The durability of vaccine-mediated immunity against infection by SARS-CoV-2 and the frequency of mRNA booster vaccination

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INTRODUCTION

Regarding the COVID-19 pandemic, several of the most pressing questions remaining are those that require decades of empirical research and data collection to answer.

1. If I have already had COVID-19, will I get it again?
2. If I am fully vaccinated, will I get it again?
3. Will I need to get COVID-19 boosters forever?

We have previously demonstrated that the use of comparative evolutionary analyses can provide predictive answers to these questions.

METHODS

We incorporated previous decades of antibody level and reinfection data collected and published by Edridge et al. 2020 for SARS-CoV-2's closest endemic relatives:

1. HCoV-229E
2. HCoV-NL63
3. HCoV-OC43

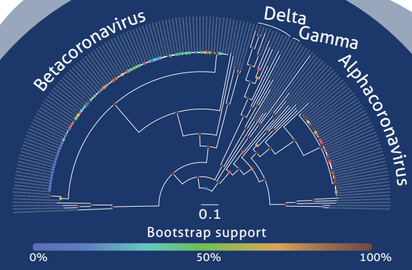
In addition to waning antibody data for MERS and SARS-CoV-1.

We extended our models relative to natural infection to provide predictions for four of the most popular vaccines in the world:

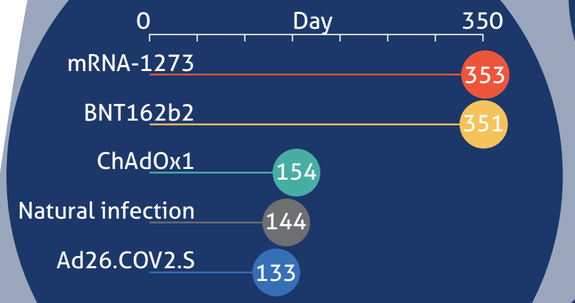
1. Moderna
2. Pfizer-BioNtech
3. Oxford-Astrazeneca
4. J&J /Janssen

Additionally, we projected the cumulative probability of breakthrough infection over the next 6 years for mRNA vaccines given different boosting schedules.

To extend our natural infection model to the other four vaccines, we first needed to determine what the peak antibody response was for each vaccine relative to natural infection



Using the waning data from SARS-CoV-2's relatives, as well as the short term SARS-CoV-2 antibody waning data published just months after the pandemic began, we performed ancestral and descendent state reconstruction on the coronavirus phylogeny and were able to impute the durability of immunity against SARS-CoV-2 over time.



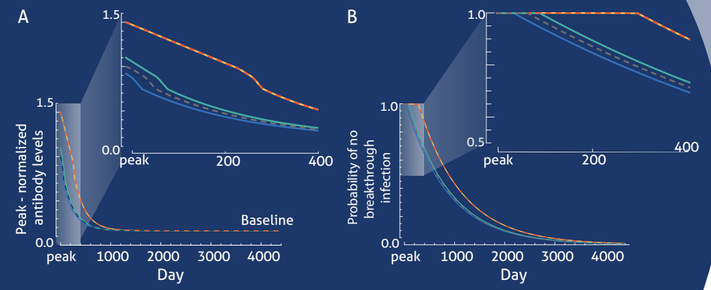
The mean time by which there is a 5% cumulative risk of breakthrough infection for mRNA vaccines is more than twice that of natural infection or viral vector vaccines.

Table 1. Peak antibody levels subsequent to vaccination and natural infection

Stimulus	Subjects (avg.)	IgG antibody	Day (avg)*	Peak (avg)†,‡	Studies
mRNA-1273	56	anti-RBD/S/S1	26	1.50044	6
BNT161b2	374	anti-RBD/S/S1	23	1.50004	14
Natural infection	620	anti-S/S1	40	1.00000‡	4
ChAdOx1	62	anti-S/S1	25	1.09977	4
Ad26.COV2.S	34	anti-RBD/S	56	0.91936	4

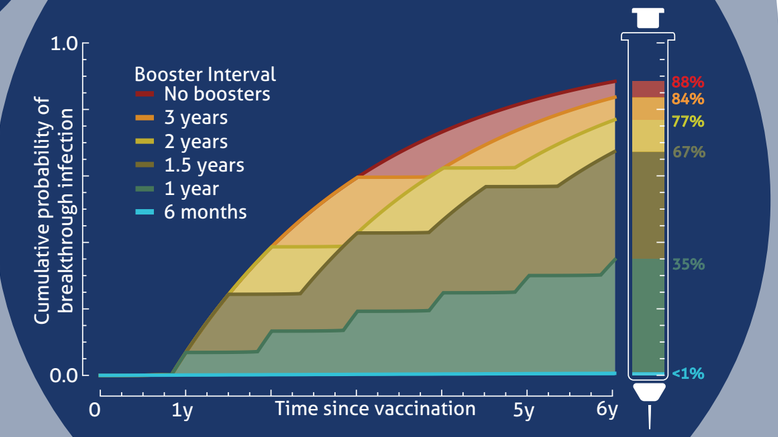
RESULTS

Peak antibody levels for mRNA vaccines were higher than natural infection, while viral vector vaccines were similar to that of natural infection



Breakthrough infections in those vaccinated by either mRNA vaccine were predicted to typically occur after a longer period than natural reinfections or breakthrough infections following either viral vector vaccination

Shorter intervals between booster administration result in the lowest cumulative probability of breakthrough infection over 6 years



CONCLUSIONS

mRNA vaccines provide immunity over a longer duration compared to natural infection or viral vector vaccines.

Delayed or infrequent boosting will substantially increase cumulative probability of SARS-CoV-2 breakthrough infection.

Population-wide booster vaccination—updated to the predominant variant—can forestall and potentially eliminate COVID-19.

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