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COVID-19 Scenario Projections: The Emergence of Omicron in the US

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December 16, 2021

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COVID-19 Modeling Consortium

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Overview

On November 24, 2021, South African scientists announced the rapid spread of a new SARS-CoV-2 variant. Within days, the WHO named the variant Omicron and classified it as a variant of concern (VOC). As of December 15, 2021, many of Omicron's epidemiological characteristics remain uncertain, including its intrinsic transmissibility, ability to evade vaccine-acquired and infection-acquired immunity, and severity. To support situational awareness and planning in the United States, we simulated the emergence and spread of Omicron in the US across a range of plausible scenarios.

Using a stochastic compartmental model that tracks population-level immunity against the Delta and Omicron variants derived from infections, primary vaccines, and booster vaccines, we project COVID-19 cases, hospitalizations and deaths over a six month period beginning on December 1, 2021 under 18 different scenarios. Our projections suggest:

- Under a pessimistic scenario in which Omicron is as transmissible as Delta and more evasive of infection-acquired and vaccine-acquired immunity than Delta (with 85%, 32%, and 22% reduced protection against infection, hospitalization, and death, respectively), Omicron could lead to the largest healthcare surge to date, unless measures are taken to slow spread. In this extreme scenario, we project a wave that peaks on February 3, 2022, with cases, hospital admissions, and deaths reaching levels that are 2.2 (95% CrI: 1.3-3.2), 1.8 (95% CrI: 1.2-2.5), and 1.2 (95% CrI: 0.8-1.5) times higher than the January 2021 peak.

- Under an optimistic scenario in which Omicron is 50% more transmissible than Delta, but far less immune evasive (with only 10% reduction in protection against infection and no reduction in protection against severe outcomes), we project a significantly milder Omicron surge that peaks in January 18, 2022 with cases, hospital admissions, and deaths reaching levels that are 0.92 (95% CrI: 0.41-1.61), 0.57 (95% CrI: 0.28-0.98), 0.46 (95% CrI: 0.32-0.64) times the the January 2021 peak.

- If 80% of previously vaccinated individuals are boosted by March 1, 2022, rather than our baseline assumption of 57%, we project that reported cases, hospital admissions, and deaths would be reduced by 5%, 12%, and 13%, respectively. In our most pessimistic Omicron scenario, this translates into averting an expected 1.3 million

reported COVID-19 cases, 168,000 hospitalizations, and 39,000 deaths between December 1, 2021 and May 1, 2022.

We are posting these results prior to peer review to provide intuition for both policy makers and the public regarding the immediate threat of the Omicron variant. We will update our estimates as additional information regarding the spread, vaccine evasiveness, and severity of Omicron become available.

Epidemiological model

The appendix describes the model in detail. We use mathematical equations to project the changing numbers of individuals who are susceptible, infected, hospitalized, recovered, and deceased and to track changing levels of immunity in the population. The projections below make the following assumptions:

- Based on seroprevalence and vaccination data [1,2] we assume that, as of August 14, 2021, 19.2% of the population has immunity from prior infection and 51.8% of the US population has been fully vaccinated.
- Between August 14 and November 8, 2021, we estimate the transmission rate in three week intervals by fitting the model to daily case report data for the US [3]. Between November 6, 2021 and May 1, 2022, we assume that policies and behavior remain constant. We initialize the transmission rate during this period with the value estimated from November 6, 2021 to November 27, 2021 and then assume that changes in transmission rate are entirely driven by the emergence of Omicron and our assumptions about its relative transmissibility and immune evasiveness.
- Hospitalization and mortality rates are fit according to time-dependent polynomial functions that ensure consistency between case, hospitalization, and mortality estimates. The average hospitalization and mortality rates calculated during the fitting are used during the projection period.
- We assume that 25% of all infections are reported as cases, though reporting rates can fluctuate according to variant severity
- Immune waning is assumed to occur an average of eight months following vaccination and twelve months following natural infection
- Our model incorporates age-specific hospitalization and mortality rates. We assume that age groups interact with one another according to contact rates estimated from the POLYMOD study (Age-specific contact patterns in the Technical Appendix)

Omicron scenarios

We consider a total of twenty different scenarios that vary with respect to Omicron's transmission rate and immune evasiveness relative to Delta (Table 1), as well as the rate of vaccine booster uptake.

- *Transmission scenarios*: Following discussions with the CDC, we investigated four scenarios in which Omicron has a different transmission rate and level of immune

escape (with respect to infection) than the Delta variant (Table 1, *Transmission Characteristics*). Assuming that Omicron is at 0.01% prevalence in the United States as of December 1, 2021, it is expected to quickly overtake Delta in the country in all four scenarios (Figure 1).

- *Severity scenarios*: For unvaccinated individuals with no prior infections, we assume that the severity of Omicron is the same as Delta. For vaccinated and previously infected individuals, we assume that they have significant but somewhat reduced protection against severe illness from Omicron relative to Delta. We investigate a range of scenarios for the reduction in protection against hospitalizations and deaths (Table 1), based on guidance from the CDC and COVID-19 scenario modeling hub [4]. We assume that Omicron infections provide a high level of protection against future Omicron infections, comparable to the protection that Delta infections provide against future Delta infections.

- *Vaccine booster scenarios*: Our low and high uptake scenarios assumes that 57% and 80% of fully vaccinated individuals in the US receive a booster dose by March 1, 2022, respectively. We assume that booster doses confer the same level of immediate protection as a primary dose.

Table 1. Eight transmission and severity scenarios for the Omicron variant in the US.

Omicron scenario	Transmission Characteristics		Severity Characteristics	
	Transmissibility relative to Delta	Immune escape relative to Delta (infections)*	Immune escape relative to Delta (hospitalizations)**	Immune escape relative to Delta (deaths)**
Baseline (no Omicron)	NA	NA	NA	NA
Scenario 1A	155%	42.5%	32%	22%
Scenario 1B	150%	10%	22%	12%
Scenario 1C	100%	85%	32%	22%
Scenario 1D	80%	50%	22%	12%
Scenario 2A	155%	42.5%	10%	10%
Scenario 2B	150%	10%	0%	0%
Scenario 2C	100%	85%	10%	10%
Scenario 2D	80%	50%	0%	0%

* These values indicate the reduction in protection against infection and symptoms for individuals that were previously vaccinated or infected by a non-Omicron variant.
** These values indicate the reduction in protection against hospitalization and death for individuals that were previously vaccinated or infected by a non-Omicron variant.

Results

We assume that policies and behavior remain constant from December 1, 2021 through May 1, 2022 and project the number of cases, hospital admissions, and deaths across 18 scenarios for the emergence and spread of the Omicron variant in the US. Each scenario is defined by the inherent transmissibility and immune evasiveness of Omicron relative to Delta and rate of booster uptake in the US (Table 1). Under all scenarios, we expect that Omicron will quickly overtake Delta as the dominant variant (Figure 1) and has the potential to cause the most severe COVID-19 healthcare surges to date (Figure 2-4, Tables 2-3).

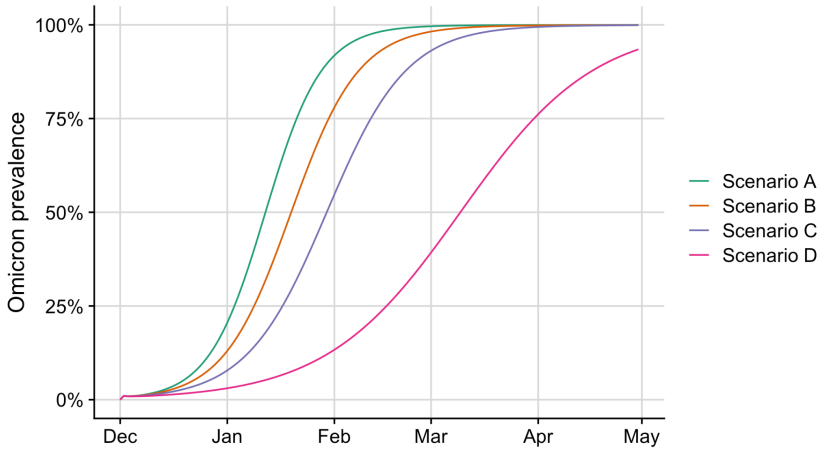

Figure 1. Projected proportion of infections caused by Omicron for four Omicron transmission scenarios (Table 1) assuming an initial prevalence of 0.01% on December 1, 2021.

Assuming a modest rate of booster uptake (57% of eligible individuals boosted by March 1), scenarios that assume a high level of immune escape yield the most pessimistic projections (Figure 2-4, orange and pink curves). The left and right graphs in Figures 2-4 compare the lower severity to higher severity scenarios (in which initial protection against hospitalizations is reduced from 90% to 70% and protection against mortality is reduced from 95% to 85%). Under both severity scenarios, hospitalizations could surge to unprecedented levels (Figure 3); under the high severity scenarios but not the low severity scenarios, mortality could also reach an all-time high (Figure 4).

Increasing vaccine booster rates is expected to decrease the cumulative COVID-19 burden during the projection period (Figure 5). Across all scenarios, increasing booster rates from 57% to 80% boosted by March 1 decreases the projected reported cases, hospitalizations, and deaths by roughly 5%, 12%, and 13%, respectively. In a scenario where Omicron has low transmission, high immune escape, and high severity, increasing booster coverage can reduce absolute disease burden by a median of 1.3 million reported cases, 168,000 hospitalizations, and 39,000 deaths from December 1, 2021 and May 1, 2022 (Table 2).

Under the most pessimistic scenario considered—low transmissibility, high immune escape, high severity and low booster uptake—we project that the peak numbers of reported cases, hospital admissions, and deaths would be 2.2 (95% CrI: 1.3-3.2), 1.8 (95% CrI: 1.2-2.5), and 1.2 (95% CrI: 0.8-1.5) times larger than the peaks that occurred during the large surge in January 2021 (Table 3). In the most optimistic scenario considered—high transmissibility,

low immune escape, low severity and high booster uptake—we project peaks that are 0.92 (95% CrI: 0.41-1.61), 0.57 (95% CrI: 0.28-0.98), 0.46 (95% CrI: 0.32-0.64) times the height of the January 2021 peaks. **Importantly, these projections assume that the US does NOT enact policies or change behavior to slow transmission.** Early and effective mitigation could avert the overwhelming surges projected under these scenarios.

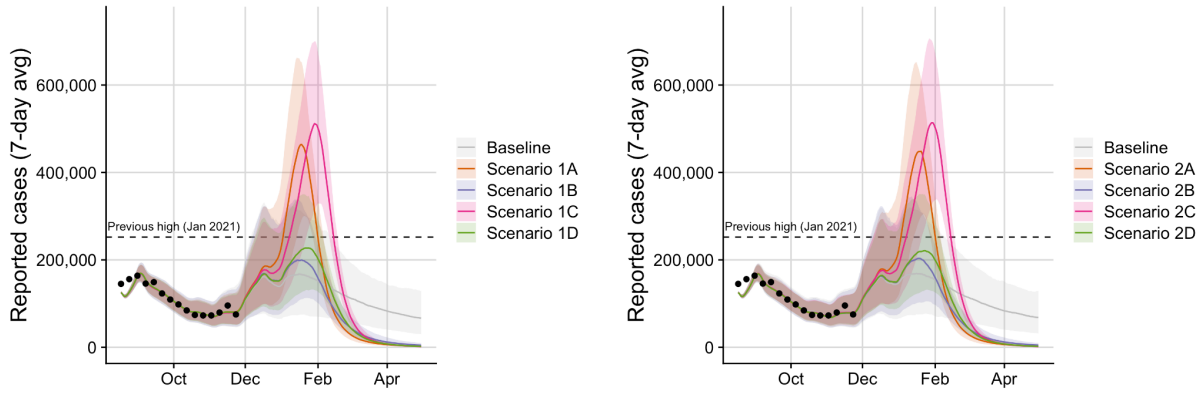

Figure 2. Projected COVID-19 case counts in the US from December 1, 2021 to May 1, 2022 under eight different Omicron emergence scenarios. Black points represent reported 7-day average COVID-19 cases in the US [3]. Colored lines represent median projections across the scenarios specified in Table 1, with ribbons indicating 90% projection intervals. The horizontal dashed line indicates the previous maximum 7-day average for reported cases in the US, which occurred on January 11, 2021. The left and right graphs correspond to the low and high severity scenarios described in Table 1, respectively. These projections assume a low rate of booster uptake, resulting in 57% of eligible individuals boosted by March 1, 2022.

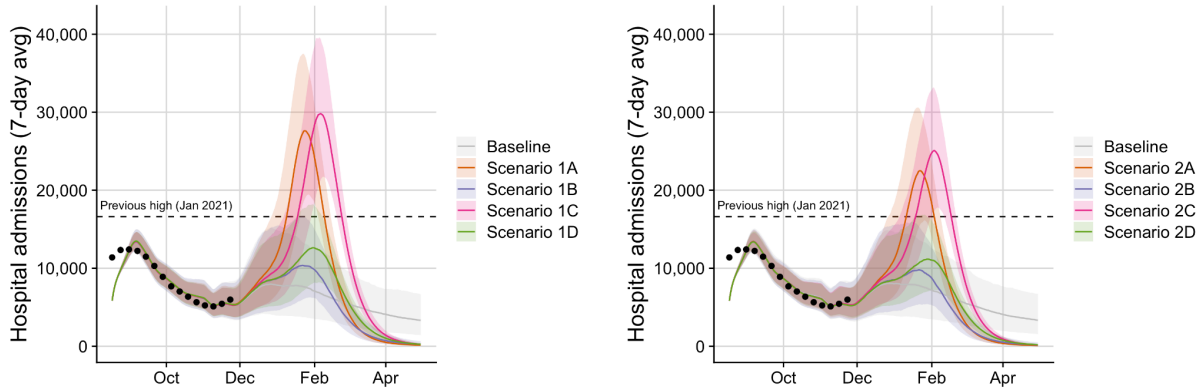

Figure 3. Projected COVID-19 hospital admissions in the US from December 1, 2021 to May 1, 2022 under eight different Omicron emergence scenarios. Black points represent reported 7-day average COVID-19 hospital admissions in the US [5]. Colored lines represent median projections across the scenarios specified in Table 1, with ribbons indicating 90% projection intervals. The horizontal dashed line indicates the previous maximum 7-day average for reported hospital admissions in the US, which occurred on January 10, 2021. The left and right graphs correspond to the low and high severity scenarios described in Table 1, respectively. These projections assume a low rate of booster uptake, resulting in 57% of eligible individuals boosted by March 1, 2022.

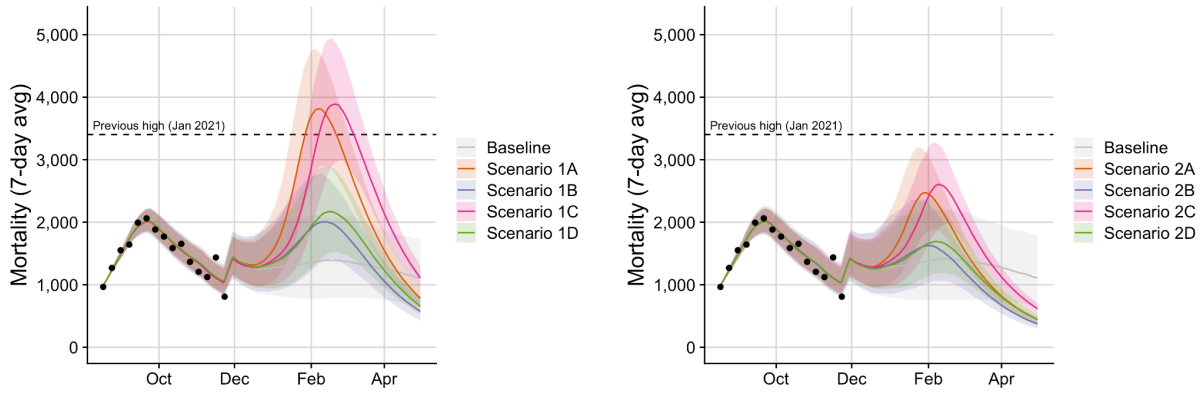

Figure 4. Projected COVID-19 mortality in the US from December 1, 2021 to May 1, 2022 under eight different Omicron emergence scenarios. Black points represent reported 7-day average COVID-19 mortality in the US [3]. Colored lines represent median projections across the scenarios specified in Table 1, with ribbons indicating 90% projection intervals. The horizontal dashed line indicates the previous maximum 7-day average for reported deaths in the US, which occurred on January 13, 2021. The left and right graphs correspond to the low and high severity scenarios described in Table 1, respectively. These projections assume a low rate of booster uptake, resulting in 57% of eligible individuals boosted by March 1, 2022.

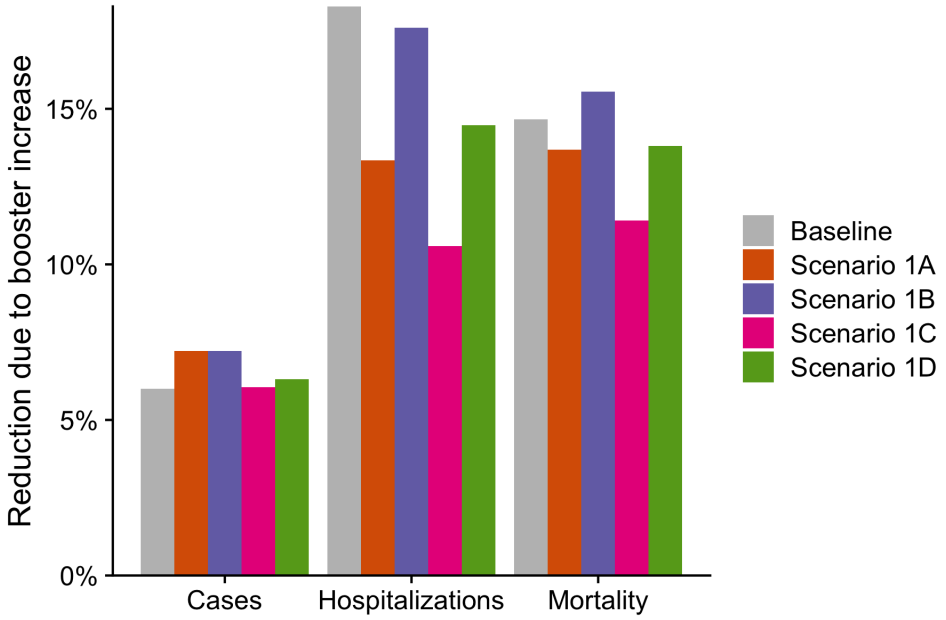

Figure 5. Projected impact of increasing SARS-CoV-2 booster uptake in the US from 57% to 80% by March 1, 2022. Bars indicate the median percent reduction in reported COVID-19 cases, hospitalizations, and mortality between December 1, 2021 and May 1, 2022. Values are based on a pairwise comparison between disease burden across 1,000 stochastic simulations for the Low and High booster scenarios.

Table 2. Projected SARS-CoV-2 burden between December 1, 2021 and May 1, 2022 in the US under 18 scenarios for the emergence of the Omicron variant. Values are medians and 95% prediction intervals based on 1,000 stochastic simulations.

Omicron Emergence Scenario		Reported cases	Hospitalizations	Deaths
Omicron scenario	**Booster uptake**			
Baseline (no Omicron)	High	19,126,000 (8,562,000 - 30,217,000)	774,000 (410,000 - 1,149,000)	170,000 (102,000 - 239,000)
Baseline (no Omicron)	Low	20,482,000 (10,086,000 - 31,972,000)	941,000 (518,000 - 1,380,000)	200,000 (122,000 - 278,000)
Scenario 1A	High	20,405,000 (14,201,000 - 27,593,000)	1,196,000 (894,000 - 1,527,000)	282,000 (219,000 - 348,000)
Scenario 1A	Low	21,912,000 (15,091,000 - 29,064,000)	1,378,000 (1,047,000 - 1,712,000)	325,000 (257,000 - 392,000)
Scenario 2A	High	20,531,000 (14,371,000 - 27,450,000)	1,019,000 (751,000 - 1,306,000)	197,000 (155,000 - 242,000)
Scenario 2A	Low	21,550,000 (15,181,000 - 28,911,000)	1,146,000 (874,000 - 1,481,000)	220,000 (176,000 - 270,000)
Scenario 1B	High	14,373,000 (8,753,000 - 21,496,000)	682,000 (461,000 - 958,000)	183,000 (133,000 - 238,000)
Scenario 1B	Low	15,436,000 (9,691,000 - 22,365,000)	824,000 (575,000 - 1,108,000)	217,000 (158,000 - 276,000)
Scenario 2B	High	14,529,000 (8,656,000 - 20,809,000)	637,000 (414,000 - 899,000)	152,000 (110,000 - 198,000)
Scenario 2B	Low	15,326,000 (9,117,000 - 22,689,000)	753,000 (499,000 - 1,069,000)	175,000 (126,000 - 231,000)
Scenario 1C	High	24,790,000 (16,293,000 - 33,417,000)	1,458,000 (1,087,000 - 1,838,000)	303,000 (230,000 - 379,000)
Scenario 1C	Low	26,107,000 (17,132,000 - 34,841,000)	1,626,000 (1,189,000 - 2,048,000)	342,000 (256,000 - 422,000)
Scenario 2C	High	25,076,000 (16,593,000 - 34,143,000)	1,245,000 (914,000 - 1,578,000)	215,000 (164,000 - 264,000)
Scenario 2C	Low	26,376,000 (17,124,000 - 35,385,000)	1,386,000 (1,007,000 - 1,752,000)	241,000 (183,000 - 297,000)
Scenario 1D	High	15,340,000 (8,918,000 - 22,990,000)	836,000 (548,000 - 1,159,000)	199,000 (137,000 - 265,000)
Scenario 1D	Low	16,311,000 (9,723,000 - 24,075,000)	964,000 (649,000 - 1,318,000)	229,000 (162,000 - 303,000)
Scenario 2D	High	15,466,000 (8,891,000 - 22,834,000)	771,000 (502,000 - 1,087,000)	166,000 (115,000 - 222,000)
Scenario 2D	Low	16,198,000 (9,711,000 - 24,011,000)	870,000 (592,000 - 1,202,000)	185,000 (136,000 - 245,000)

Table 3. Projected peak values in SARS-CoV-2 cases, hospitalizations, and deaths between December 1, 2021 and May 1, 2022 in the US under 18 scenarios for the emergence of the Omicron variant. Values are median and 95% prediction intervals based on 1,000 stochastic simulations.

Omicron Emergence Scenario		Peak reported cases (7-day average)	Peak hospitalizations (7-day average)	Peak deaths (7-day average)
Omicron scenario	**Booster uptake**			
Prior Maximum (January 2021)		252,000	16,600	3,400
Baseline (no Omicron)	High	221,400 (96,900 - 417,000)	8,900 (4,500 - 16,500)	1,600 (1,100 - 2,200)
Baseline (no Omicron)	Low	228,700 (96,100 - 433,000)	10,000 (4,700 - 18,600)	1,700 (1,100 - 2,600)
Scenario 1A	High	461,900 (267,400 - 709,500)	24,100 (15,300 - 35,500)	3,300 (2,300 - 4,400)
Scenario 1A	Low	508,200 (289,900 - 758,800)	28,600 (18,600 - 40,500)	3,900 (2,800 - 5,000)
Scenario 2A	High	467,200 (273,700 - 701,500)	20,200 (12,700 - 29,600)	2,200 (1,500 - 2,900)
Scenario 2A	Low	497,300 (303,600 - 744,000)	23,400 (15,600 - 33,400)	2,500 (1,800 - 3,400)
Scenario 1B	High	230,700 (110,500 - 410,000)	9,800 (5,300 - 16,300)	1,700 (1,200 - 2,500)
Scenario 1B	Low	246,200 (121,600 - 423,900)	11,900 (6,600 - 18,800)	2,100 (1,400 - 2,900)
Scenario 2B	High	231,800 (102,300 - 405,600)	9,500 (4,600 - 16,300)	1,500 (1,100 - 2,200)
Scenario 2B	Low	243,400 (110,000 - 432,200)	11,100 (5,600 - 18,700)	1,700 (1,100 - 2,600)
Scenario 1C	High	510,400 (307,200 - 746,900)	26,900 (18,100 - 38,100)	3,400 (2,500 - 4,600)
Scenario 1C	Low	548,000 (327,900 - 799,000)	30,500 (20,500 - 42,300)	3,900 (2,800 - 5,200)
Scenario 2C	High	518,800 (311,700 - 764,300)	22,500 (14,900 - 31,800)	2,300 (1,600 - 3,000)
Scenario 2C	Low	552,400 (335,300 - 795,500)	25,500 (17,100 - 35,100)	2,600 (1,800 - 3,400)
Scenario 1D	High	236,000 (116,000 - 394,200)	11,000 (6,300 - 17,300)	1,900 (1,200 - 2,600)
Scenario 1D	Low	254,700 (131,300 - 414,700)	13,100 (7,600 - 19,900)	2,200 (1,400 - 3,100)
Scenario 2D	High	239,700 (115,100 - 388,300)	10,300 (5,600 - 16,100)	1,600 (1,100 - 2,200)
Scenario 2D	Low	251,600 (130,100 - 410,200)	11,900 (6,900 - 18,600)	1,800 (1,200 - 2,500)

Technical appendix

Epidemiological model

We use an age-structured COVID-19 SEIRS compartment model that tracks changes in the level of protection acquired from past infection and vaccination (Figure A1). We describe the changes in population-wide immunity resulting from three sources: Delta infections, Omicron infections, and vaccination. The level of each source of protection is explicitly modeled through a state variable. Natural infections increase the infection-acquired protection variables and primary and booster vaccines increase the vaccine-acquired protection variable. The levels of immunity wane at different speeds that are based on published estimates. The variables are used to reduce disease susceptibility and severity by inhibiting infections, symptomatic disease, hospitalizations, and deaths. The efficacy of each form of immunity depends on the relative prevalence of the circulating variants.

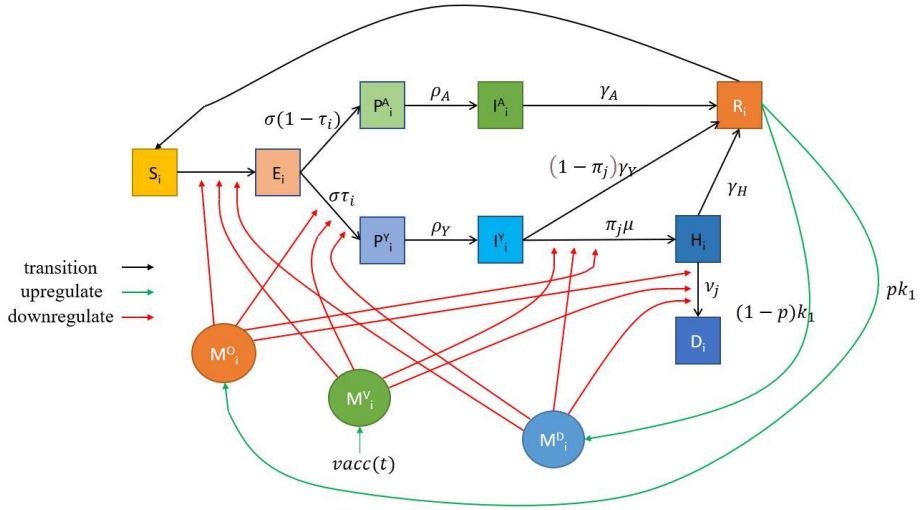

Figure A1. Schematic representation of the mathematical model of SARS-CoV-2 transmission and vaccination. Each subgroup (defined by age) is modeled by a separate set of compartments. Upon infection, susceptible individuals (S) progress to the exposed state (E). Exposed individuals either transition into the pre-symptomatic (P^Y) or the pre-asymptomatic (P^A) compartment. Pre-asymptomatic cases first transition to the infectious asymptomatic compartment (I^A) and then to the recovered compartment (R) where they are fully immune to reinfection. Pre-symptomatic individuals first move to the symptomatic compartment (I^Y); a fraction of individuals moves directly to the recovered compartment, while the remaining transition to the hospitalized compartment (H). Hospitalized cases will either move to the recovered compartment (R) or die (D). Recovered individuals eventually become partially susceptible again and move into the susceptible compartment (S). At the same time, we describe the changes in population-immunity acquired from Omicron (M_O), Delta (M_D), vaccination and other variants (M_V). These immunity levels increase through natural infections and vaccination. Each of these immunities downregulates infection rates, symptomatic disease, hospitalization, and death with efficacies that depend on the circulating virus.

Changes in immunity are captured through specific non-dimensional state variables. We begin by describing the changes in the population-level immunity acquired from Delta infections:

$$\frac{dM_D^I}{dt} = \frac{k_1(1-p)R_l}{N_l(1+K_{s,1}M_D^I+K_{s,1}M_V^I+(1-(1-p)\epsilon)K_{s,1}M_O^I)} - \omega_1 M^D,$$

where the first term on the right-hand side of the equation describes the development of immunity upon recovery from Delta infections. R_l is the number of recovered individuals among the age group *l,* and *p* denotes the relative prevalence of Omicron to Delta. Saturation of immunity reduces its upregulation because most of the people who get infected while having antibodies do not generate as many antibodies as during primary infections. The second term represents the waning of immunity. Next, we describe the changes in the population-immunity acquired through vaccination:

$$\frac{dM_V^I}{dt} = k_2 \frac{Vacc(t)}{N_l(1 + K_{s,2} M_l^V)} - \omega_2 M_V^I,$$

where *Vacc(t)* is a time-dependent function that describes the daily administered dose two weeks before during the vaccination program. The model does not make a distinction between doses administered as primary series or as third doses. The effect of each dose on immunity is considered two weeks after their administration. The last term on the right-hand side of the equation describes the waning of immunity acquired from vaccination and all variants except Delta and Omicron. After that, we describe the evolution of the immunity acquired from Omicron as follows:

$$\frac{dM_O^I}{dt} = k_1 p \frac{R_l}{N_l(1 + (1 - p\epsilon) K_{s,1}(M_D^I + M_V^I) + K_{s,1} M_O^I)} - \omega_1 M_O^I.$$

Then, we describe the transition among the different compartment for each specific age group *l* as follows:

$$\frac{dS_l}{dt} = -S_l \cdot \sum_{i \in A} \frac{\beta_i \phi_{l,i} (I_i^Y + I_i^A \omega^A + P_i^Y + P_i^A \omega^A)}{N_i(1 + K_1^1 M_D^I + K_1^2 M_V^I + K_1^3 M_O^I)} + \eta R$$

$$\frac{dE_l}{dt} = S_l \cdot \sum_{i \in A} \frac{\beta_i \phi_{l,i} (I_i^Y + I_i^A \omega^A + P_i^Y + P_i^A \omega^A)}{N_i(1 + K_3^1 M_D^I + K_3^2 M_V^I + K_3^3 M_O^I)} - \sigma E_l$$

$$\frac{dP_l^A}{dt} = (1 - \tau_l + K_2^1 M_D^I + K_2^2 M_V^I + K_2^3 M_O^I)\sigma E_l - \rho^A P_l^A$$

$$\frac{dP_l^Y}{dt} = (\tau_l - K_2^1 M_D^I - K_2^2 M_V^I - K_2^3 M_O^I)\sigma E_l - \rho^Y P_l^Y$$

$$\frac{dI_l^A}{dt} = \rho^A P_l^A - \gamma^A I_l^A$$

$$\frac{dI_l^Y}{dt} = \rho^Y P_l^Y - (1 - \pi_m)\gamma^Y I_l^Y - \frac{\pi_m \mu I_l^Y}{1 + K_3 M_l^H}$$

$$\frac{dH_l}{dt} = \frac{\pi_m \mu I_l^Y}{1 + K_3^1 M_D^I + K_3^2 M_V^I + K_3^3 M_O^I} - \gamma_H H_l - \frac{\nu_m H_l}{1 + K_4^1 M_D^I + K_4^2 M_V^I + K_4^3 M_O^I}$$

$$\frac{dR_l}{dt} = \gamma^A I_l^A + (1 - \pi_m)\gamma^Y I_l^Y + \gamma_H H_l - \eta R_l$$

$$\frac{dD_l}{dt} = \frac{\nu_m H_l}{1 + K_4^1 M_D^I + K_4^2 M_V^I + K_4^3 M_O^I},$$

where *A,* are all possible age groups, ω^A is the relative infectiousness of the infectious

compartments I^A, I^{PA}, β is the transmission rate, $\phi_{a,i}$ is the mixing rate between age group a, $i \in A$, and γ^A, γ^Y, γ^H are the recovery rates for the I^A , I^Y, H compartments, respectively, σ is the exposed rate, ρ^A, ρ^Y are the pre-(a)symptomatic rates, τ is the symptomatic ratio, π is the proportion of symptomatic individuals requiring hospitalization, μ is the rate at which hospitalized cases enter the hospital following symptom onset, ν is the mortality rate for hospitalized cases, and η is the rate at which recovered individuals become susceptible again, K_i^j with *i* in *[1, 2, 3, 4]* and *j* in *[1, 2, 3]* are positive constants that describe the efficacy of immunity in reducing the rates of infection, symptomatic disease, hospitalization, and death, *p* describes the relative prevalence of Omicron to Delta. Numerical values of the epidemiological parameters are provided in Table A1 and values of immunological parameters are presented in Table A2.

Model parameters

Table A1: list of epidemiological parameter values used in the numerical simulations.

Parameters	Value	Source
γ^A: recovery rate on asymptomatic compartment	Equal to γ^Y	Assumption
γ^Y: recovery rate on symptomatic non-treated compartment	0.25	[6]
τ: symptomatic proportion (%)	0.35	Adjusted to have 1 symptomatic case out of 4 in the steady-state for Delta
σ: exposed rate	1/1.5	increased from 1/2.9 to 1/1.5 because of Delta [3]
ρ^A: pre-asymptomatic rate	Equal to ρ^Y	
ρ^Y: pre-symptomatic rate	$\frac{1}{2.3}$	[6]
ω^A: relative infectiousness of infectious individuals in compartment I^A	$\frac{2}{3}$	[7]
IFR: infected fatality ratio, age specific (%)	Low risk: [0.0009, 0.0022, 0.0022, 0.0339, 0.2520, 0.6440]	Age adjusted from Verity et al. [8]
YFR: symptomatic fatality ratio, age specific (%)	Low risk: [0.001608, 0.003823, 0.003823, 0.05943, 0.4420, 1.130]	$YFR = \frac{IFR}{\tau}$

Age-specific contact patterns

Contact matrices for the US were used to describe mixing rates between age groups [9]. We use three matrices to describe the contact patterns in all locations, schools and workplaces to describe the reduction in mobility during holidays and weekends. We consider that schools close during weekends and from December 18 to January 02, and also during the months of June, July and August. We also consider that workplaces are closed during the weekends. Then, the overall contact matrix is taken as follows:

$$CM = CM_{all} - \alpha_s(t)CM_s - \alpha_w(t)CM_w,$$

where CM_{all}, CM_s, CM_w, are the contact matrices for all locations, schools, and workplaces, respectively. $\alpha_s(t)$ and $\alpha_w(t)$ are time-dependent functions that describe the opening or closure of schools and workplaces, they take the value of 0 if the corresponding location is opened and 1 if it is closed. The three considered contact matrices are as follows:

$$CM_{all} = \begin{bmatrix} 2.598237 & 1.600682 & 0.1895988 & 4.1198752 & 0.912514 & 0.112739 \\ 0.640235268 & 8.428533343 & 0.400015072 & 4.028603965 & 0.709643468 & 0.103204179 \\ 0.173684 & 2.0999574 & 6.663684 & 8.710766 & 0.5601588 & 0.0327582 \\ 0.490443671 & 1.516968944 & 0.759891199 & 10.27014274 & 1.714438659 & 0.095919246 \\ 0.431143971 & 1.339346998 & 0.592373724 & 6.379632659 & 3.196133287 & 0.188612431 \\ 0.204998347 & 0.718001781 & 0.182731115 & 2.136319698 & 1.558267141 & 0.602532372 \end{bmatrix},$$

$$CM_s = \begin{bmatrix} 1.196597632 & 0.269627261 & 0.03173379 & 0.38262616 & 0.049755762 & 0 \\ 0.139739606 & 3.973684579 & 0.051319078 & 0.369792419 & 0.075075384 & 0.000263253 \\ 0.016961126 & 0.903246574 & 3.427856164 & 2.582830513 & 0.060321191 & 0 \\ 0.058180033 & 0.331477088 & 0.188215674 & 0.461408137 & 0.042344186 & 0.000352703 \\ 0.093904827 & 0.568170143 & 0.243358213 & 0.35953993 & 0.073783363 & 0.0005338 \\ 0.000729122 & 0.021954765 & 0.006167126 & 0.029787663 & 0.03474166 & 0.011651215 \end{bmatrix},$$

$$CM_w = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 1.20585 \times 10^{-05} \\ 0 & 0.039768604 & 0.005775822 & 0.091897952 & 0.006139445 & 0 \\ 0 & 0.020170591 & 0.386451333 & 1.666005478 & 0.136647372 & 0 \\ 0 & 0.056904943 & 0.171469933 & 4.893999929 & 0.792456512 & 0 \\ 0 & 0.069619305 & 0.071928236 & 2.526315884 & 0.70871039 & 0 \\ 0 & 0 & 0 & 0.00026916 & 8.88673 \times 10^{-05} & 2.02847 \times 10^{-05} \end{bmatrix}.$$

Validating the estimated immunity in model

The model dynamics were inspired by the numerical simulations of an agent-based within- and between-host model. This multiscale model has revealed that population immunity reduces disease susceptibility and severity. The parameters for immunity development and saturation (k_1, k_2, $K_{s,1}$) were estimated by fitting the results of the multiscale model.

Initializing the epidemiological model

Age-specific patterns for immunity history were assumed to match the data for seroprevalence [1,10]. We start accounting for vaccination dose allocation on August 01, 202. The first date for vaccination is considered to be two weeks before the beginning of the simulation. This is because we consider that each allocated dose upregulates

vaccine-acquired immunity two weeks of its administration. Vaccine-induced immunity was initiated by considering the vaccination coverages, in terms of administered doses per age group, until this date. We assume that all individuals who received vaccine shots until July 31 2021, did not lose their immunity because the considered half-life time for vaccine-acquired immunity waning is 8 months. Then, vaccination acquired from Delta infections is computed as the remaining immunity, such that 70% are immunized either through vaccination or natural infection [10]. Thus, we obtain the following initial age-specific values for Delta-induced and vaccine-induced immunities:

$$M_{D0} = [0.22, 0.42, 0.86, 0.61, 0.39, 0.26], \quad M_{V0} = [0, 0.0017, 0.4997, 0.6628, 0.6040, 0.8739].$$

Table A2: list of immunological parameter values used in the numerical simulations.

Rate of population immunization from natural infections (k_1)	153.55	Fitted to multiscale model results
Rate of population immunization from vaccination (k_2)	0.112	Fitted to data
Constant of saturation from natural infection ($K_{s,1}$)	100	Fitted to multiscale model results
Constant of saturation from vaccination ($K_{s,2}$)	10	Fitted to data
M_D and M_O immune waning rate (ω_1)	$1/(12 \times 30)$	Immunity acquired from infection is considered to last longer than vaccine-induced one [11]
M_D and M_O immune waning rate (ω_2)	$1/(8 \times 30)$	[11]

Fitting the epidemiological model to United States data

In the absence of immune escape, we consider the values for the rate of immunity efficacy in blocking infections, symptoms, hospitalizations, and deaths summarized in Table A3.

Estimating the effect of immune escape

The model considers that immune escape reduces the efficacy of a type of immunity in reducing susceptibility and severity of another immunity type. Omicron escape to immunity acquired through vaccines and other variants is simulated by reducing the efficacy of Omicron as follows:

$$K_1^i(p) = 4(1 - p\epsilon), \quad K_2^i(p) = 0.15(1 - p\epsilon),$$
$$K_3^i(p) = 19(1 - p\epsilon_2), \quad K_4^i(p) = 38(1 - p\epsilon_2),$$

where *i* can be either 1 or 2, *p* is the relative prevalence of Omicron to Delta, ϵ_1 and ϵ_2 represent the levels of Omicron immune escape to infection/symptoms and to severe

disease, respectively. We assume that Delta has the same chances to escape immunity acquired through Omicron infections.

Table A3. Efficacy levels against the same variant in the absence of immune escape.

	Value	Corresponding efficacy against infection for the fully immunized
$K_{1,}^{1}, K_{1}^{3}$	4	80%
K_{1}^{2}	3 for under 65 and 1.33 for over 65	75% for under 65 and 57% for over 65
$K_{2,}^{1}, K_{2}^{3}$	0.15	90%
K_{2}^{2}	0.15	90%
$K_{3,}^{1}, K_{3}^{3}$	19	95%
K_{3}^{2}	19 for under 65 and 9 for over 65	95% for under 65 and 90% for over 65
$K_{4,}^{1}, K_{4}^{3}$	38	97.5%
K_{4}^{2}	38 for under 65 and 19 for over 65	97.5% for under 65 and 95% for over 65

Estimating the prevalence of the Omicron variant

The model is designed to simulate the spread of a single virus. However, several parameters can be tuned to describe a double-strain epidemic by considering that they depend on the relative prevalence of Omicron to Delta. Thus, we need to simulate the ascent of Omicron for each scenario to parameterize the model. To achieve this, we fit a two-strain model to US data to describe the competition between Omicron and Delta. A schematic representation of the model is provided in Figure A2.

Estimating age-specific vaccination rates

Vaccination is modelled by considering the daily number of allocated doses. These doses can be either administered during primary series or as additional shots. We assume that each administered dose upregulates the age-specific immunity M^{I}_{V} two weeks after its administration. The number of administered doses per age group is taken from the CDC dataset [2]. Then, the average number of daily administered doses for each age group during November is computed as a rollout for the next month. Booster dose rollout is increased by 2- or 4-folds depending on the considered booster coverage scenario. The administration of doses stops as soon as it reaches the age-specific levels of vaccine hesitancy summarized in Table A4. Hesitancy among children is assumed to be higher than among adults.

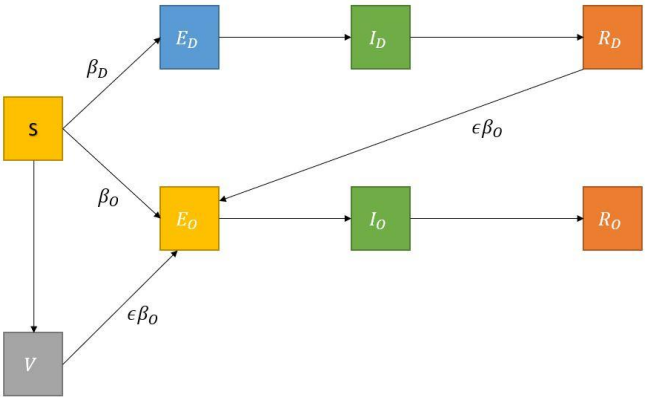

Figure A2. Schematic representation of the two-strain model used to estimate the growth of Omicron. Susceptible individuals (S) can either get infected by Delta or Omicron and become exposed (E_D and E_O). They can also become vaccinated with a constant rollout similar to the one of the US. Omicron transmission rate (β_O) is taken superior to the one of Delta depending on the considered scenario. Furthermore, Omicron can infect individuals who are vaccinated or recovered from Delta because of immune escape. For instance, an immune escape level of ϵ suggest that ϵR_D and ϵV are susceptible to Omicron infection.

The model is parameterized using the US data for immunity and vaccination history. Next, it is fitted to the latest trends in Delta COVID-19 cases until December 01, 2021. Then, Omicron is introduced to the system by considering that its relative prevalence is equal to 0.01 on December 01, 2021.

Table A4. Assumed hesitancy levels for each age group.

	Assumed hesitancy level to vaccination
[0-4]	-
[5-11]	30 %
[12-18]	26 %
[19-49]	24.9 % [12]
[50-64]	12 % [13]
[65+]	7 % [13]

Making projections

The model is fitted using US data for cases, hospitalization, and mortality ([5], [3]) for the period from 08/21/2021 to 11/30/2021. Then, projections are made for the period between 12/01/2021 and 05/01/2022. Microstochasticities are introduced using the Euler-Maruyama Method. Furthermore, the daily transmission rate is sampled from the distribution $N(\beta_F, \sigma_\beta)$, where β_F is the transmission rate for the period between 12/09/2021 and 12/30/2021 fitted

using US data, σ_β describes the difference between the 95% confidence interval and the median for the fitted transmission rates values during the fitting period.

For each scenario projection, we made 1000 simulation runs and computed the 7-day rolling averages. Then, the 0.05, 0.50, 0.95 quantities are computed for each day.

References

1. Center of Disease Control. Nationwide Antibody Seroprevalence Survey. Available: https://covid.cdc.gov/covid-data-tracker/#national-lab. Accessed on December 01, 2021.

2. Center of Disease Control. COVID-19 Vaccination and Case Trends by Age Group, United States. Available: https://data.cdc.gov/Vaccinations/COVID-19-Vaccination-and-Case-Trends-by-Age-Group-/gxj9-t96f. Accessed on December 01, 2021.

3. Johns Hopkins University. COVID-19 Data Repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Available: https://github.com/CSSEGISandData/COVID-19. Accessed on December 01, 2021.

4. Home - COVID 19 scenario model hub. [cited 15 Dec 2021]. Available: https://covid19scenariomodelinghub.org/

5. U.S. Department of Health & Human Services. COVID-19 Reported Patient Impact and Hospital Capacity by State Timeseries. Available: https://healthdata.gov/Hospital/COVID-19-Reported-Patient-Impact-and-Hospital-Capa/g62h-syeh. Accessed on December 01, 2021.

6. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med. 2020. doi:10.1038/s41591-020-0869-5

7. He D, Zhao S, Lin Q, Zhuang Z, Cao P, Wang MH, et al. The relative transmissibility of asymptomatic COVID-19 infections among close contacts. Int J Infect Dis. 2020;94: 145–147.

8. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of COVID-19 disease. Epidemiology. medRxiv; 2020. doi:10.1101/2020.03.09.20033357

9. Prem K, Cook AR, Jit M. Projecting social contact matrices in 152 countries using contact surveys and demographic data. PLOS Computational Biology. 2017. p. e1005697. doi:10.1371/journal.pcbi.1005697

10. Moghadas SM, Sah P, Shoukat A, Meyers LA, Galvani AP. Population Immunity

Against COVID-19 in the United States. Annals of Internal Medicine. 2021. pp. 1586–1591. doi:10.7326/m21-2721

11. Gazit S, Shlezinger R, Perez G, Lotan R, Peretz A, Ben-Tov A, et al. Comparing SARS-CoV-2 natural immunity to vaccine-induced immunity: reinfections versus breakthrough infections. doi:10.1101/2021.08.24.21262415

12. Baack BN, Abad N, Yankey D, Kahn KE, Razzaghi H, Brookmeyer K, et al. COVID-19 Vaccination Coverage and Intent Among Adults Aged 18–39 Years — United States, March–May 2021. MMWR. Morbidity and Mortality Weekly Report. 2021. pp. 928–933. doi:10.15585/mmwr.mm7025e2

13. Trinidad B, Ruhter J, Kolbe A, Marus J, et al.. COVID-19 Vaccine Hesitancy: Demographic Factors, Geographic Patterns, and Changes Over Time. Office of the Assistant Secretary for Planning and Evaluation. Published online in May 2021. https://aspe.hhs.gov/sites/default/files/private/pdf/265341/aspe-ib-vaccine-hesitancy.pdf