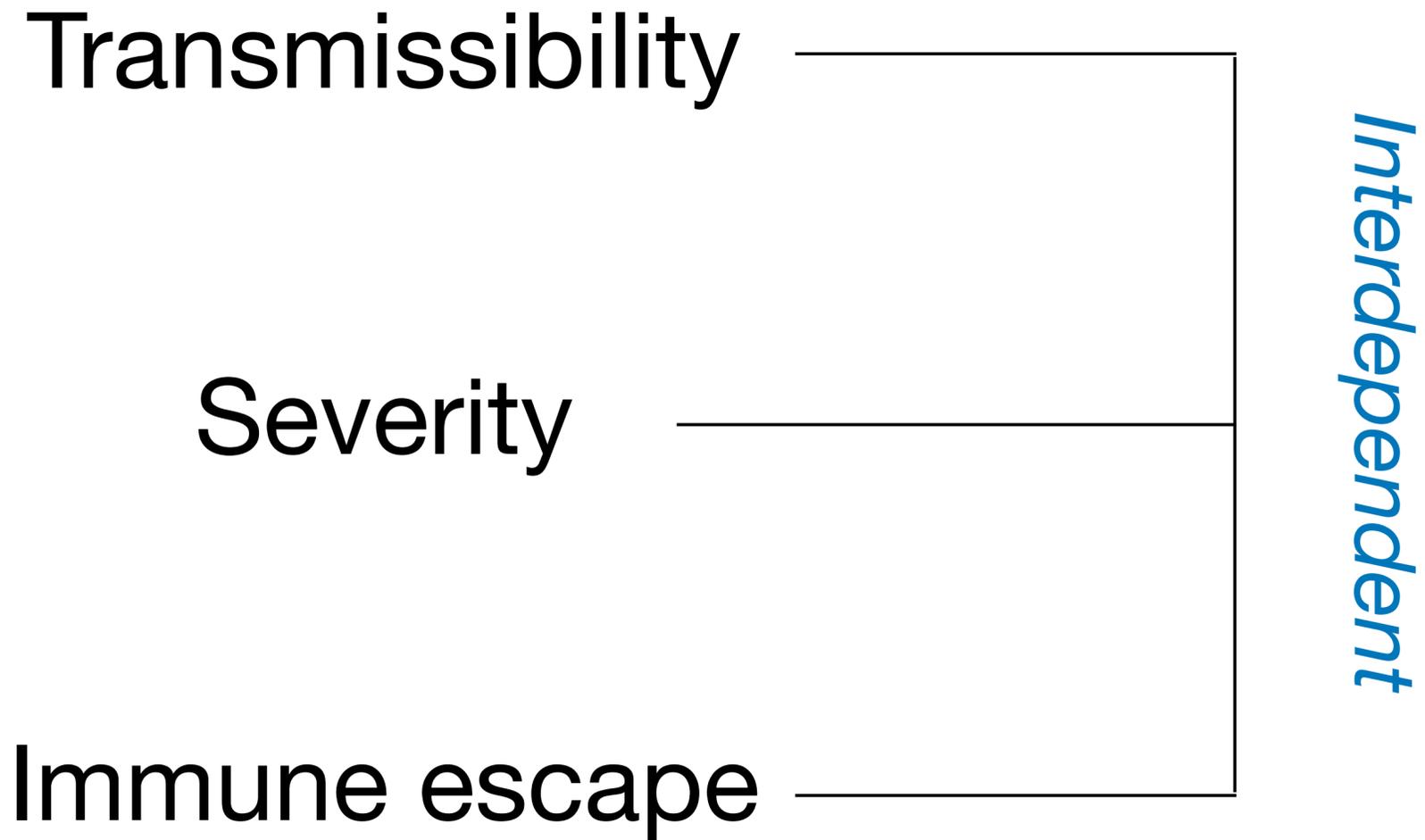
# The devil in the details

Transmissibility

Severity

Immune escape

*Interdependent*

A diagram illustrating the interdependence of three factors: Transmissibility, Severity, and Immune escape. The terms are arranged vertically from top to bottom. A vertical line on the right side connects the three terms, with the word "Interdependent" written vertically along it. Horizontal lines extend from each term to the vertical line, indicating their connection to the overall concept.

# Variants of Concern in the UK

A variant first appears through **mutation** in the unknown source location

The variant **establishes transmission** in that location

The variant is **imported** to the UK

The variant **establishes transmission** in the UK.

# The big picture

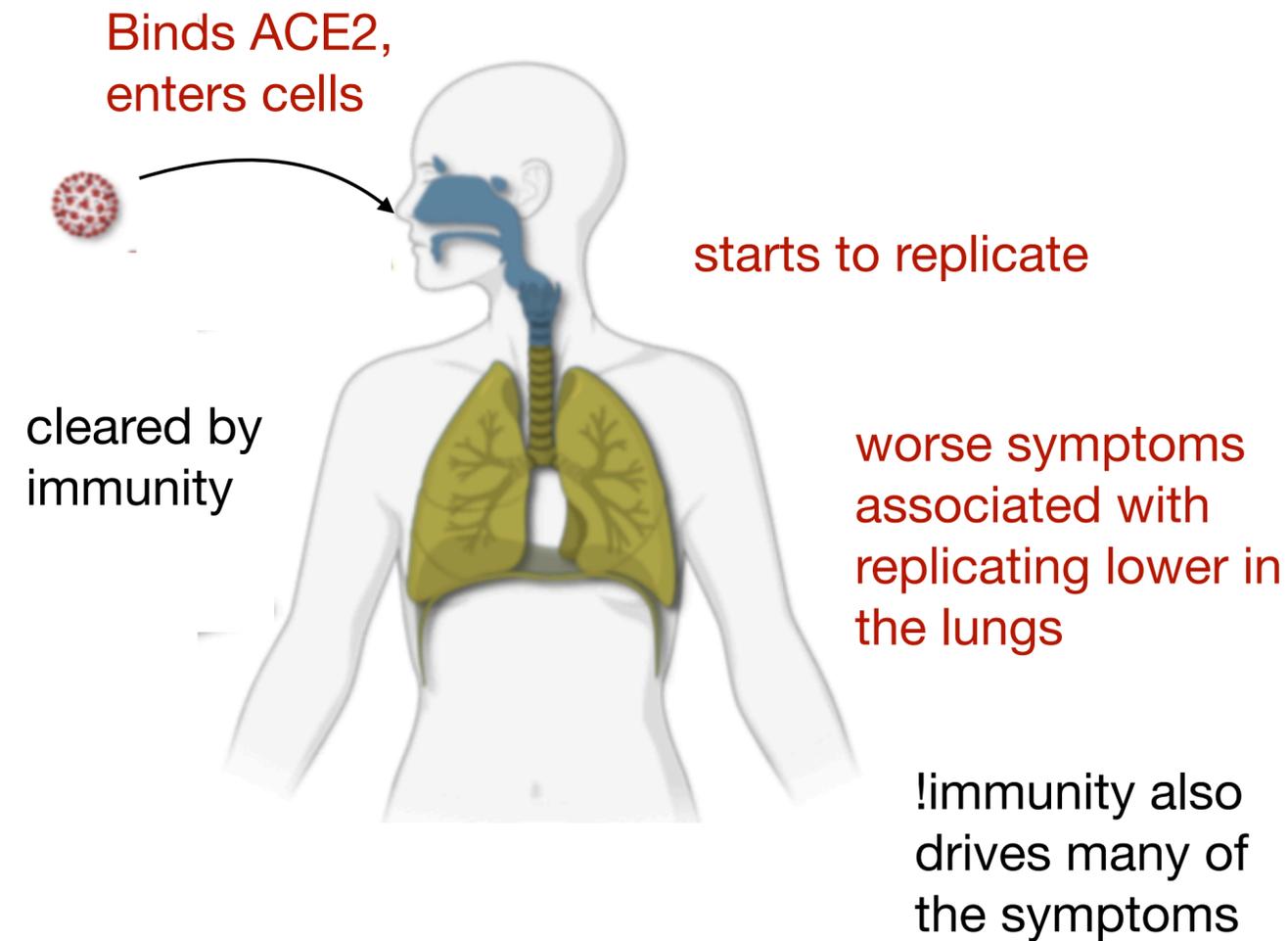
More **circulation** globally means more opportunity for variants to emerge

Circumstances **most propitious** for spread of particular variants are very hard to predict

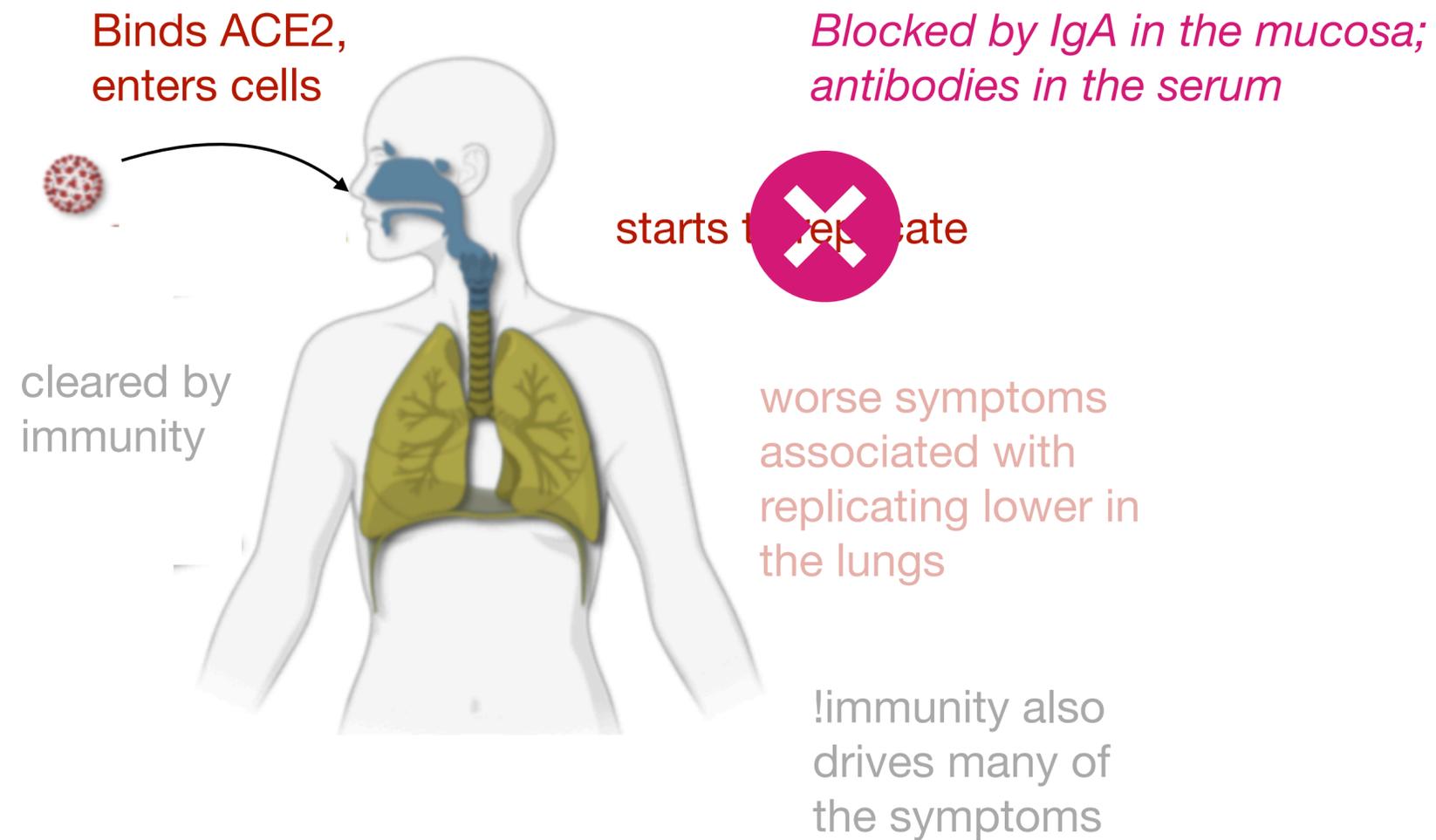
**The spread of immune escape**

**The future of severity**

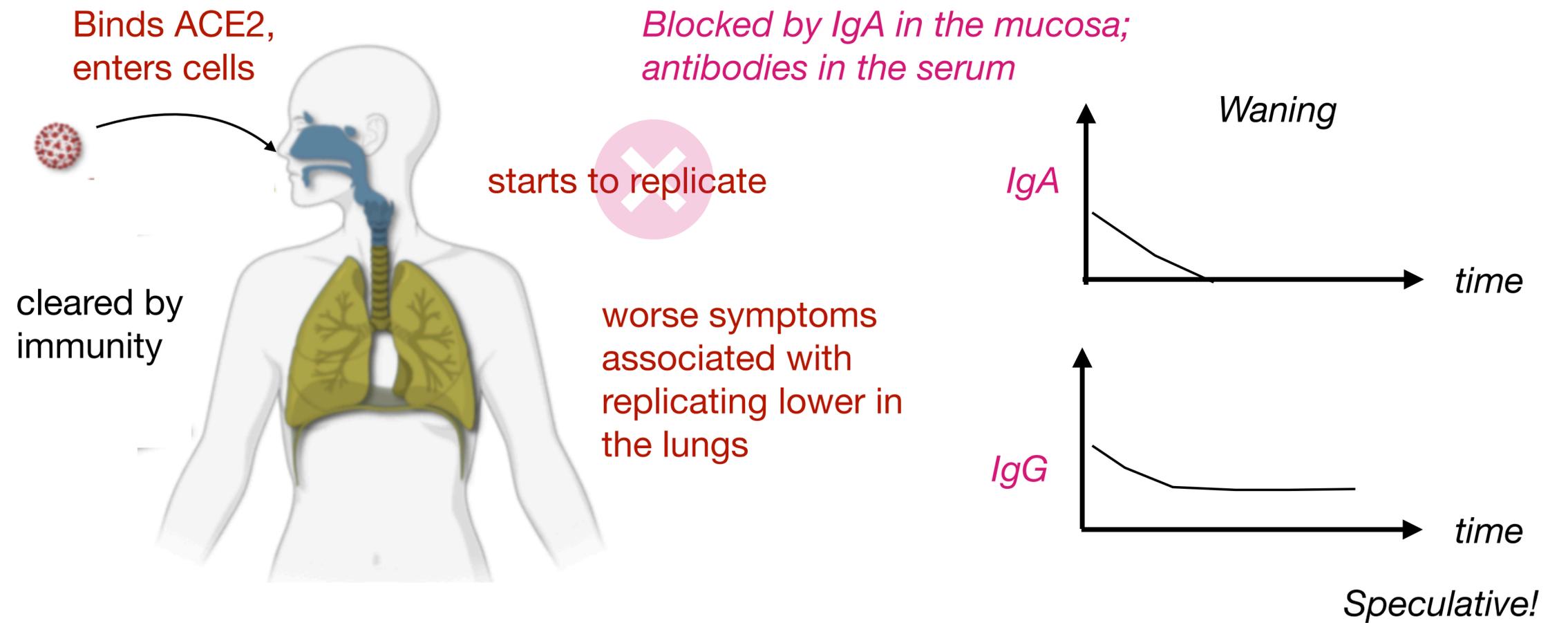
# The spread of immune escape



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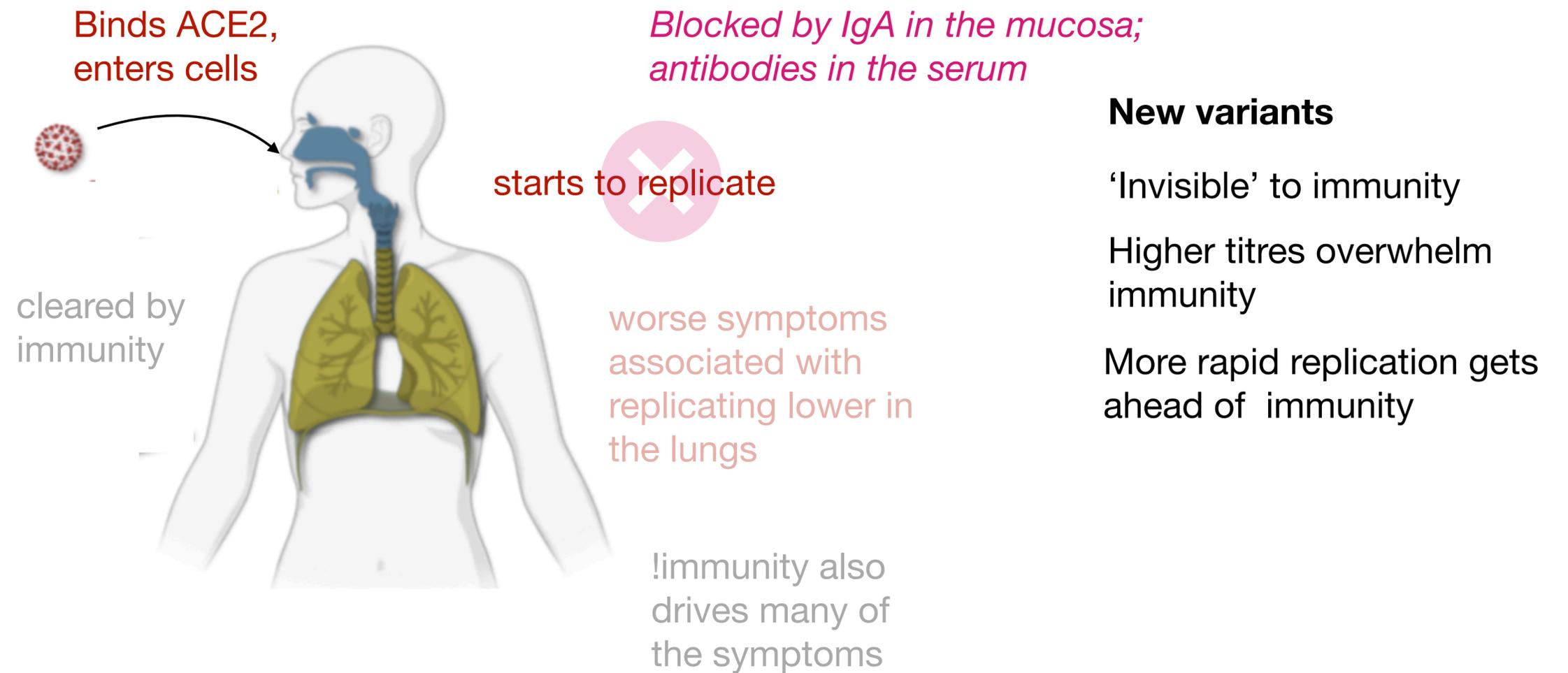


# The spread of immune escape



**Host characteristics enable 'breakthroughs'**

# The spread of immune escape



**Viral characteristics enable 'breakthroughs'**

# The spread of immune escape



**Population context? Two key parameters:**

**$\alpha$ :** relative transmission rate of secondarily-infected individuals, compared to that following infection of naive susceptibles

**$\epsilon$ :** the relative susceptibility to breakthrough infection

# The spread of immune escape



**Population context? Two key parameters:**

**$\alpha$ :** relative transmission rate of secondarily-infected individuals, compared to that following infection of naive susceptibles

**$\epsilon$ :** the relative susceptibility to breakthrough infection

What happens in a country at **herd immunity** where an **immune escape variant** is introduced?

# The spread of immune escape



the relative susceptibility to  
breakthrough infection

$$\frac{\beta S(t)}{\gamma} + \frac{\epsilon \beta V(t)}{\gamma} > 1$$

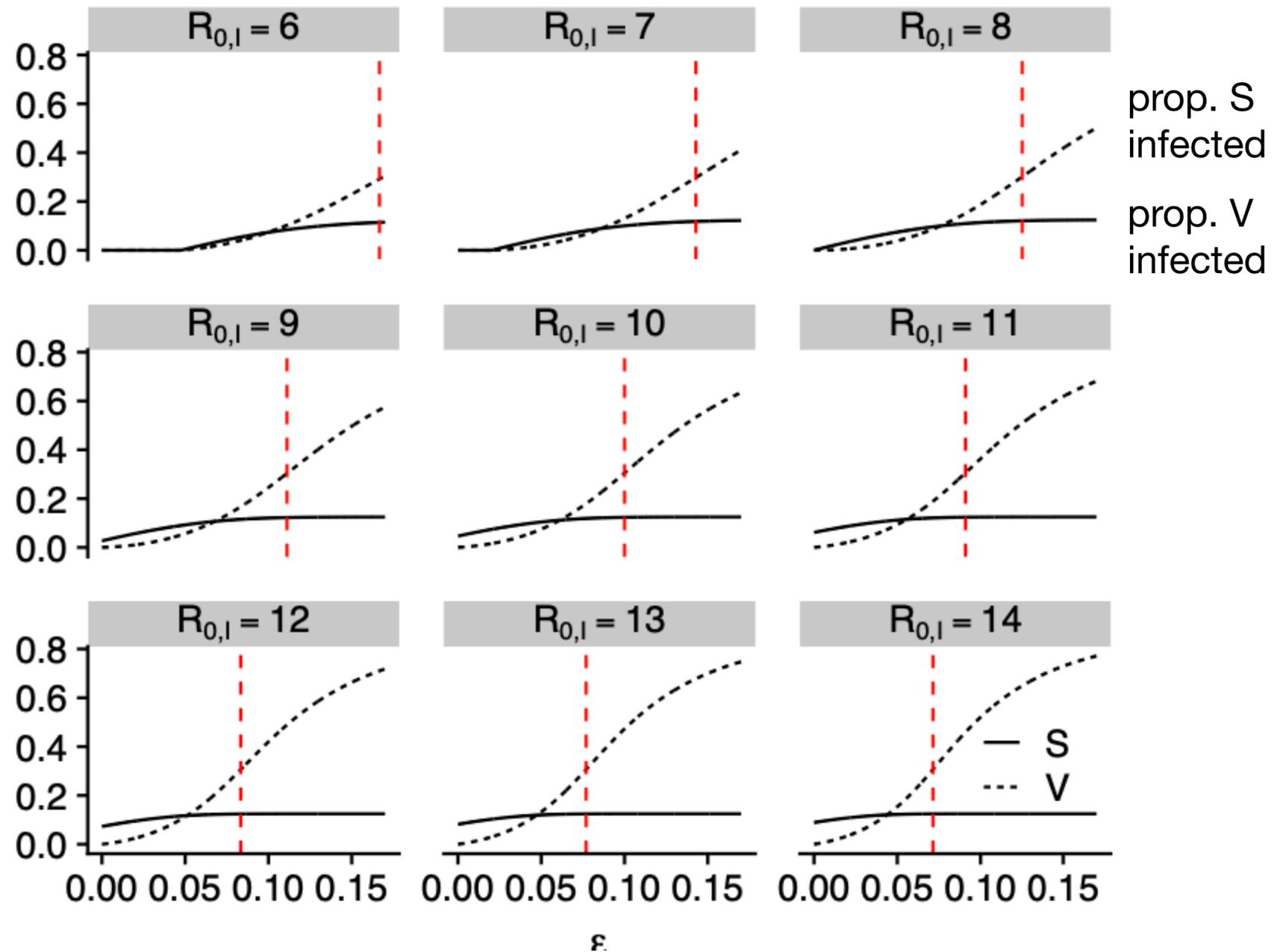
# The spread of immune escape



value of  $\epsilon$  for  
which  $\epsilon R_{0,I} = 1$

the relative susceptibility to  
breakthrough infection

$$\frac{\beta S(t)}{\gamma} + \frac{\epsilon \beta V(t)}{\gamma} > 1$$



# The spread of immune escape

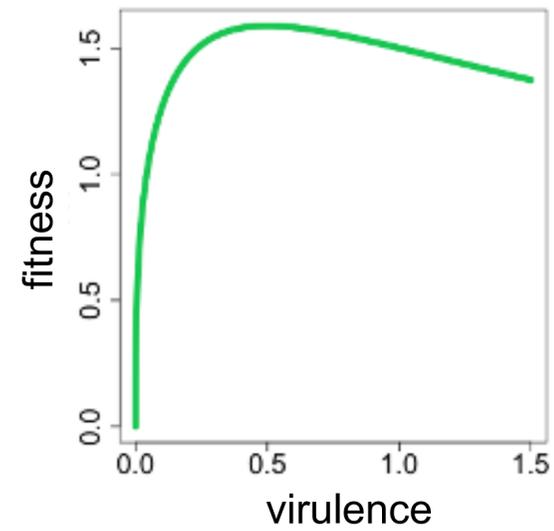
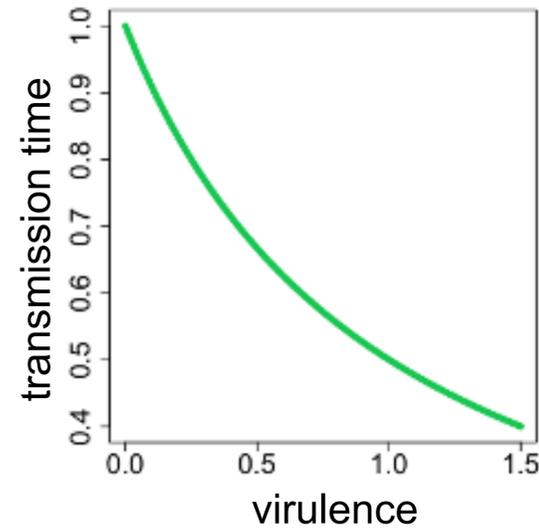
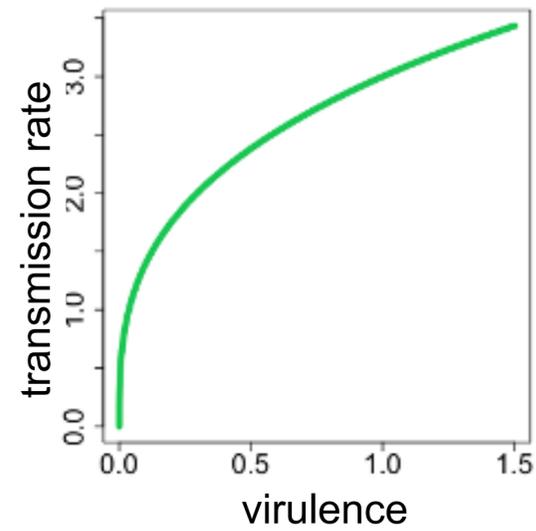


The combination of **infection of remaining susceptibles** and **breakthrough infections of vaccinees** can promote infection of invading variants, even when vaccination rates are high and onward transmission from vaccinees relatively weak.

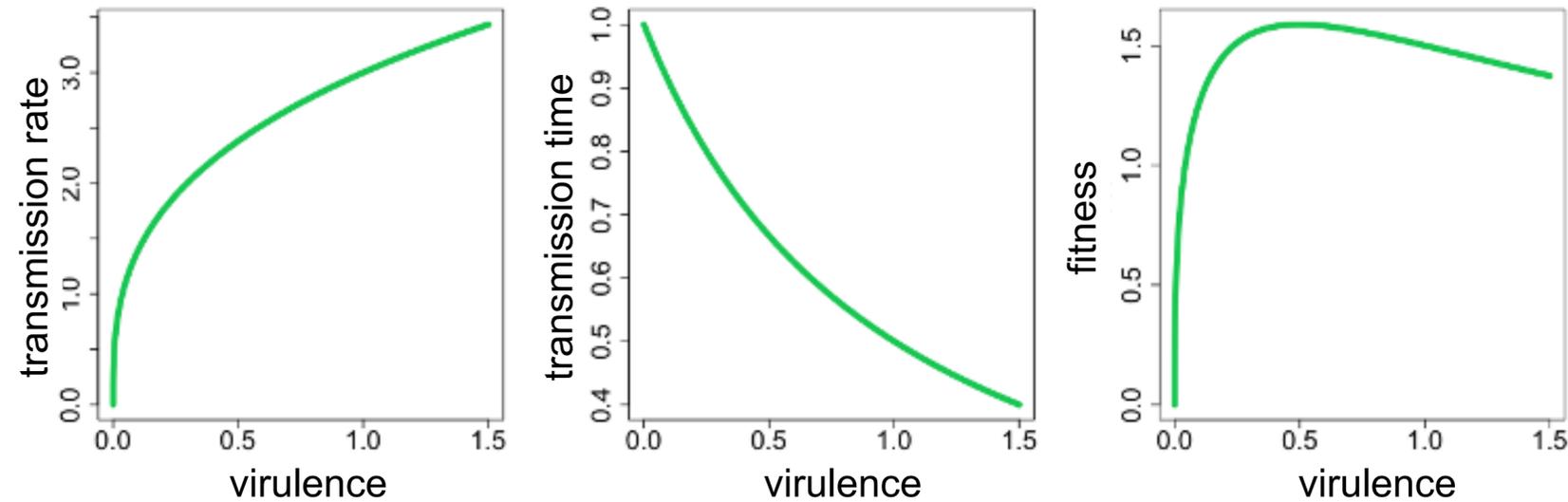
**The spread of immune escape**

**The future of severity**

# The future of severity

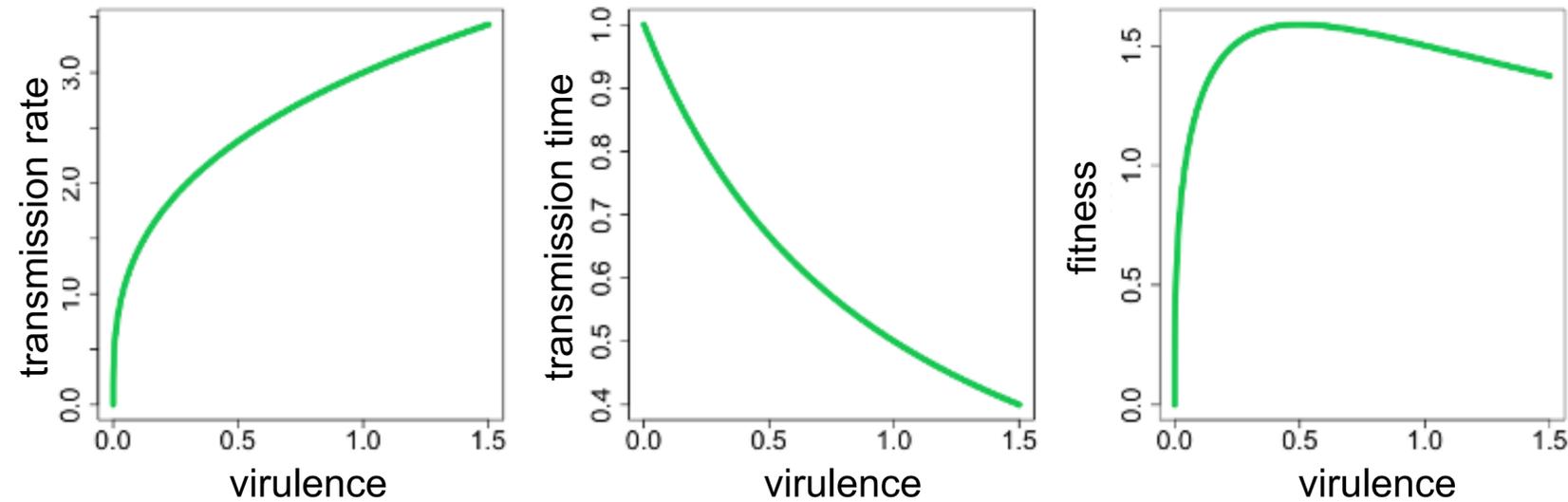


# The future of severity



Is the evolution of increased transmission possible?  
Is increased transmission linked to increased virulence?

# The future of severity



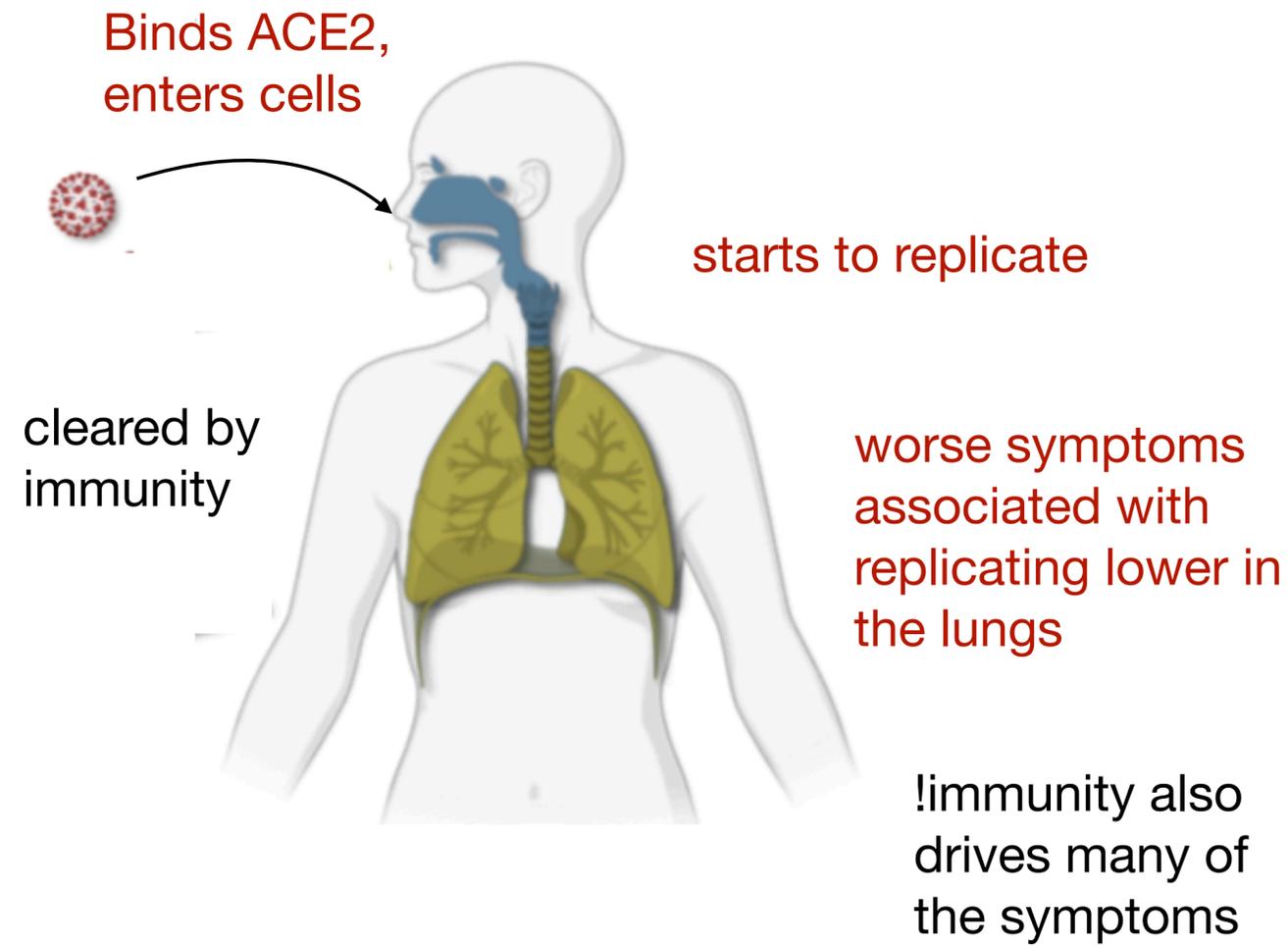
Is the evolution of increased transmission possible?

**Yes**

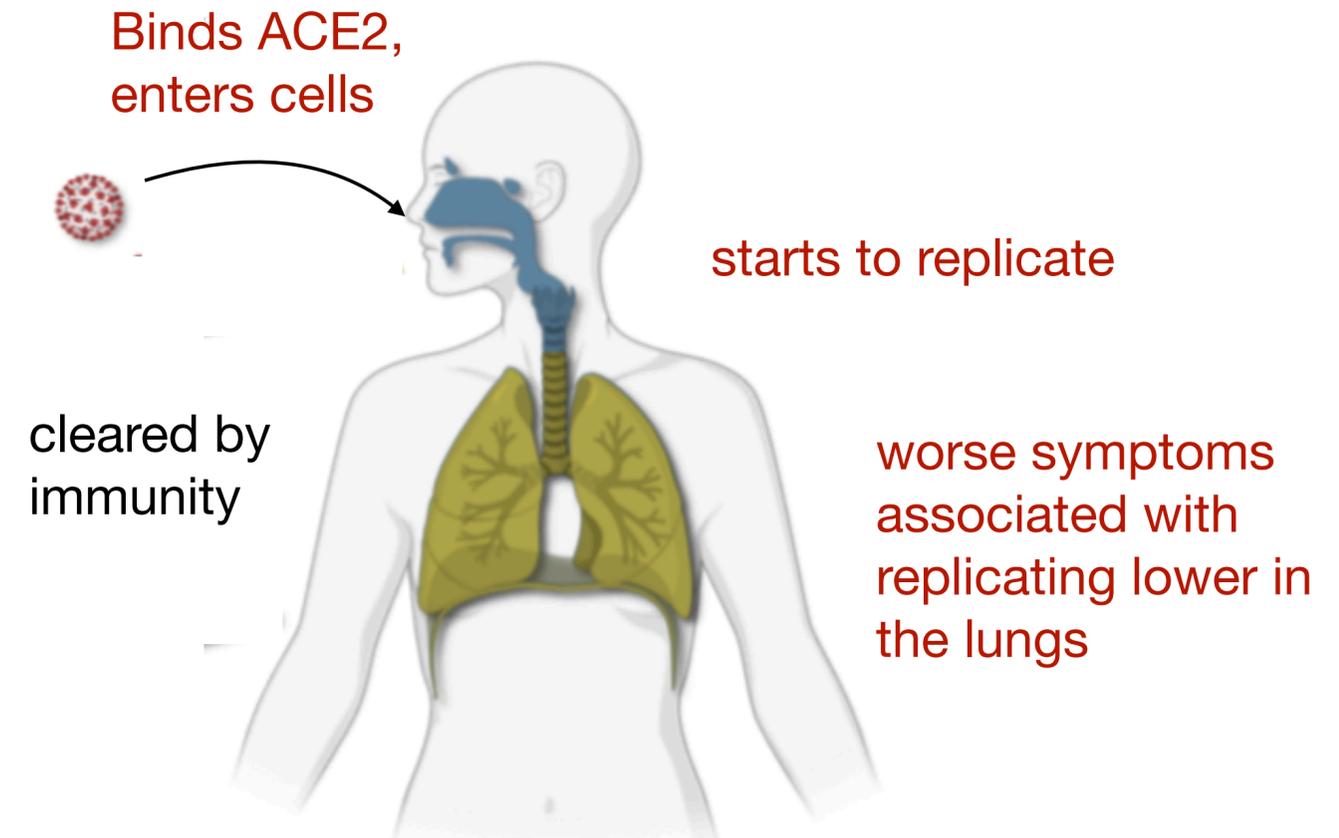
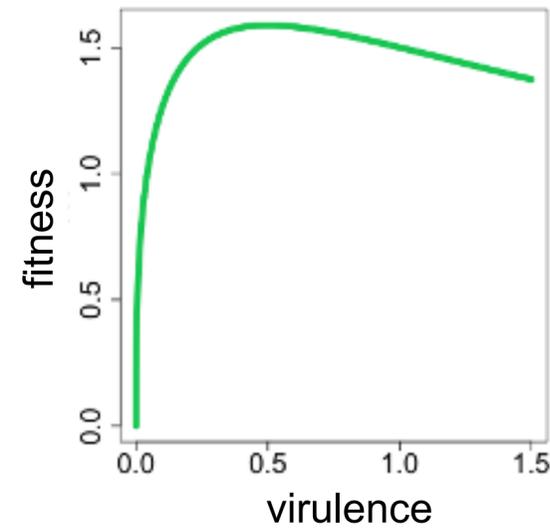
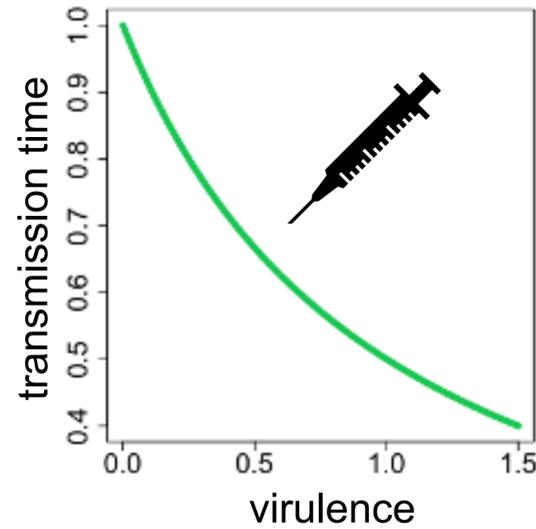
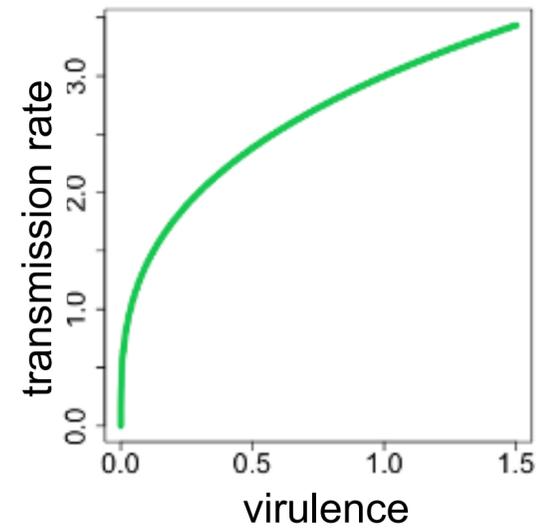
Is increased transmission linked to increased virulence?

***Sometimes***

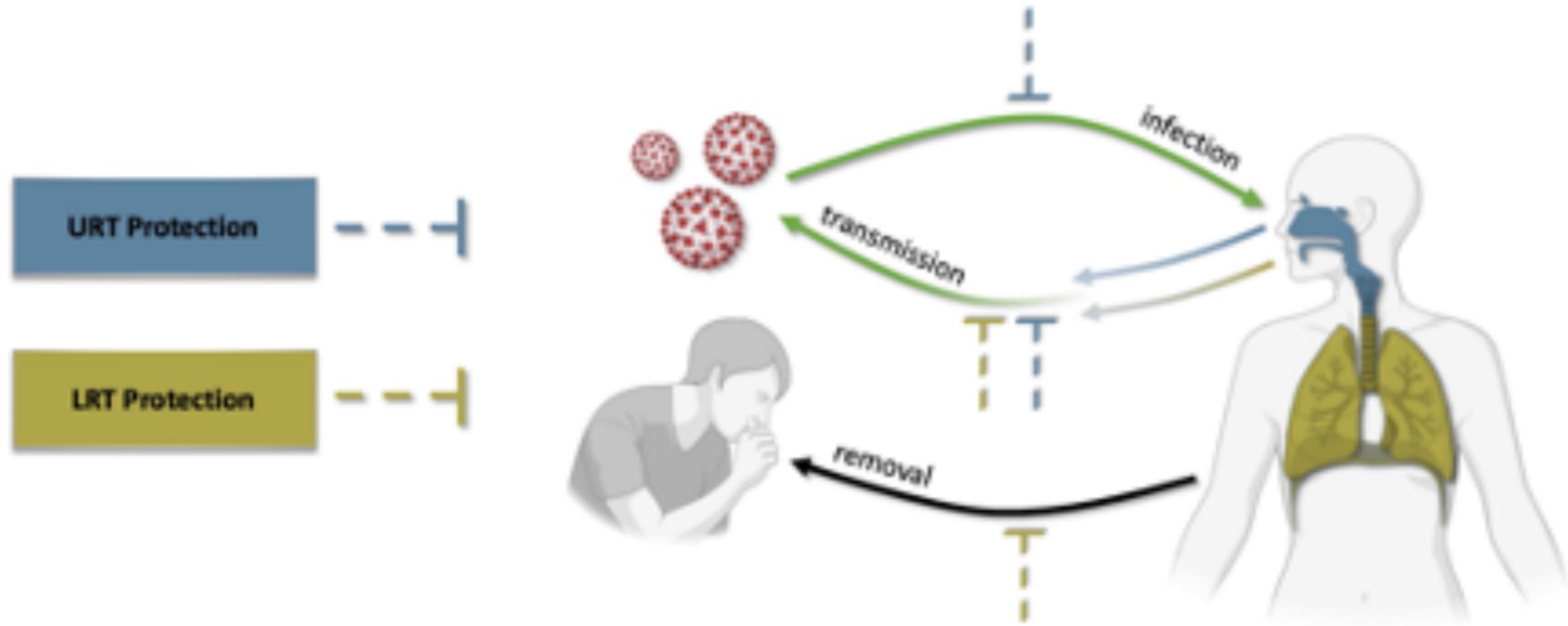
# The future of severity



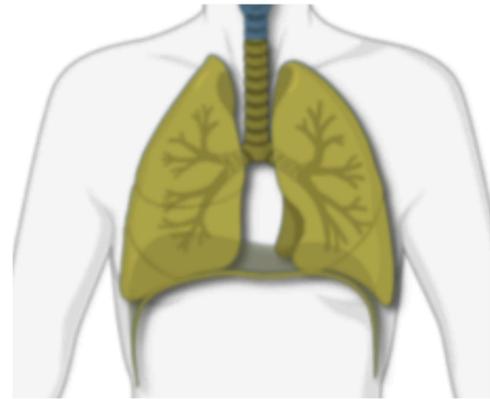
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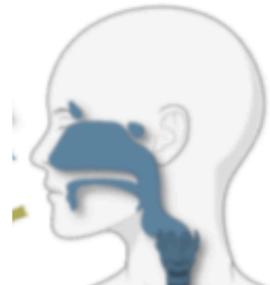
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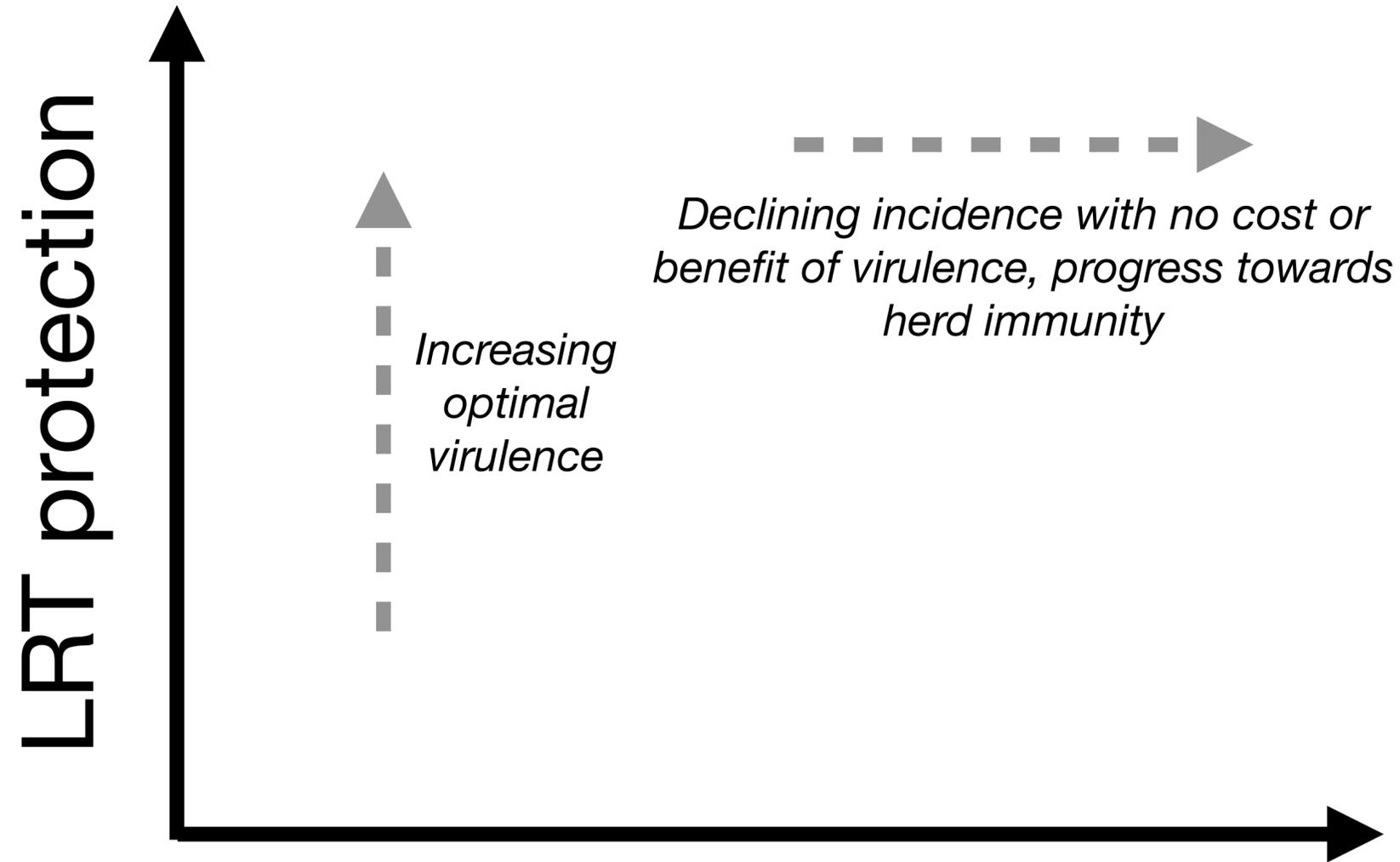
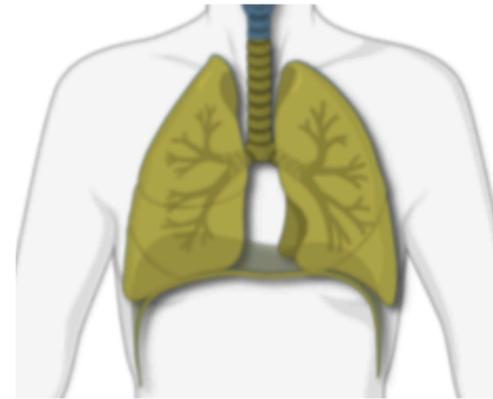
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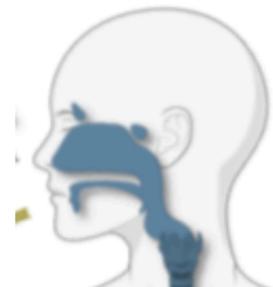
URT protection



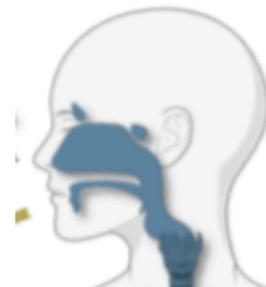
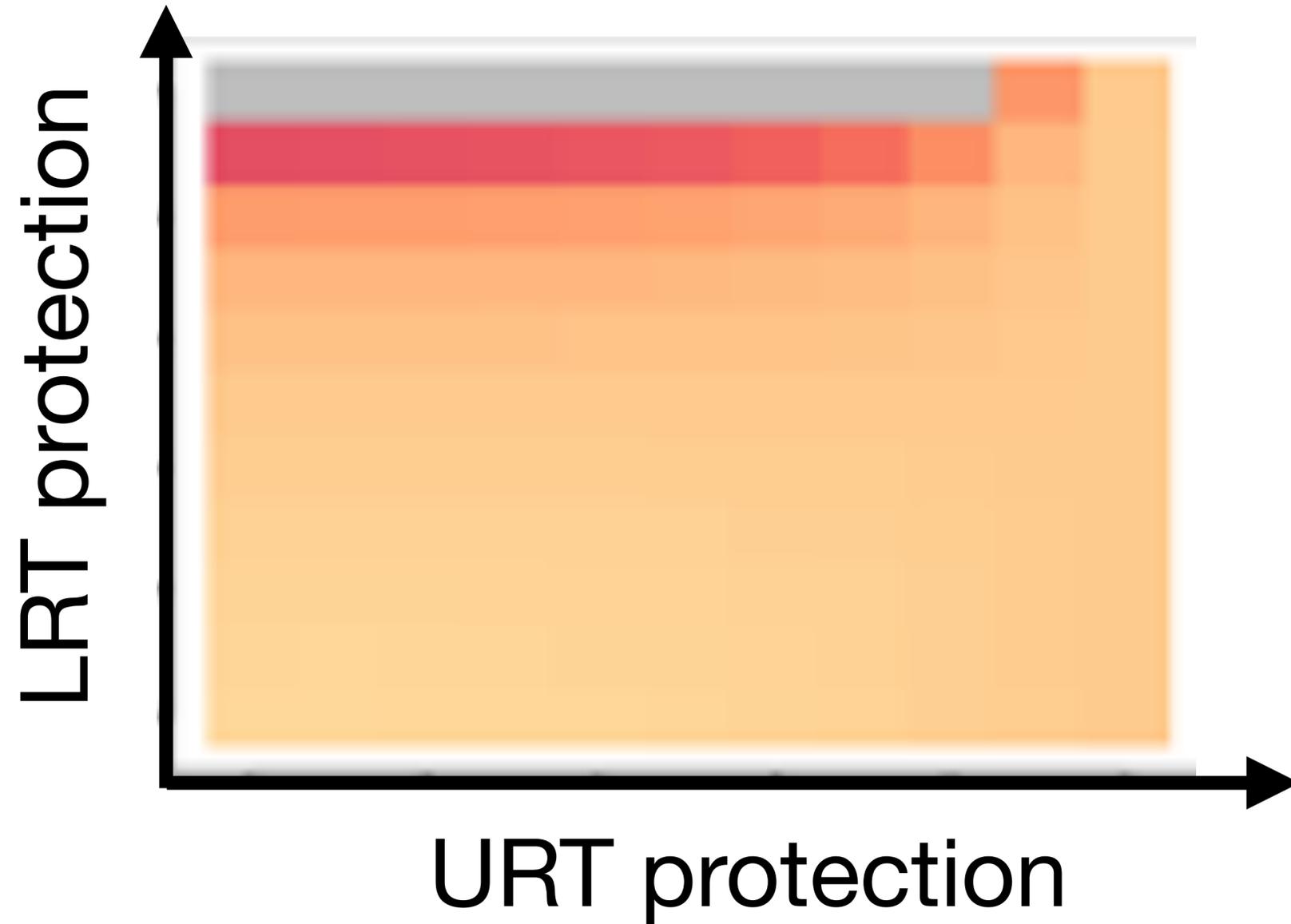
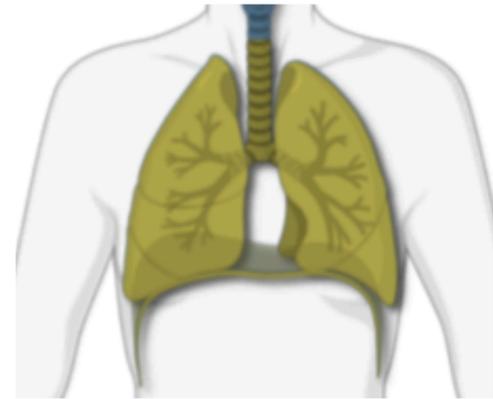
# The future of severity



URT protection



# The future of severity



# The future of severity

If severity and transmission are linked, under pessimistic assumptions around this, possible futures are:

1. Unbounded selection for increased virulence
2. An intermediate optimal of increased virulence
3. Herd immunity blocks/reduces evolutionary potential

**The spread of immune escape**

**The future of severity**

# The big picture

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**Thank you!**

Samuel Clifford, Rosalind Eggo, Julia Gog,  
Bryan Grenfell, Deirdre Hollingsworth,  
Petra Klepac, Billy Quilty, Robin Thompson

# The future of severity

