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This supplemental material has been provided by the authors to give readers additional information about their work.
eMethods

Model structure
We extended our previous agent-based model of COVID-19 transmission and vaccination \(^1,2\) to include B.1.1.7 (Alpha), P.1 (Gamma) and B.1.617.2 (Delta) variants of SARS-CoV-2 with different transmissibilities in addition to the original pandemic strain. The model implemented the natural history of disease with epidemiological classes for susceptible; exposed and infected (not yet infectious); asymptomatic (and infectious); pre-symptomatic (and infectious); symptomatic (and infectious) with either mild or severe illness; recovered; and dead. The population was stratified into six age groups of 0 to 4, 5 to 19, 20 to 49, 50 to 64, 65 to 79, and 80+ years and incorporated age-specific risk of hospitalizations and deaths, contact patterns, and a two-dose vaccination rollout. Daily contacts between individuals were sampled from a negative-binomial distribution parameterized (eTable 1) using empirical data on pre-pandemic and pandemic-era interactions \(^3,4\).

Transmissibility
Risk of infection for susceptible individuals depended probabilistically on their interaction with infectious individuals in the pre-symptomatic, symptomatic, or asymptomatic stages of infection. The transmission probability of the original strain of SARS-CoV-2 was calibrated by fitting the model to case incidence data per 100,000 population in the entire US from October 1, 2020, to June 30, 2021.\(^5\) We chose October 1 as the starting point for our calibration and simulations because it was a time of a relatively low incidence preceding the fall/winter wave in the US. The calibration (in the presence of only the original strain of SARS-CoV-2) resulted in a transmission probability of 0.109. This transmission probability corresponds to an effective reproduction number of 1.17 in early October 2020 \(^6\), which accounted for the effect of non-pharmaceutical interventions (NPIs) in simulated scenarios. We then introduced the Alpha variant on December 1, 2020 (12 days prior to the start of vaccination in the US) \(^7\) with a 50% higher transmissibility compared to the original strain \(^8–10\). We introduced the Gamma variant on January 5 \(^11\) and the Delta variant (B.1.617.2) in the model on March 13, 2021 \(^12\). The transmissibility of Gamma was 60% higher compared to the original strain \(^13\), while the transmissibility of the Delta variant was set as 30% higher than the Alpha variant \(^14\).

Disease dynamics
We parameterized the infectivity of asymptomatic, mild symptomatic, and severe symptomatic individuals to be 26%, 44%, and 89% relative to the pre-symptomatic stage \(^15–17\). We assumed that these relative infectivities remained the same for all variants in the model. The incubation period was sampled from a log-normal distribution with a mean of 5.2 days \(^18\), and parameters of 1.434 (shape) and 0.661 (scale). An age-dependent proportion of infected individuals progressed to a pre-symptomatic stage with a mean duration of 2.3 days, sampled from a Gamma distribution with parameters of 1.058 (shape) and 2.17 (scale) \(^16,19\). Pre-symptomatic cases developed symptomatic disease with a mean infectious period of 3.2 days, which was also sampled from a Gamma distribution with parameters of 2.77 (shape) and 1.1563 (scale) \(^20,21\). The remaining proportion of infected individuals experienced asymptomatic infection until recovery, with a mean infectious period of 5 days sampled from a Gamma distribution with parameters of 5 (shape) and 1 (scale) \(^20,21\).

Recent studies indicate that antibodies from prior infection with other variants of SARS-CoV-2 may have reduced neutralizing activity against Gamma and Delta \(^22–25\). We therefore assumed that both the Gamma and Delta variants evade naturally acquired immunity by an average of
21% (95% CI: 11-36%)\textsuperscript{26,27}. This evasion rate was implemented as a reduction of immune protection for individuals recovered from the original strain or the Alpha variant, corresponding to an average transmission probability of \(0.21 \times 0.109 = 0.0229\) per contact. We further assumed that recovery from infection due to the Gamma or Delta variant provides protection against all variants in the model, preventing reinfection for at least one year.

**Infection outcomes**

We assumed that asymptomatic and mild symptomatic cases recover from infection without hospitalization. A proportion of those with severe disease were hospitalized within 2-5 days of symptom onset\textsuperscript{28,29} and were therefore removed from the transmission chain. We also assumed that all symptomatic cases who were not hospitalized self-isolated within 24 hours of symptom onset, and reduced their number of daily contacts by an additional 72\% (eTable 1). Intensive care unit (ICU) and non-ICU hospitalization rates were parameterized (eTable 2) by clinical and epidemiological data stratified by age and comorbidities\textsuperscript{30-32}. Infection with Alpha variant was associated with 64\% higher risk of death\textsuperscript{9,10}, and infections with Gamma or Delta variants were assigned the case fatality of the original strain.

**Vaccination**

We implemented a two-dose vaccination campaign with a sequential prioritization of: (i) healthcare workers (5\% of the total population)\textsuperscript{35}, adults with comorbidities, and those aged 65 and older; and (ii) other individuals aged 16-64\textsuperscript{36,37}. Based on vaccine uptake data, we assigned 60\% probability of vaccination for individuals aged 40-64 years and 40\% vaccination probability for individuals aged 16-39 years\textsuperscript{38}. The minimum age-eligibility for vaccination was 16 years before May 13, 2021 after which children aged 12 to 15 years became eligible for vaccination. We used reported daily vaccine doses administered since the start of vaccination to parameterize a rolling 7-day average of vaccine distribution per 100,000 population\textsuperscript{39}.

We specified Pfizer-BioNTech vaccines with an interval of 21 days between the first and second doses\textsuperscript{40}. This interval was 28 days for Moderna vaccines\textsuperscript{41}. We parameterized the model with published estimates of vaccine efficacy following each dose of Pfizer-BioNTech and Moderna vaccines against infection, symptomatic disease, and severe disease caused by the original strain\textsuperscript{1,42}. The mean efficacies, reported in eTable 3, were implemented in the model as a reduction of transmission probability (for efficacy against infection), reduction in probability of developing symptomatic disease, and reduction of severe illness if symptomatic disease occurred.

**Data sources**

The overall demographic characteristics and temporal distribution of individuals receiving COVID-19 vaccines was obtained from the CDC data repository\textsuperscript{39}. Daily COVID-19 infections (i.e., confirmed by a test), and deaths (reported as associated with COVID-19) were obtained from New York Times Github repository\textsuperscript{43}. Daily new COVID-19 hospital admissions were retrieved from the HealthGov data repository\textsuperscript{44}.

**Model implementation**

Assuming 10\% pre-existing immunity generated by the original strain prior to October 2020\textsuperscript{56,57}, we simulated the model with a population of 100,000 individuals from October 1, 2020 to December 1, 2021. To incorporate the age distribution of pre-existing immunity in the population, we ran the model with only the original strain in the absence of vaccination and determined the infection rates in different age groups when the overall attack rate reached 10\%. The distribution of this immunity was used to parameterize the initial population at the start of simulations.
On April 2, the guidelines by the US Centers for Disease Control and Prevention indicated a minimal risk for fully vaccinated individuals to travel and engage in certain social activities while taking COVID-19 precautions. We therefore allowed vaccinated individuals to return to pre-pandemic behaviour 14 days after the second dose of vaccine from April 3, 2021.

During the calibration process (in the presence of only the original strain of SARS-CoV-2), we used a 50% lower rate of contacts (compared to pre-pandemic normal behaviour) and determined the transmission probability of 0.109 per contact in the pre-symptomatic stage of infection. Transmissibility during other stages of infection was adjusted according to their infectivity relative to the pre-symptomatic stage. The transmission probability obtained during the calibration corresponds to an effective reproduction number of 1.17 in early October 2020, accounting for the effect of NPIs. After the calibration, the transmission probability of the original strain remained fixed and the age-specific contact rates were adjusted throughout the simulations (in all scenarios with and without vaccination) to implicitly account for the change in various NPIs implemented in the US and fit the model to observed incidence data. The model was implemented in Julia, which is an open-source, high-performance, dynamic programming language that allows rapid analysis of computationally intensive problems, such as agent-based modelling. Simulations were averaged over 500 independent Monte-Carlo realizations, and 95% credible intervals derived using a bias-corrected and accelerated bootstrap method. The simulation codes are available at:

https://github.com/thomasvilches/multiple_strains/tree/rapid_vaccination
**eTable 1. Mixing Patterns and the Daily Number of Contacts Derived From Empirical Observations**

| Age group | Proportion of contacts between age groups | No. of daily contacts without self-isolation Mean (SD) | No. of daily contacts for self-isolated individuals Mean (SD) |
|-----------|-----------------------------------------|--------------------------------------------------|-----------------------------------------------------|
| 0-4       | 0.2287 0.1839 0.4219 0.1116 0.0539      | 10.21 (7.65)                                      | 2.86 (2.14)                                          |
| 5-19      | 0.0276 0.5964 0.2878 0.0591 0.0291      | 16.793 (11.7201)                                  | 4.70 (3.28)                                          |
| 20-49     | 0.0376 0.1454 0.6253 0.1423 0.0494      | 13.795 (10.5045)                                  | 3.86 (2.95)                                          |
| 50-65     | 0.0242 0.1094 0.4867 0.2723 0.1074      | 11.2669 (9.5935)                                  | 3.15 (2.66)                                          |
| 65+       | 0.0207 0.1083 0.4071 0.2193 0.2446      | 8.0027 (6.9638)                                   | 2.24 (1.95)                                          |

*Daily numbers of contacts were sampled from negative binomial distributions for different scenarios*
**eTable 2. Model Parameters Associated With Hospitalization of Severe Cases**

| Parameter                                                                 | Value                                      | Source     |
|---------------------------------------------------------------------------|--------------------------------------------|------------|
| Proportion of severe cases hospitalized with one or more comorbidities    | 100%                                       | 30–32      |
| Non-ICU                                                                   | 60.4%                                      |            |
| ICU                                                                       | 39.6%                                      |            |
| Proportion of severe cases hospitalized without any comorbidities         | 10.8%                                      | 30–32      |
| Non-ICU                                                                   | 75%                                        |            |
| ICU                                                                       | 25%                                        |            |
| Length of non-ICU stay (days)                                            | Gamma(shape: 4.5, scale: 2.75)             | Derived from 33,34 |
| Length of ICU stay (days)                                                | Gamma(shape: 4.5, scale: 2.75) + 2         | Derived from 33,34 |
**eTable 3.** Estimated Vaccine Efficacies (%) and Their 95% CIs From Published Studies

| Vaccine efficacy (%) | Weeks after the first dose | Weeks after the second dose | Reference |
|----------------------|---------------------------|-----------------------------|-----------|
| **Original strain**  |                           |                             |           |
| Infection            | None                      | 46 (40, 51)                 | 60 (53, 66) | 86.1 (82.4, 89.1) | 41,45–49 |
| Symptomatic disease  | None                      | 57 (50, 63)                 | 66 (57, 73) | 94 (87, 98)     |           |
| Severe disease       | None                      | 62 (39, 80)                 | 80 (59, 94) | 92 (75, 100)    |           |
| **Alpha variant**    |                           |                             |           |
| Infection            | None                      | 29.5 (22.9, 35.5)           | 60 (53, 66) | 89.5 (85.9, 92.3) | 50–52    |
| Symptomatic disease  | None                      | 53.6 (50, 63)               | 62 (57, 73) | 93.7 (91.6, 95.3) |           |
| Severe disease       | None                      | 54.1 (26.1, 71.9)           | 80 (59, 94) | 94 (87, 98)     |           |
| **Gamma variant**    |                           |                             |           |
| Infection            | None                      | 36.8 (32., 40.8)            | 48 (42.4, 52) | 73.6 (70.4, 76) | 50,51    |
| Symptomatic disease  | None                      | 33.2 (8.3, 51.4)            | 66 (57, 73) | 94 (87, 98)     |           |
| Severe disease       | None                      | 34 (0, 50)                  | 68 (64, 75) | 97.4 (92.2, 99.5) |           |
| **Delta variant**    |                           |                             |           |
| Infection            | None                      | 36.8 (32.0, 40.8)           | 48 (42.4, 52) | 64 (57, 70)     | 52–55    |
| Symptomatic disease  | None                      | 33.5 (20.6, 44.3)           | 62 (57, 73) | 88 (85.3, 90.1) |           |
| Severe disease | None | 34 (0, 50) | 68 (64, 75) | 80 (73–85) |

\(^a\) Vaccine efficacy against the Gamma variant was assumed to be the same as those reported for Beta.
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