

# **Asymptomatic infection fuels spread of more infectious SARS-CoV-2 variants**

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## **Sars-CoV-2 has a highly 'insidious' strategy**

Sars-CoV-2 shed and transmitted by asymptotically infected people



suboptimal anti-S Abs

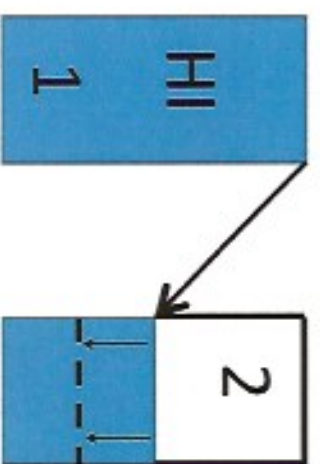
Promote fitness & propagation of immune escape variants capable of overcoming suboptimal immune pressure on spike (S) protein



This will breed 'more infectious' variants

## Natural CoV pandemic: Infection pressure and occurrence of 2<sup>nd</sup> wave of disease

- The level of infection pressure determines the time length between the first and second wave of disease
- After 1<sup>st</sup> wave, the infection pressure will steadily increase and lead to 2<sup>nd</sup> wave of disease in an important part of naturally protected people (in blue)



Erosion of natural immunity in large part of AI population +  
infection pressure rapidly grows at high level  
→ 2<sup>nd</sup> wave of (severe) disease in younger age groups

→ Erosion of natural immunity in smaller, additional part  
of AI population + infection pressure slowly grows at low  
level → enabling (local) viral replication on background  
of suboptimal  $\alpha$ S-Abs → 'more infectious' variants (plateau)

HI: Herd immunity  
AI: Asymptomatically infected

Infection pressure will ultimately increase till 'more infectious' variants  
break through innate immune barrier of those who asymptotically  
resisted 2<sup>nd</sup> wave → delayed 3<sup>rd</sup> wave of (severe) disease in

Youngsters

## Infection pressure and occurrence of 2<sup>nd</sup> wave of disease (cont'nd)

- Stringent infection prevention measures will delay 2<sup>nd</sup> wave of disease in previously protected subjects while promoting breeding of infectious variants
- Introduction of highly infectious variants will expedite this process
- Mass vaccination on the background of 'more infectious' variants will enhance immune pressure exerted on their infectiousness, regardless of viral infection pressure\* (due to anti-RBD Abs)

Due to suboptimal immunity in an important part of vaccinees (mass vaccination!), viral variants will increasingly select escape mutations within RBD. As those will have a competitive advantage, this will promote breeding of variants that are even more infectious and finally lead to vaccine-resistant variants



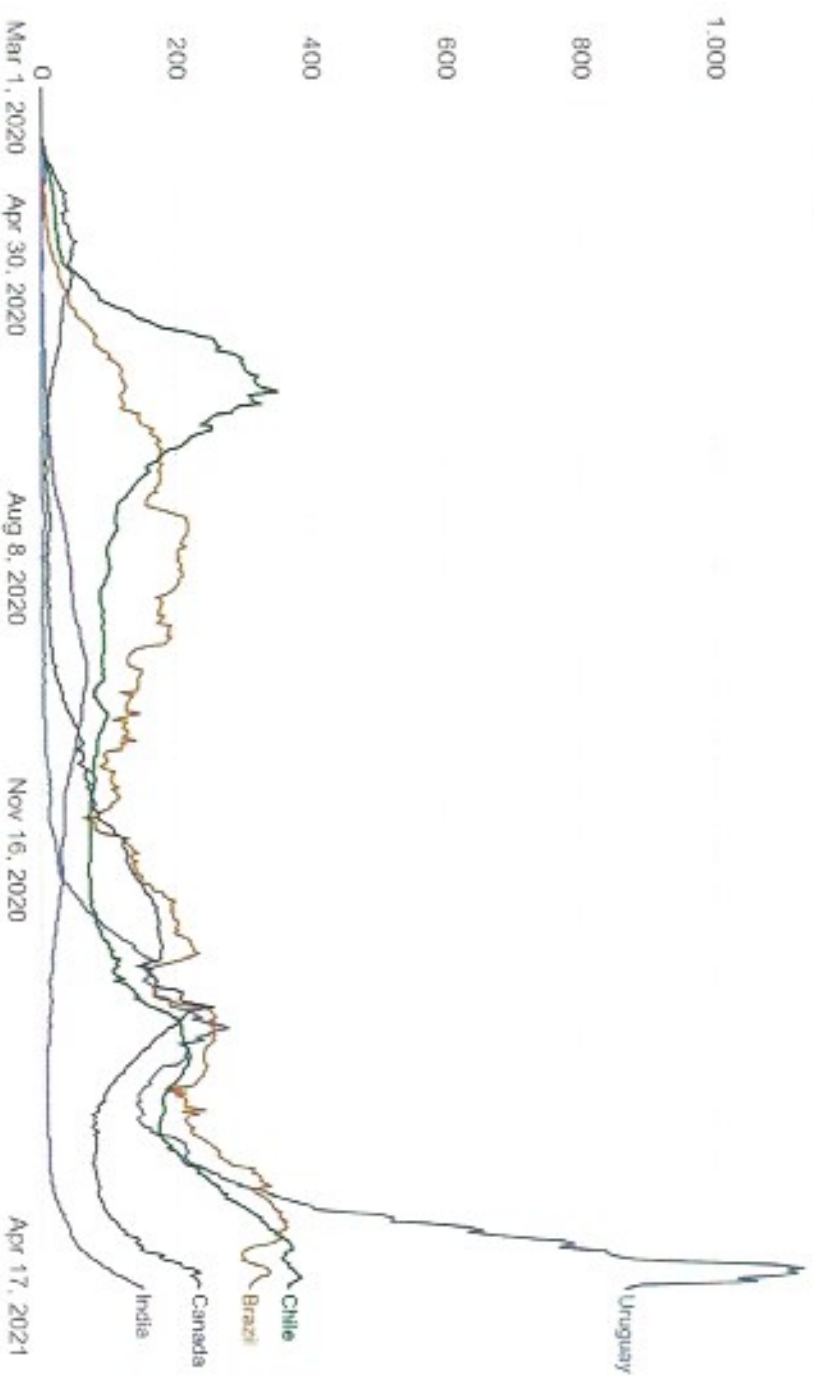
RBD: receptor-binding domain

\* except if full lock-down

# Starting mass vaccination on backgrounds of different infectivity

## Daily new confirmed COVID-19 cases per million people

Shown is the rolling 7-day average. The number of confirmed cases is lower than the number of actual cases; the main reason for that is limited testing.



Source: Johns Hopkins University CSSE COVID-19 Data

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## Efficiency of conventional vaccines to control a pandemic is *conditional*

- Pandemic: NEW virus; innate herd immunity only
- Mass vaccination with conventional (i.e., non-sterilizing vaccines) *could control and even eradicate infection* IF and only IF:
  - not highly mutable virus
  - no asymptomatic/ animal reservoir

Conditions NOT fulfilled in case of SARS-CoV-2:

- highly mutable virus
- $\exists$  asymptomatic carriers  $\rightarrow$  'more infectious' variants  
(especially if more infection-prevention measures)

**Mass vaccination of youngsters is going to result in enhanced morbidity and mortality rates in this age group!**

