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The University of Texas at Austin

Scenario projections for the spread of SARS-CoV-2 Omicron BA.4 and BA.5 subvariants in the US and Texas

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August 4, 2022

The University of Texas at Austin
COVID-19 Modeling Consortium

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Overview

This report projects the spread and burden of the highly-transmissible SARS-CoV-2 Omicron BA.4 and BA.5 variants based on data through July 5, 2022. By that date, BA.4 and BA.5 were the predominant variants in the US[1] and COVID-19 hospitalizations were increasing.

Using a stochastic compartmental model that tracks population-level immunity derived from infections, primary vaccines, and booster vaccines, we project COVID-19 cases, hospitalizations, and deaths over a twelve month period for both the entire United States and the state of Texas. We simulate sixteen different scenarios in which we vary the transmission properties of the Omicron BA.4/BA.5 variants and the rate of SARS-CoV-2 vaccine booster uptake.

The timing and size of the imminent Omicron BA.4/BA.5 waves depend on the severity of the scenario, as follows.

- In a *pessimistic scenario* in which the BA.4 and BA.5 variants are highly transmissible, immunity wanes rapidly, and booster uptake is low, we project:

  US: A growing wave that peaks around October 10, 2022 with reported cases, hospital admissions, and deaths reaching 26% (95% CrI: 13%-42%), 49% (95% CrI: 28%-75%), and 42% (95% CrI: 25%-60%) the maximum levels that occurred during the large Omicron surge in January 2022, respectively.

  For the six month period between July 5, 2022 and January 5, 2023, a total of 38.07 (95% CrI: 23.84-55.50) million reported cases, 1.76 (95% CrI: 1.18-2.43) million hospitalizations, and 164.2 (95% CrI: 116.8-215.5) thousand deaths.

  Texas: A growing wave that peaks around September 16, 2022 with reported cases, hospital admissions, and deaths reaching 45% (95% CrI:

33%-58%), 97% (95% CrI: 74%-120%), and 67% (95% CrI: 53%-81%) the maximum levels that occurred during the large Omicron surge in January 2022, respectively.

For the six month period between July 5, 2022 and January 5, 2023, a total of 4.56 (95% CrI: 3.51-5.7) million reported cases, 245 (95% CrI: 194.3-298.1) thousand hospitalizations, and 15.5 (95% CrI: 12.6-18.5) thousand deaths.

- In an *optimistic scenario* in which the BA.4/BA.5 variants are not more more transmissible than other recently circulating variants but more easily escape infection-acquired protection, immunity wanes more slowly, and booster uptake is high, we project:

  US: A growing wave that peaks around July 26, 2022 with reported cases, hospital admissions, and deaths reaching 12% (95% CrI: 8%-15%), 23% (95% CrI: 19%-28%), and 17% (95% CrI: 15%-21%) the maximum levels that occurred during the large Omicron surge in January 2022, respectively.

  For the six month period between July 5, 2022 and January 5, 2023, a total of 16.2 (95% CrI: 11.73-23.66) million reported cases, 691.77 (95% CrI: 544.5-910.82) thousand hospitalizations, and 70.7 (95% CrI: 59.32-87.14) thousand deaths.

  Texas: A growing wave that peaks around August 16, 2022 with reported cases, hospital admissions, and deaths reaching 19% (95% CrI: 14%-26%), 39% (95% CrI: 30%-49%), and 23% (95% CrI: 18%-29%) the maximum levels that occurred during the large Omicron surge in January 2022, respectively.

  For the six month period between July 5, 2022 and January 5, 2023, a total of 2.44 (95% CrI: 1.79-3.19) million reported cases, 108.83 (95% CrI: 83.5-135.2) thousand hospitalizations, and 6.2 (95% CrI: 4.9-7.6) thousand deaths.

Epidemiological model

In late 2021, we developed a stochastic compartmental model to provide Omicron scenario projections for the US Centers for Disease Control and Prevention (CDC)[2]. The model tracks the changing numbers of individuals who are susceptible, infected, hospitalized, recovered, and deceased, as well as the changing levels of immunity acquired through infection and vaccination. The projections make the following assumptions:

- As of February 7, 2022, 57.7% of the US population had been infected[1,3] and 64.9% had been fully vaccinated[1,3]; for Texas, 69.7% had been infected and 59.2% fully vaccinated.
- From February 7 through June 22, 2022, we estimate the transmission rate in five week intervals from daily case report data[4]. Between July 1 and January 1, 2023, we

assume that policies and behavior remain constant. We initialize the transmission rates during this period with the values estimated for May 18 to June 22, 2022 and then increase the rates depending on the specific BA.4 and BA.5 scenario.

- We estimate age-specific hospitalization and mortality rates directly from data[5].
- We assume that 25% of all infections are reported prior to the emergence of the Omicron BA.4 and BA.5 variants, and that reporting rates during the projection period depend on immune-mediated severity of infection which vary across scenarios.
- We consider two scenarios for immune waning. Slow waning assumes a half-life time of eight months following vaccination or natural infection; fast waning assumes a half-life of four months.
- Based on CDC Variants & Genomic Surveillance data[1], the Omicron BA.4 and BA.5 variants appeared in the US on April 30, 2022 and were the predominant variants circulating in the US by July 2022.
- We assume that BA.2 has a 40% transmissibility advantage over BA.1 [6], and that BA.2.12.2 has 30% chances to escape prior immunity from BA.1 and BA.2 [7].

Additional details are provided in the Appendix.

Omicron BA.4/BA.5 transmission and boosting scenarios

Table 1. Four scenarios for the transmission of the BA.4 and BA.5 Omicron variants. The rightmost columns indicate the speed of immune waning following infection with any Omicron subvariant.

Scenario	BA.4/BA.5 advantage	Waning of protection against infection	Waning of protection against severity
T1	40% more transmissible than BA.2.12.1	8 month half life	No waning
T2	42.5% immune evasive from past Omicron infections than BA.2.12.1	8 month half life	No waning
T3	40% more transmissible than BA.2.12.1	4 month half life	12 month half life
T4	42.5% more immune evasive from past Omicron infections than BA.2.12.1	4 month half life	12 month half life

Table 2. Four scenarios for the rollout of SARS-CoV-2 boosters. Each scenario assumes that boosters continue to roll out at the current rate until the date specified in the second column, at which point uptake increases as specified in the third column.

Scenario	Date of rate change	New booster rate/policy
B1	No Increase	N/A
B2	July 15, 2022	Five-fold increase in uptake for over 12y Second boosters authorized for 18-49y
B3	August 15, 2022	
B4	September 15, 2022	

We consider a total of 16 different scenarios, all combinations of four scenarios for the transmissibility of Omicron BA.4/BA.5 variants (Table 1) and four scenarios for the rate of

booster uptake (Table 2). Each transmissibility scenario specifies whether BA.4/BA.5 is more transmissible or more immune evasive than the BA.2.12.1 variant and the rates at which immune protection against BA.4/BA/5 infection and severe disease wanes following infection (Table 1). Two scenarios assume that BA.4 and BA.5 can evade immunity against infection while the other two consider that BA.4 and BA.5 have more intrinsic transmissibility than BA.2.12.1. All scenarios assume that BA.4 and BA.5 have the same intrinsic severity (i.e., hospitalization and mortality rates) as prior Omicron variants. The four booster scenarios (Table 2) assume that boosters continue to roll out until 70% of fully vaccinated individuals have received two boosters.

Scenario Projections for Omicron BA.4/BA.5 Variant

The following projections assume that non-pharmaceutical intervention policies and cautionary behavior remain constant from July 5, 2022 through August 17January 5, 2023.

US Projections

First, we assume that vaccine booster rates do not change and project reported SARS-CoV-2 cases, hospitalizations and deaths under the four different Omicron BA.4/BA.5 scenarios specified in Table 1 (Figure 1). Then, we project the impact of increasing the rate of booster uptake on hospital admissions (Figure 2). Table 3 provides the projected cumulative SARS-CoV-2 reported cases, hospital admissions, and deaths from July 5, 2022 to August 17, 2023 for all 16 scenarios. Table 4 provides the projected peak values.

Across the sixteen scenarios, the seven-day average in reported cases is expected to peak between July 24 and October 12, 2022. Seven-day average COVID-19 hospital admissions are expected to peak between August 2 and October 18, 2022, with a median estimate of August 21, 2022.

Under the most pessimistic scenario (T3-B1), which assumes high BA.4/BA.5 transmissibility, fast immune waning, and no increasing in booster uptake—we project that the peak numbers of reported cases, hospital admissions, and deaths would reach 26% (95% CrI: 13%-42%), 49% (95% CrI: 28%-75%), and 42% (95% CrI: 25%-60%) the maximum levels reached during the large Omicron surge that occurred in January 2022 (Table 4). In this scenario, we estimate that the total reported cases, hospital admissions, and deaths between July 5, 2022 and January 5, 2023 will be 32.09 (95% CrI: 17.96-49.57) million, 1.54 (95% CrI: 0.96-2.22) million, and 150.26 (95% CrI: 100.49-203.72) thousand, respectively (Table 3).

In the most optimistic scenario (T2-B2), which assumes high BA.4/BA.5 immune evasiveness, low immune waning, and immediate expansion of booster uptake, we project that the peak numbers of reported cases, hospital admissions, and deaths would reach 12% (95% CrI: 8%-15%), 23% (95% CrI: 19%-28%), and 17% (95% CrI: 15%-21%) the maximum levels reached during the January surge (Table 4). In this scenario, we estimate that the total reported cases, hospital admissions, and deaths between July 5, 2022 and January 5, 2023 will be 9.70 (95% CrI: 5.58-16.92) million, 439.23 (95% CrI: 298.90-654.88) thousand, and 50.30 (95% CrI: 38.59-66.89) thousand, respectively (Table 3).

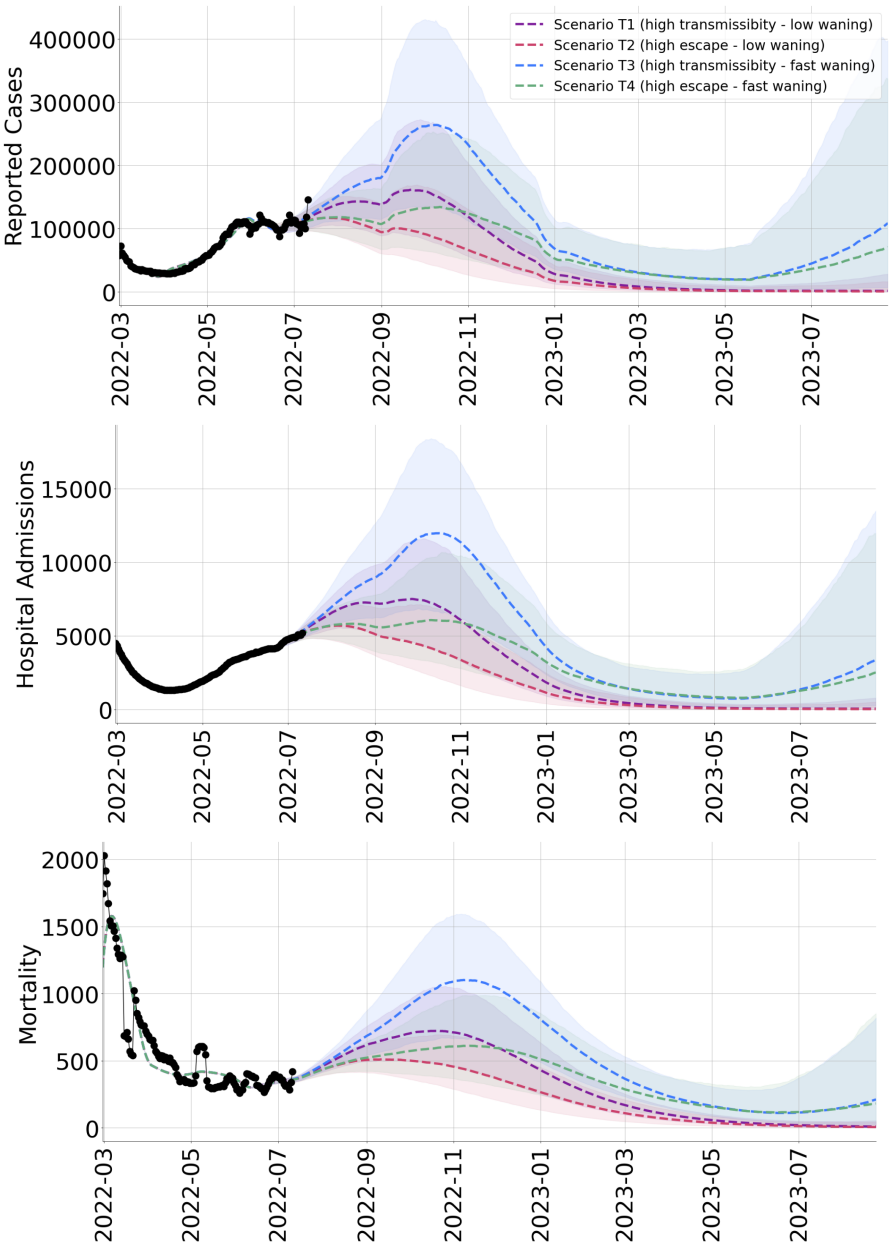

Figure 1. Seven-day rolling average of daily reported COVID-19 cases (top), hospital admissions (middle), and deaths (bottom) in the US for four Omicron BA.4/BA.5 scenarios, as specified in Table 1. Black dots indicate reported values from February 28, 2022 to July 4, 2022. Dashed lines and shaded ribbons represent median values and 95% prediction intervals from July 5, 2022 to August 17, 2023, respectively, based on 1000 stochastic simulations.

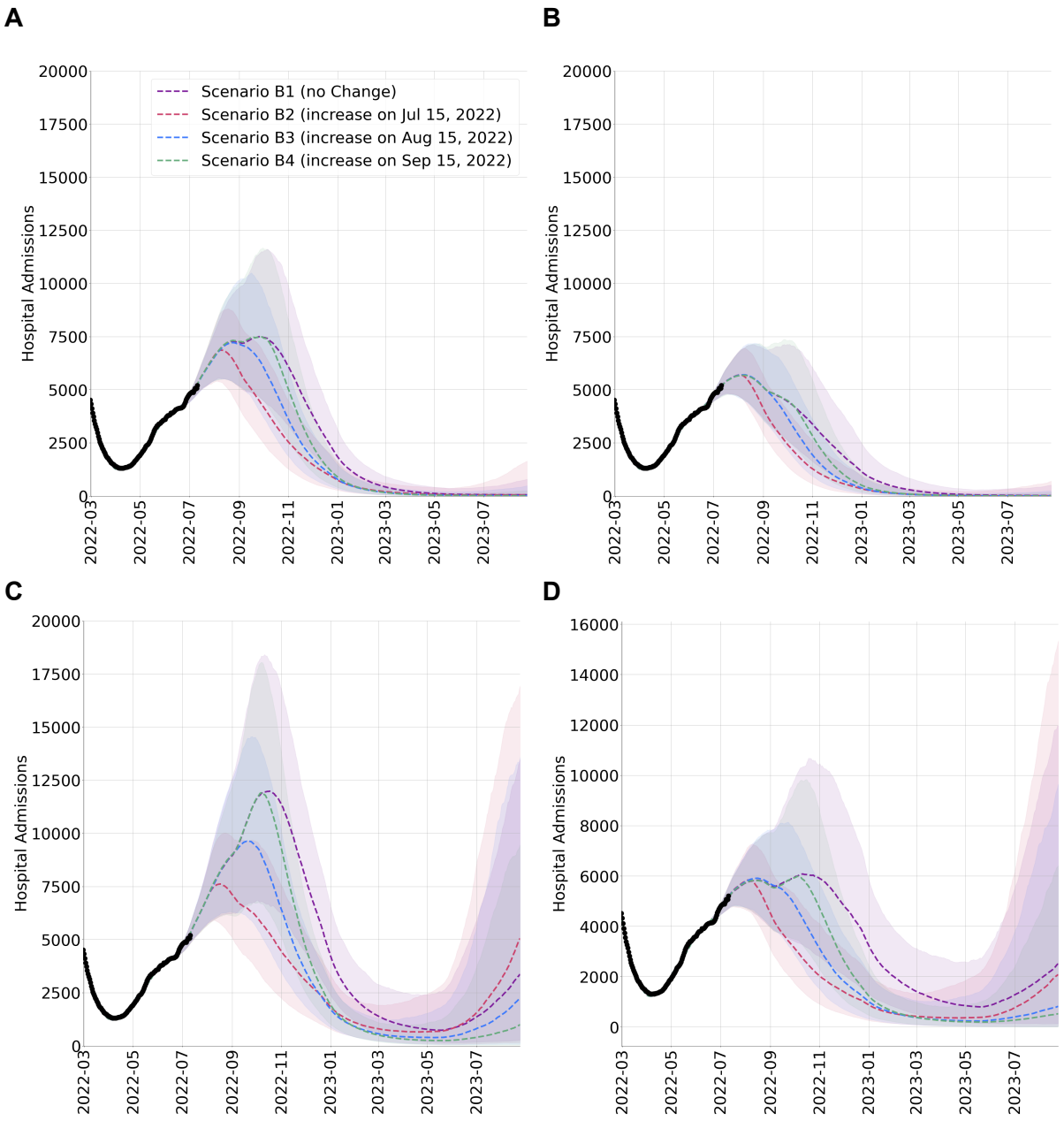

Figure 2. Projected COVID-19 hospital admissions in the US under various booster uptake scenarios. Graphs A through D correspond to the BA.4/BA.5 scenarios T1 through T4 described in Table 1, respectively. Each graph compares scenarios in which boosters continue to roll out at the current pace (purple); roll out at a faster pace to a broader group of adults starting on July 15, 2022 (red); roll out at a faster pace to a broader group of adults starting on August 15, 2022 (blue); roll out at a faster pace to a broader group of adults starting on September 15, 2022 (green). The colored ribbons represent 95% prediction intervals across 1000 stochastic simulations.

Table 3. Projected cumulative SARS-CoV-2 burden between July 5, 2022 and January 5, 2023 in the US under sixteen scenarios for Omicron BA.4/ BA.5 transmission rates and booster uptake. Scenarios T1-T4 and B1-B4 are defined in Tables 1 and 2, respectively. Values are medians and 95% prediction intervals based on 1,000 stochastic simulations.

Scenario	Reported Cases	Hospitalizations	Deaths
T1-B1	26,272,900 (17,643,000 - 38,102,400)	1,238,800 (882,700 - 1,693,100)	123,400 (93,100 - 160,200)
T1-B2	21,388,900 (14,573,300 - 31,694,500)	898,300 (671,900 - 1,213,100)	86,500 (69,200 - 109,100)
T1-B3	23,416,800 (16,043,200 - 34,263,700)	1,033,800 (768,100 - 1,403,100)	100,700 (79,800 - 129,300)
T1-B4	25,037,200 (16,770,300 - 36,797,800)	1,145,200 (826,200 - 1,571,700)	112,700 (86,100 - 146,700)
T2-B1	19,491,500 (13,466,500 - 28,656,800)	909,500 (663,400 - 1,256,500)	95,100 (73,700 - 122,700)
T2-B2	16,202,500 (11,739,600 - 23,666,300)	691,700 (544,500 - 910,800)	70,700 (59,000 - 87,000)
T2-B3	17,735,000 (12,599,600 - 25,633,300)	787,600 (602,200 - 1,045,600)	81,200 (65,600 - 101,300)
T2-B4	18,757,400 (13,129,700 - 27,980,800)	853,700 (637,600 - 1,177,400)	88,500 (69,800 - 114,100)
T3-B1	38,078,300 (23,842,000 - 55,504,800)	1,763,100 (1,184,800 - 2,434,500)	164,200 116,800 - 215,500)
T3-B2	28,864,200 (18,495,800 - 43,479,800)	1,133,300 (807,200 - 1,564,900)	101,700 (79,000 - 130,900)
T3-B3	32,335,100 (20,917,300 - 47,794,000)	1,361,900 (960,800 - 1,874,800)	124,300 (93,400 - 161,400)
T3-B4	35,144,500 (22,145,200 - 50,423,300)	1,559,800 (1,062,300 - 2,110,800)	143,600 (104,800 - 185,600)
T4-B1	25,466,800 (15,974,800 - 39,785,500)	1,170,600 (786,100 - 1,713,000)	113,700 (82,700 - 155,000)
T4-B2	19,385,700 (12,931,700 - 30,015,000)	782,800 (582,200 - 1,081,900)	76,700 (61,500 - 96,900)
T4-B3	21,670,600 (14,370,600 - 32,913,800)	920,000 (671,600 - 1,273,000)	90,300 (70,800 - 116,000)
T4-B4	23,306,500 (15,202,500 - 35,550,500)	1,028,600 (727,900 - 1,452,700)	101,000 (77,200 - 132,800)

Table 4. Projected peak SARS-CoV-2 burden (seven-day average) between July 5, 2022 and January 5, 2023 in the US under sixteen scenarios for Omicron BA.4/ BA.5 transmission rates and booster uptake. Scenarios T1-T4 and B1-B4 are defined in Tables 1 and 2, respectively. Values are medians and 95% prediction intervals based on 1,000 stochastic simulations.

Scenario	Peak Reported Cases	Peak Hospitalizations	Peak Deaths
T1-B1	161,405 (105,710 - 272,401)	7,506 (5,547 - 11,611)	723 (504 - 1,055)
T1-B2	141,700 (103,463 - 206,490)	6,858 (5,403 - 8,811)	535 (436 - 663)
T1-B3	150,839 (103,886 - 252,447)	7,217 (5,507 - 10,497)	630 (499 - 858)
T1-B4	160,309 (103,897 - 276,610)	7484 (5,504 - 11,682)	713 (503 - 1,014)
T2-B1	116,791 (94,932 - 169,155)	5,696 (4,835 - 7,135)	510 (415 - 695)
T2-B2	117,276 (95,046 - 152,643)	5,700 (4,804 - 6,948)	458 (397 - 543)
T2-B3	117,106 (93,742 - 159,525)	5,701 (4,798 - 7,191)	508 (412 - 627)
T2-B4	116,598 (94,050 - 175,601)	5,677 (4,781 - 7,378)	508 (411 - 701)
T3-B1	263,728 (135,651 - 430,470)	11,982 (6,860 - 18,414)	1,101 (672 -1,593)
T3-B2	172,043 (116,200 - 297,193)	7,615 (5,907 - 10,019)	586 (471 - 774)
T3-B3	230,381 (127,133 - 379,988)	9,631 (6,312 - 14,560)	788 (555 - 1,113)
T3-B4	265,592 (135,438 - 426,250)	11,924 (6,747 - 18,051)	983 (641 - 1,408)
T4-B1	134,136 (94,646 - 253,254)	6,074 (4,843 - 10,682)	612 (423 - 989)
T4-B2	119,548 (93,106 - 165,597)	5,834 (4,770 - 7,272)	471 (396 - 563)
T4-B3	123,095 (94,545 - 207,538)	5,906 (4,808 - 8,137)	535 (425 - 700
T4-B4	132,555 (93,719 - 249,552)	5,981 (4,799 - 9,832)	575 (426 - 840)

Texas Projections

First, we assume that vaccine booster rates do not change and project reported SARS-CoV-2 cases, hospitalizations and deaths under the four different Omicron BA.4/BA.5 scenarios specified in Table 1 (Figure 3). Then, we project the impact of increasing the rate of booster uptake on hospital admissions (Figure 4). Table 5 provides the projected cumulative SARS-CoV-2 reported cases, hospital admissions, and deaths from XX to XX for all 16 scenarios. Table 6 provides the projected peak values.

Across the sixteen scenarios, the seven-day average in reported cases is expected to peak between August 16th and September 24, 2022. Seven-day average COVID-19 hospital admissions are expected to peak between August 19 and October 1, 2022, with a median estimate of September 19, 2022.

Under the most pessimistic scenario (T3-B1), which assumes high BA.4/BA.5 transmissibility, fast immune waning, and no increasing in booster uptake—we project that the peak numbers of reported cases, hospital admissions, and deaths would reach 45% (95% CrI: 33%-58%), 97% (95% CrI: 74%-120%), and 67% (95% CrI: 53%-81%) the maximum levels reached during the large Omicron surge that occurred in January 2022 (Table 6). In this scenario, we estimate that the total reported cases, hospital admissions, and deaths between July 5, 2022 and January 5, 2023 will be 4.12 (95% CrI: 3.10-5.25) million, 228.04 (95% CrI: 177.56-281.08) thousand, and 15.41 (95% CrI: 12.40-18.44) thousand (Table 5).

In the most optimistic scenario (T2-B2), which assumes high BA.4/BA.5 immune evasiveness, low immune waning, and immediate expansion of booster uptake, we project that the peak numbers of reported cases, hospital admissions, and deaths would reach 9% (95% CrI: 14%-26%), 39% (95% CrI: 30%-49%), and 23% (95% CrI: 18%-29%) the maximum levels reached during the January surge (Table 6). In this scenario, we estimate that the total reported cases, hospital admissions, and deaths between July 5, 2022 and January 5, 2023 will be 1.98 (95% CrI: 1.36-2.70) million, 89.86 (95% CrI: 66.00-116.53) thousand, and 5.64 (95% CrI: 4.33-7.04) thousand, respectively (Table 5).

As of August 4, 2022, the daily reported cases are slightly lower than the projected numbers for the optimistic scenario, while the trends of hospital admissions and mortality are consistent with the projections. We speculate that this mismatch stems from a decrease in the proportion of cases reported, as mild cases increasingly opt not to test or to use at-home tests.

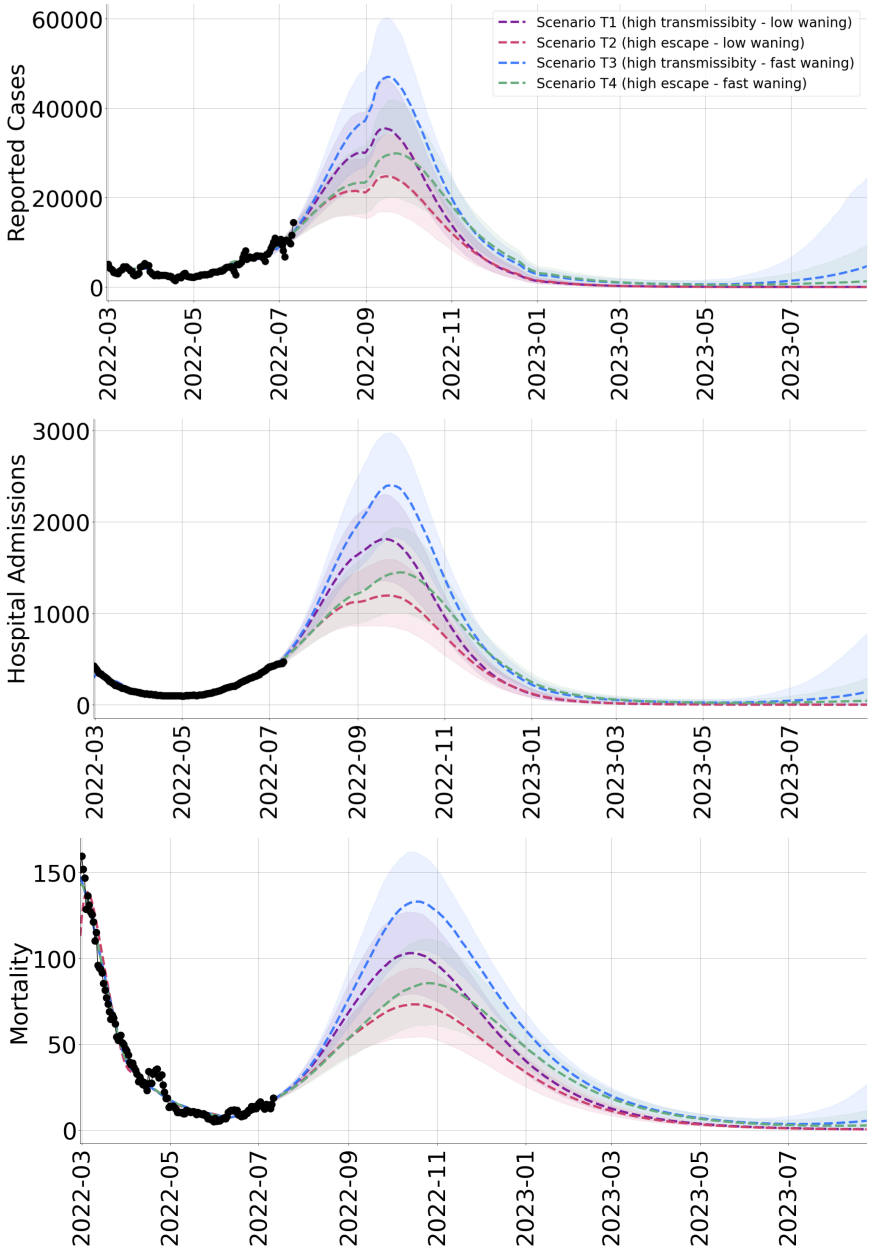

Figure 3. Seven-day rolling average of daily reported COVID-19 cases (top), hospital admissions (middle), and deaths (bottom) in Texas for four Omicron BA.4/BA.5 scenarios, as specified in Table 1. Black dots indicate reported values from February 28, 2022 to July 4, 2022. Dashed lines and shaded ribbons represent median values and 95% prediction intervals from July 5, 2022 to August 17, 2023, respectively, based on 1000 stochastic simulations.

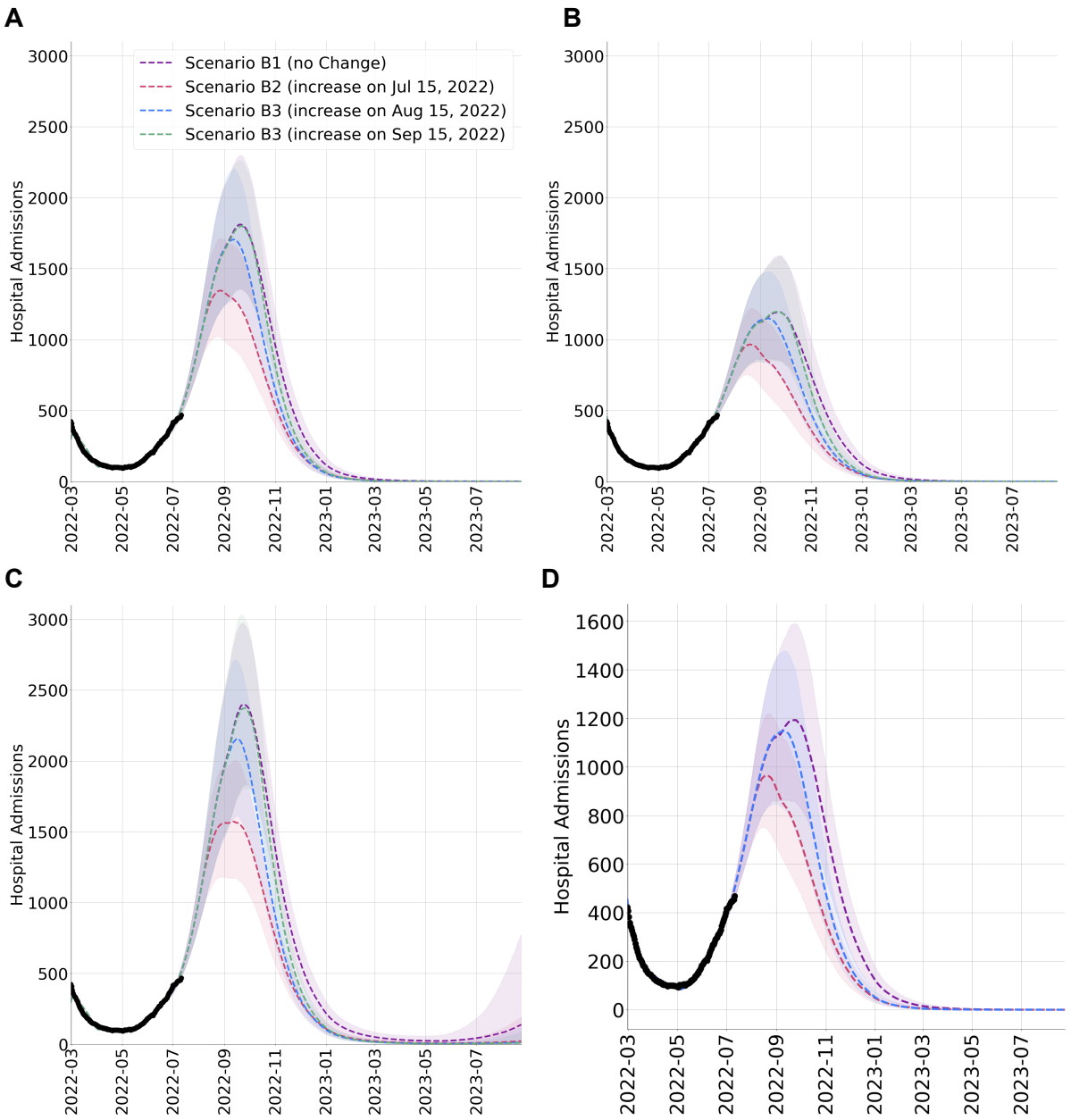

Figure 4. Projected COVID-19 hospital admissions in Texas under various booster uptake scenarios. Graphs A through D correspond to the BA.4/BA.5 scenarios T1 through T4 described in Table 1, respectively. Each graph compares scenarios in which boosters continue to roll out at the current pace (purple); roll out at a faster pace to a broader group of adults starting on July 15, 2022 (red); roll out at a faster pace to a broader group of adults starting on August 15, 2022 (blue); roll out at a faster pace to a broader group of adults starting on September 15, 2022 (green). The colored ribbons represent 95% prediction intervals across 1000 stochastic simulations.

Table 5. Projected cumulative SARS-CoV-2 burden between July 5, 2022 and January 5, 2023 in Texas under sixteen scenarios for Omicron BA.4/ BA.5 transmission rates and booster uptake. Scenarios T1-T4 and B1-B4 are defined in Tables 1 and 2, respectively. Values are medians and 95% prediction intervals based on 1,000 stochastic simulations.

Scenario	Reported Cases	Hospitalizations	Deaths
T1-B1	3,609,200 (2,747,300 - 4,579,400)	193,300 (152,300 - 238,200)	12,500 (10,000 - 15,100)
T1-B2	3,089,800 (2,303,600 - 3,973,400)	144,700 (112,700 - 179,200)	8,100 (6,400 - 9,800)
T1-B3	3,360,000 (2,546,600 - 4,266,700)	169,000 (133,300 - 208,300)	10,100 (8,000 - 12,200)
T1-B4	3,500,300 (2,683,500 - 4,416,400)	183,600 (145,600 - 224,900)	11,400 (9,200 - 13,700)
T2-B1	2,949,600 (2,210,900 - 3,846,300)	148,700 (115,200 - 187,800)	9,700 (7,600 - 12,000)
T2-B2	2,447,600 (1,796,700 - 3,196,600)	108,000 (83,500 - 135,200)	6,200 (4,900 - 7,600)
T2-B3	2,722,700 (2,010,300 - 3,507,300)	128,300 (98,900 - 159,400)	7,700 (6,100 - 9,500)
T2-B4	2,845,900 (2,117,700 - 3,710,300)	140,000 (107,900 - 176,500)	8,800 (6,900 - 10,900)
T3-B1	4,561,800 (3,513,300 - 5,703,300)	245,000 (194,300 - 298,100)	15,500 (12,600 - 18,500)
T3-B2	3,812,400 (2,867,300 - 4,774,300)	174,700 (137,200 - 212,300)	9,500 (7,500 - 11,300)
T3-B3	4,146,000 (3,129,600 - 5,185,100)	206,700 (161,600 - 251,300)	12,000 (9,500 - 14,300)
T3-B4	4,401,700 (3,383,700 - 5,522,100)	230,100 (182,600 - 281,600)	14,000 (11,300 - 17,000)
T4-B1	3,579,500 (2,612,800 - 4,657,900)	180,000 (136,000 - 227,400)	11,100 (8,500 - 13,800)
T4-B2	2,860,400 (2,069,700 - 3,770,800)	122,100 (92,900 - 154,400)	6,600 (5,200 - 8,100)
T4-B3	3,173,200 (2,291,100 - 4,132,700)	146,600 (110,600 - 184,100)	8,400 (6,500 - 10,400)
T4-B4	3,365,000 (2,484,600 - 4,414,700)	163,600 (125,300 - 208,600)	9,700 (7,600 - 12,200)

Table 6. Projected peak SARS-CoV-2 burden (seven-day average) between July 5, 2022 and January 5, 2023 in Texas under sixteen scenarios for Omicron BA.4/ BA.5 transmission rates and booster uptake. Scenarios T1-T4 and B1-B4 are defined in Tables 1 and 2, respectively. Values are medians and 95% prediction intervals based on 1,000 stochastic simulations.

Scenario	Peak Reported Cases	Peak Hospitalizations	Peak Deaths
T1-B1	35,533 (25,415 - 46,860)	1,811 (1,356 - 2,302)	103 (79 - 127)
T1-B2	28,732 (19,713 - 39,389)	1,346 (1,019 - 1,713)	64 (48 - 81)
T1-B3	34,623 (24,614 - 46,356)	1,705 (1,276 - 2,205)	86 (66 - 109)
T1-B4	35,339 (25,587 - 46,108)	1,802 (1,355 - 2,266)	101 (77 - 125)
T2-B1	24,780 (16,915 - 34,282)	1,193 (864 - 1,592)	73 (54 - 94)
T2-B2	20209 (15,034 - 27,240)	966 (752 - 1,220)	46 (36 - 58)
T2-B3	24,415 (16,322 - 33,050)	1,148 (849 - 1,479)	61 (47 - 78)
T2-B4	24,656 (16,862 - 34,212)	1,196 (856 - 1,596)	72 (53 - 92)
T3-B1	47,016 (34,739 - 60,321)	2,399 (1,834 - 2,975)	133 (105 - 162)
T3-B2	36,720 (26,074 - 47,693)	1,571 (1,181 - 2,007)	75 (57 - 94)
T3-B3	44,784 (31,640 - 57,269)	2,157 (1,611 - 2,714)	105 (80 - 130)
T3-B4	46,508 (34,206 - 61,368)	2,374 (1,809 - 3,031)	128 (99 -162)
T4-B1	29,906 (20,147 - 41,928)	1,447 (1,012 - 1,944)	86 (62 - 112)
T4-B2	22,596 (15,694 - 31,774)	1,002 (781 - 1,276)	48 (37 - 60)
T4-B3	28,234 (18,476 - 39,156)	1,287 (896 - 1,697)	66 (48 - 85)
T4-B4	29,344 (19,898 - 41,357)	1,423 (1,011 - 1,928)	79 (58 -105)

Appendix:

Estimating the emergence of Omicron variants

To estimate the rising proportion of cases caused by Omicron BA.4/ BA.5 during May 2022, we fit logistic functions to CDC Variants & Genomic Surveillance data[1] (Figure A1).

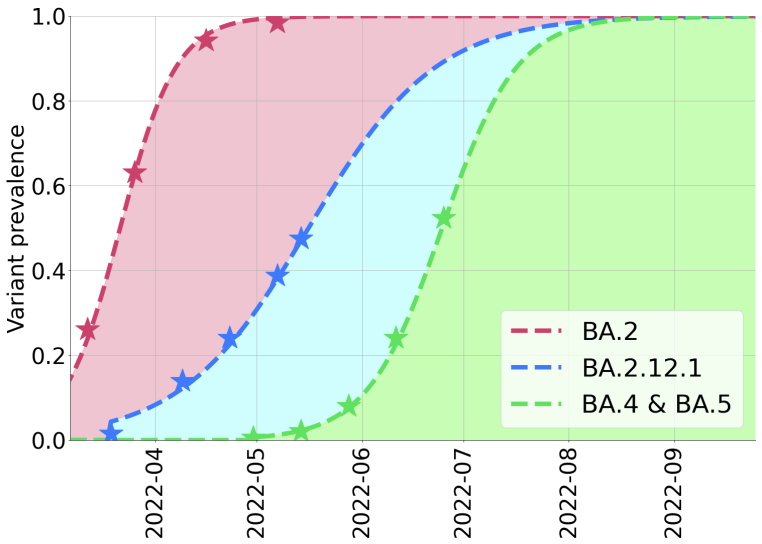

Figure A1. Estimated ascent of the Omicron subvariants BA.2, BA.2.12.1, and BA.4/BA.5 in US. Values represent the proportion of cases caused by the Omicron subvariants. Stars indicate the reported proportion of each variant in a sample of US COVID-19 specimens, according to Nowcast[8]; the dashed line is the fitted logistic curve.

Additional modeling assumptions

Historic trends of cases, deaths, and hospital admissions [9], [10] were used to calibrate the model. We assume that seroprevalence is equal to 57.5% and 69.7% in the US and Texas, respectively as of February 21, 2022 [11,12]). Initial coverages of primary and booster vaccination were taken from available data ([11,12]). As a baseline, we consider 25% of infections to be reported as cases, though the reporting rate can fluctuate according to population-immunity. Immune waning is assumed to occur with half-life times that depend on the immunity source. Vaccine-induced immunity is assumed to wane with half-life times equal to 6 months and 3 months for primary shots and boosters, respectively [13]. Hence, immunity derived from booster vaccination provides strong but short lived protection [14]. Age groups interact with each other according to contact rates provided from the POLYMOD study [15].

The model is fitted using data from February 21, 2022 to July 4, 2022. Then, we make projections for COVID-19 cases, hospitalizations, and deaths over the period from July 5, 2022 to August 17, 2023. The transmission rate is fitted using a piecewise function. Then, it is kept constant through the projection window. Hospitalization and mortality rates are fitted using time-dependent polynomial functions during the fitting period. Then, they are kept constant through the projection interval.

Details of the epidemiological model

Model structure. A previously developed age-structured SEIRS model is extended to include the variants BA.2, BA.2.12.1, and BA.4/BA.5 and booster vaccination [2] (Figure A1). The model explicitly tracks the changes in the population immunity resulting from infections with different variants as well as primary and booster vaccination. The changes in the population-immunity determine the average susceptibility and severity of the population depending on the circulating variants.

We describe the changes in the population-immunity acquired by infections with Omicron BA.1, BA.2, BA.2.12.1, and BA.4/BA.5 through specific non-dimensional state variables. For each variant, we consider two state variables that describe protection against infection and severe disease and we assume that immunity against infection wanes faster and protection against severe disease[16]. First, We describe the states variables for population-immunity that protects against infection, derived from natural infection, for the age group l:

$$\frac{dM^I_{O1-l}}{dt} = \frac{k_1 p_O 1 R_l}{N_l(1+K_s M^H_l)} - \omega_1 M^I_{O1-l},$$

$$\frac{dM^I_{O2-l}}{dt} = \frac{k_1 p_{O2} R_l}{N_l(1+K_s M^H_l)} - \omega_1 M^I_{O2-l},$$

$$\frac{dM^I_{O12-l}}{dt} = \frac{k_1 p_{O12} R_l}{N_l(1+K_s M^H_l)} - \omega_1 M^I_{O12-l},$$

$$\frac{dM^I_{O45-l}}{dt} = \frac{k_1 p_{O45} R_l}{N_l(1+K_s M^H_l)} - \omega_1 M^I_{O45-l},$$

where $M^I_{O1\text{-}l}$, $M^I_{O2\text{-}l}$, $M^I_{O12\text{-}l}$, and $M^I_{O45\text{-}l}$ represent the population-immunity levels derived from infection with Omicron BA.1, Omicron BA.2, and BA.2.12.2, and BA.4/BA.5, among the age group l, respectively, p_{O1}, p_{O2}, p_{O12}, p_{O45} denote the prevalence of Omicron BA.1, Omicron BA.2, BA.2.12.2, and BA.4/BA.5 across all infections, K_s is a positive constant modeling the saturation of antibody production in individuals who were previously infected and developed severe disease, M^I_l is the aggregate of immunities that protect against infection for the age group l. Next, we describe the evolution of population-immunity derived by vaccination:

$$\frac{dM^I_{V-l}}{dt} = k_2 V(t) - k_3 B(t) + \omega_3 M^I_{B-I} - \omega_2 M^I_{V-l},$$

$$\frac{dM^I_{B-l}}{dt} = k_3 B(t) - \omega_3 M^I_{B-l},$$

where $M^I_{V\text{-}l}$ and $M^I_{B\text{-}l}$ are the population-wide immunities derived from vaccination with primary series and booster dose, V(t) and B(t) are the number of vaccine doses administered as primary series or boosters, respectively. We account for the delay between vaccine administration and the development for protection and we consider that immunity increases two weeks after the administration of a single dose, and one week after administration of a booster. Similarly, we describe the changes in the population-immunities that protect against hospitalization and death but we consider different waning rates:

$$\frac{dM_{O1-H}^{H}}{dt} = \frac{k_1 p_{O1} R_l}{N_l(1+K_s M_H^H)} - \omega_4 M_{O1-H}^{H},$$

$$\frac{dM_{O2-H}^{H}}{dt} = \frac{k_1 p_{O2} R_l}{N_l(1+K_s M_H^I)} - \omega_4 M_{O2-H}^{H},$$

$$\frac{dM_{O12-H}^{H}}{dt} = \frac{k_1 p_{O12} R_l}{N_l(1+K_s M_H^I)} - \omega_4 M_{O12-H}^{H},$$

$$\frac{dM_{O45-H}^{H}}{dt} = \frac{k_1 p_{O45} R_l}{N_l(1+K_s M_H^I)} - \omega_4 M_{O45-H}^{H},$$

$$\frac{dM_{V-H}^{I}}{dt} = k_2 V(t) - k_3 B(t) + \omega_5 M_{B-H}^{H} - \omega_4 M_{V-H}^{H},$$

$$\frac{dM_{B-H}^{I}}{dt} = k_3 B(t) - \omega_5 M_{B-H}^{H},$$

Next, we model the transitions among the different compartment for each specific age group *l* as follows:

$$\frac{dS_l}{dt} = -S_l \cdot \sum_{i \in A} \frac{\beta_i \phi_{l,i} (I_i^Y + I_i^A \omega^A + P_i^Y + P_i^A \omega^A)}{N_i(1+\mathbf{K^I}(\mathbf{p})\mathbf{M^I})} + \eta R$$

$$\frac{dE_l}{dt} = S_l \cdot \sum_{i \in A} \frac{\beta_i \phi_{l,i} (I_i^Y + I_i^A \omega^A + P_i^Y + P_i^A \omega^A)}{N_i(1+\mathbf{K^I}(\mathbf{p})\mathbf{M^I})} - \sigma E_l$$

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

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

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

$$\frac{dI_l^Y}{dt} = \rho^Y P_l^Y - (1-\pi_m)\gamma^Y I_l^Y - \frac{\pi_m \mu I_l^Y}{1+\mathbf{K^H}(\mathbf{p})\mathbf{M^H}}$$

$$\frac{dH_l}{dt} = \frac{\pi_m \mu I_l^Y}{1+\mathbf{K^H}(\mathbf{p})\mathbf{M^H}} - \gamma_H H_l - \frac{\nu_m H_l}{1+\mathbf{K^D}(\mathbf{p})\mathbf{M^H}}$$

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

$$\frac{dD_l}{dt} = \frac{\nu_m H_l}{1+\mathbf{K^D}(\mathbf{p})\mathbf{M^H}},$$

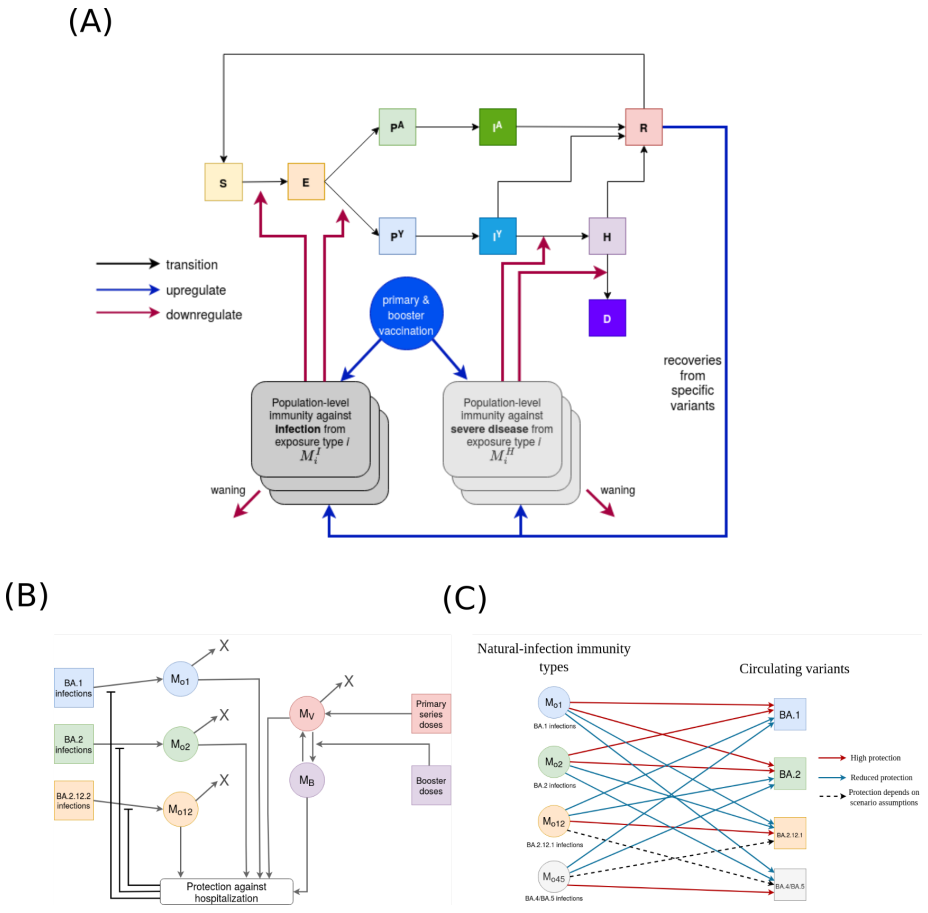

Figure A1. Schematic representation of the model of COVID-19 transmission that explicitly tracks population immunity derived from natural infection and vaccination. (A) Susceptible individuals (S) move to the exposed state (E) when they get infected. Exposed individuals transition into either the pre-symptomatic (PY) or the pre-asymptomatic (PA) compartment. Pre-asymptomatic cases first transition to the infectious asymptomatic compartment (IA) and then to the recovered compartment (R) where they are fully immune to reinfection. Pre-symptomatic individuals first move to the symptomatic compartment (IY); a fraction of those individuals move 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 enjoy a short period of full immunity before returning to the susceptible compartment (S). For each type of immune exposure (i.e., infection with a specific variant or receipt of a specific type of vaccine dose), the model uses two state variables to track the resulting population-level average protection against infection and against severe disease. These variables increase as individuals recover from infections and receive vaccines and they decrease according to waning (half-life) parameters, specific to each exposure type. Immunity state variables modify overall rates of infection and risk of hospitalization/death with efficacies that can vary depending on currently circulating virus variants and the age and risk group of the exposed individual. Variables tracking population-level immunity can be readily modified to capture immunity with respect to future variants as well as multiple types of vaccines and boosters. **(B)** Infection upregulates the population-immunities depending on the evolution of variant distribution among infections. The administration of primary series vaccine dose increases the vaccination-derived immunity, while booster doses transfer vaccination-derived immunity to the more effective booster-derived one. The contribution of natural infections to population-immunities decreases as the overall protection against severe disease increases. That's because less severe infections leave a lower number of antibodies than severe cases. **(C)** The effectiveness of the different population-immunities derived from natural infection captured by the model against the considered circulating variants.

where *A,* represent all possible age groups, ω^A describes 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, $\mathbf{K^I(p)}$ = [K^I_{O1}(p), K^I_{O2}(p), K^I_{O12}(p), K^I_{O45}(p), K^I_V(p), K^I_B(p)), $\mathbf{K^H(p)}$ = [K^H_{O1}(p), K^H_{O2}(p), K^H_{O12}(p), K^H_{O45}(p), K^H_V(p), K^H_B(p], and $\mathbf{K^D(p)}$ = [K^D_{O1}(p), K^D_{O2}(p), K^D_{O12}(p), K^D_{O45}(p), K^D_V(p), K^D_B(p)] are vectors of positive constants that describe the efficacy of immunity in reducing the rates of infection, disease, hospitalization, and death, while $\mathbf{M^I}$ = [M^I_{O1}, M^I_{O2}, M^I_{O12}, M^I_{O45}, M^I_V, M^I_B] and $\mathbf{M^H}$ = [M^H_{O1}, M^H_{O2}, M^H_{O12}, M^H_{O45}, M^H_V, M^H_B] are two vectors consisting of state variables that describe the protection levels derived from vaccination and natural infection against infection and protection, respectively, *p* describes the relative prevalence of each Omicron subvariant. Numerical values of the epidemiological parameters are provided in Table A1 and values of immunological parameters are presented in Table A2.

Age-specific contact patterns. Contact matrices for the US are used to describe mixing patterns between age groups [15]. The model uses three matrices to describe the contact patterns in all locations, schools and workplaces in order to represent 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. Workplaces are considered to be closed during the weekends. The overall contact matrix is calculated as follows:

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

where CM_{all}, CM_s, CM_w, are the contact matrices in 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:

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

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

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	[18]
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	$\frac{1}{2.3}$	[18]
ω^A: relative infectiousness of infectious individuals in compartment I^A	$\frac{2}{3}$	[19]
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. [20]
YFR: symptomatic fatality ratio, age specific (%)	Low risk: [0.001608, 0.003823, 0.003823, 0.05943, 0.4420, 1.130]	$YFR = \frac{IFR}{\tau}$

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

Validation of the immunological dynamics of the 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_3, K_s) were estimated by fitting the results of the multiscale model. Waning rates were calculated depending on the scenario assumptions (Table 1).

Initializing the epidemiological model. Age-specific patterns for immunity history were assumed to match the data for seroprevalence [11,17]. We start accounting for vaccination dose allocation on February 7, 2022. The first date for vaccination is considered to be two weeks before the beginning of the simulation for primary series, and one week for boosters. Vaccine-induced immunity was initiated by considering the vaccination coverages, in terms of administered doses per age group, until the starting date of the fitting period.

In the US, population-immunity generated from Omicron B.1 infections is taken from seroprevalence and corresponds to 57.5% of the population[11]. We estimate that roughly 65.5% and 29% are immunized through vaccination with primary series and boosters, respectively [12]. We assume that there is no significant immunity generated by Omicron infections. Thus, we obtain the following initial age-specific values for Delta-induced and vaccine-induced immunities:

$$M_{O10} = [0.175, 0.2625, 0.455, 0.3955, 0.3255, 0.224],$$

$$M_{V0} = [0, 0.0076, 0.475, 0.5092, 0.5092, 0.72314],$$

$$M_{B0} = [0, 0, 0.212, 0.22, 0.22, 0.32351].$$

Immune escape modeling. 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 immunity against Omicron as follows:

$$K_1^i(p) = K^I(1 - p\epsilon)$$

where *i* can be either O1, O2, O12, or V, *p* is the relative prevalence of Omicron BA.4/BA.5 to previous Omicron variants, ϵ represents the levels of Omicron immune escape to infection/symptoms and to severe disease, respectively. We assume that Omicron BA.4/BA.5 do not escape protection against severe disease. The value of ϵ is set such they reduce the rates of infection and symptomatic disease as follows:

$$\frac{r}{1 + K.(1 - p\epsilon)} = (1 - eff)r.$$

We consider that immunity acquired through infection with a specific variant provides the best protection against the same variant [212213,22]. Also, we assume that all Omicron variants do not escape immunity acquired by booster shots [14]. The protection levels provided by each time of immunities captured in the model in the absence of immune escape are provided in Table A3.

Estimating the prevalence of the Omicron variant. We fit a logistic curve to the relative frequency of Omicron and BA.2 among sequenced SARS-CoV-2 specimens in the US (Figure 1) [8].

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
M^I_V immune waning rate (ω_2)	$\ln(2)/(6 \times 30)$	[23]
M^I_B immune waning rate (ω_3)	$\ln(2)/(3 \times 30)$	[24]
M^H_V immune waning rate (ω_4)	$\ln(2)/(12 \times 30)$	[23]
M^H_B immune waning rate (ω_5)	$\ln(2)/(6 \times 30)$	[24]

Estimating age-specific vaccination rates. Vaccination is modeled 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[12]. Then, the average number of daily administered doses for each age group during April and May 2022 is computed as a rollout for the next month. Booster dose rollout is increased by 5-folds starting from a moment that depends on the considered scenario. The administration of doses stops as soon as it reaches the age-specific levels of vaccine hesitancy summarized in Table A4. For the booster vaccination scenarios 2, 3, and 4, we consider that 70% of fully vaccinated individuals received two booster shots. Hesitancy among children is assumed to be higher than among adults. While we stop the administration of boosters when the number of administered doses reaches 60% of the population.

Making projections. The model is fitted using US data for cases, hospitalization, and mortality ([10], [9]) for the period from 02/21/2022 to 07/04/2022. Then, projections are made for the period between 07/04/2022 and 08/17/2023. Microstochasticities are introduced using the Euler-Maruyama Method, 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 quantiles are computed for each day.

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

Immunity source	Protection against infection	Protection against symptoms	Protection against hospitalization	Protection against death
Infection with Delta	90%	90%	95%	97.5%
Infection with Omicron BA.1, BA.2, BA.12.2.12 and BA.4/BA.5	90%	90%	95%	97.5%
Vaccination with primary series	75% for under 65 and 57% for over 65	90% for under 65 and 80% for over 65	95%	97.5%
Vaccination with booster shots*	88%	88%	95%	97.5%

The model is parameterized using the US data for immunity and vaccination history. Next, it is fitted to the latest trends in COVID-19 cases until July 4, 2022.

Table A4. The assumed hesitancy levels for each age group.

Age groups	Assumed hesitancy level to vaccination
[0-4]	-
[5-11]	30 %
[12-18]	26 %
[19-49]	24.9 % [25]
[50-64]	12 % [26]
[65+]	7 % [26]

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