Supplemental Online Content

Lin D, Gu Y, Xu Y, et al. Association of Primary and Booster Vaccination and Prior Infection With SARS-CoV-2 Infection and Severe COVID-19 Outcomes. *JAMA.* Published online September 26, 2022. doi:10.1001/jama.2022.17876

eMethods
eFigures
eTables

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

eMethods

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Data Sources

Data Linkage

Data from the state's Covid-19 vaccination management system include a person-level view of all doses administered by providers participating in the state's Covid-19 vaccine program, as well as those administered by federal pharmacy providers participating in the Federal Retail Pharmacy Program for COVID-19 Vaccination. These data are refreshed weekly.

Records from the state's lab and case surveillance system are linked to vaccination data weekly. Lab records contain name elements, date of birth, and geographic information for linkage purposes, demographic covariates, and Covid-19 outcomes including hospitalization and death.

Matching Model

Data from NC COVID and CVMS were linked through an integration with the state's health information exchange (NC HealthConnex). NC HealthConnex contains a database that maintains a unique index (or identifier), called the "master patient index", for every patient whose information has been received by NC HealthConnex. Key identifiers (name, date of birth, and address) reported by laboratories, hospitals and health systems, retail and community pharmacies, county health departments, and other healthcare entities, are passed through NC HealthConnex, and a probabilistic algorithm is used to match records to existing identifiers in the database, or to assign a new identifier if the individual cannot be matched to an existing one. Then the master patient index is used to link CVMS and NC COVID records. It was hashed to create a hashed identifier for this study.

Expanded Death Surveillance

To improve the timeliness and completeness of information on Covid-19 deaths, surveillance data include matched electronic death certificate outcomes for Covid-19 causes of death occurring January 1, 2022 forward. North Carolina death certificates listing 'U071' as a cause of death were matched to Covid-19 case records on name, date of birth, sex, social security number, and place of residence using Match Pro 2.2.1 software (cancer.gov).

Protection of Human Subjects

This research was approved by the University of North Carolina at Chapel Hill Institutional Review Board. A data use agreement was signed between the North Carolina Department of Health and Human Services and the University of North Carolina at Chapel Hill.

Statistical Methods

Suppose that we are interested in K immunity-conferring events, such as vaccination and prior infection. For $k = 1, \ldots, K$, let V_k denote the time when the individual experiences the kth immunity-conferring event. In addition, let T denote the time when the individual experiences the clinical outcome of interest (e.g., SARS-CoV-2 infection, hospitalization,

death). Each time is measured in days from the start of the pandemic, i.e., March 2, 2020. Finally, let X denote baseline risk factors, such as demographic variables (i.e., age group, sex, race, ethnicity, geographical region, and county-level vaccination rate).

We specify that the hazard function of T is related to V_k $(k = 1, \ldots, K)$ and X through the Cox regression model[1]

$$\lambda(t|V_1, \ldots, V_K; X) = \lambda_0(t) \exp\left\{\beta^{\mathrm{T}} X + \sum_{k=1}^{K} \eta_k(t - V_k) A_k(t)\right\}, \tag{1}$$

where $\lambda_0(\cdot)$ is an arbitrary baseline hazard function, β is a set of regression parameters representing the effects of baseline risk factors, $\eta_k(\cdot)$ is a function characterizing the time-varying effect of the kth immunity-conferring event, $A_k(t) = I(V_k < t)$, and $I(\cdot)$ is the indicator function. This is a generalization of the Cox model we previously used for evaluating vaccine effectiveness.[2,3] All demographic variables are categorical, and the categories of each variable are compared to its first category. Under this formulation, the baseline hazard function varies over the calendar time, and the effect of an immunity-conferring event on the risk of the clinical outcome depends on the time elapsed since the immunity-conferring event.

Let C denote the censoring time, which is equal to the time of data lock τ but is set to the time of the booster when analyzing the effectiveness of primary series and to the time of the second booster when analyzing the effectiveness of the first booster. We observe $\widetilde{T} = \min(T, C)$ and $\Delta = I(T \leq C)$. We set V_k to infinity if the kth immunity-conferring event did not occur before τ. The data consist of $(\widetilde{T}_i, \Delta_i, V_{1i}, \ldots, V_{Ki}, X_i)$ $(i = 1, \ldots, n)$, where n is the total number of individuals in the population. We let the log hazard ratios $\eta_k(\cdot)$ $(k = 1, \ldots, K)$ be piecewise linear functions of time, with potentially different numbers of pieces and different change points. That is, for $k = 1, \ldots, K$,

$$\eta_k(t) = \sum_{l=0}^{m_k} \gamma_{kl} B_{kl}(t) = \gamma_{k0} t + \gamma_{k1}(t - t_{k1})_+ + \cdots + \gamma_{km_k}(t - t_{km_k})_+, \tag{2}$$

where $t_+ = t$ if $t > 0$ and 0 otherwise, $t_{k1}, \ldots, t_{km_k}$ are the m_k change points, and $\gamma_{k0}, \ldots, \gamma_{km_k}$ are the unknown parameters pertaining to the slope of each piece. For prior infection, we add an intercept c_k to the right side of (2) to account for the fact that the log hazard ratio upon infection is not necessarily 0. Typically, we place a change point at every 30 days; however, we may place the first change point at 2 weeks to detect an early peak or place the change points at every 60 days or even fewer time points if the data are sparse. We constraint the parameters such that the effect of a two-dose mRNA vaccine regimen between dose 1 to dose 2 is the same as the effect of the corresponding one-dose vaccine regimen and that the effect of every prior infection is the same. For $k = 1, \ldots, K$, write $\gamma_k = (\gamma_{k0}, \ldots, \gamma_{km_k})^{\mathrm{T}}$, and $Z_{ki}(t) = \big(B_{k0}(t - V_{ki})A_{ki}(t), \ldots, B_{km_k}(t - V_{ki})A_{ki}(t)\big)^{\mathrm{T}}$, where $A_{ki}(t) = I(V_{ki} < t)$. We further write $\gamma = \big(\gamma_1^{\mathrm{T}}, \gamma_2^{\mathrm{T}}, \ldots, \gamma_K^{\mathrm{T}}\big)^{\mathrm{T}}$ and $Z_i(t) = \big(Z_{1i}(t)^{\mathrm{T}}, Z_{2i}(t)^{\mathrm{T}}, \ldots, Z_{Ki}(t)^{\mathrm{T}}\big)^{\mathrm{T}}$. Then the partial likelihood for β and γ takes the form

$$L(\beta, \gamma) = \prod_{i=1}^{n} \left\{ \frac{e^{\beta^{\mathrm{T}} X_i + \gamma^{\mathrm{T}} Z_i(\widetilde{T}_i)}}{S^{(0)}(\beta, \gamma; \widetilde{T}_i)} \right\}^{\Delta_i}, \tag{3}$$

where $S^{(0)}(\beta,\gamma;t)=\sum_{j=1}^{n} I(\widetilde{T}_j \geq t)e^{\beta^{\mathrm{T}}X_j+\gamma^{\mathrm{T}}Z_j(t)}$.

The analysis dataset contains the information of all the individuals who have been vaccinated or have developed SARS-CoV-2 by the end of the study. For each stratum defined by the combination of the demographic variables, we can determine the number of individuals who have neither been vaccinated nor developed SARS-CoV-2 by the end of the study by subtracting the number of individuals in the analysis dataset from the total number of individuals in the census data. Suppose that there are $\widetilde{n}$ individuals in the analysis dataset and that there are n_g individuals in the gth stratum ($g=1,\ldots,G$) out of those who are not in the analysis dataset. Note that the individuals in the same stratum have the same value of X. Note also that, for the individuals not in the analysis dataset, $\widetilde{T}=\tau$, $\Delta=0$, and $V_k>\tau$ ($k=1,\ldots,K$). Thus, $S^{(0)}(\beta,\gamma;t)=\sum_{j=1}^{\widetilde{n}} I(\widetilde{T}_j \geq t)e^{\beta^{\mathrm{T}}X_j+\gamma^{\mathrm{T}}Z_j(t)}+\sum_{g=1}^{G} n_g e^{\beta^{\mathrm{T}}X_g}$, where X_g is the value of X for the gth stratum.

We maximize $L(\beta,\gamma)$ through the Newton-Raphson algorithm. The resulting maximum partial likelihood estimator $(\widehat{\beta},\widehat{\gamma})$ is approximately normal with mean (β,γ) and covariance matrix $\mathcal{I}^{-1}(\widehat{\beta},\widehat{\gamma})$, where $\mathcal{I}(\beta,\gamma)$ is the negative second-derivative matrix of $\log L(\beta,\gamma)$. Given $\widehat{\gamma}_k$, we estimate the effectiveness of the kth immunity-conferring event in reducing the risk of the clinical outcome by

$$\widehat{VE}_k(t)=1-e^{\widehat{\eta}_k(t)}=1-\exp\left\{\sum_{l=0}^{m_k}\widehat{\gamma}_{kl}B_{kl}(t)\right\}$$

and construct the 95% confidence interval. We also show "No. at risk", which is the number of individuals with a certain exposure (i.e., vaccination or prior infection) who are still under observation at a certain time point since the exposure.

We consider several extensions of the above framework:

First, to allow vaccine effectiveness to depend on vaccine cohort (i.e., individuals who are vaccinated during a particular calendar period), we let the log hazard ratio $\eta_k(\cdot)$ to take a different value for each vaccine cohort. Likewise, to allow the protection of prior infection to depend on the type of variant (e.g., delta or omicron), we let the log hazard ratio $\eta_k(\cdot)$ to take a different value for each type of variant.

Second, we consider SARS-CoV-2 infections as recurrent events and formulate the effects of baseline risk factors and immunity-conferring events on the rate of infection through the multiplicative intensity model[4] with the same regression parameters as model (1). We modify the partial likelihood given in (3) as follows: an individual will contribute as many terms to the product in $L(\beta,\gamma)$ as the number of infections that have been detected, and they will be included in the summation in $S^{(0)}(\beta,\gamma;t)$ as long as they are under observation at time t.

Third, to study the interacting effects of boosters and prior infections, we replace the linear predictor on the right side of (1) by

$$\sum_j I(S_j<t)\eta_S(t-S_j)+I(V<t,S_1\geq V)\eta_V(t-V)+I(S_1<V<t)\eta_{S,V}(t-V),$$

where S_j is the time of the jth prior infection, and V is the time of the booster shot. The function $\eta_{S,V}(t-V)$ characterizes the time-varying effect of the booster among those who have been infected before boosting, $\eta_V(t-V)$ characterizes the time-varying effect of the

booster among those who have not been infected before boosting, and $\eta_S(t-S)$ characterizes the time-varying effect of prior infection among individuals who have primary vaccination.

Sensitivity Analysis

We performed multiple imputation of missing hospitalization and survival data in two steps. In the first step, we estimated the probability that a SARS-CoV-2 infection leads to a clinical event of interest (i.e., hospitalization or death) by fitting a logistic regression model to the observed data with the following covariates: demographic variables, infection cohort (March 1, 2020 – October 15, 2020; October 16, 2020 – December 15, 2020; December 16, 2020 – January 31, 2021; February 1, 2021 – May 31, 2021; June 1, 2021 – July 15, 2021; July 16, 2021 – September 30, 2021; October 1, 2021 – December 15, 2021; December 16, 2021 – May 3, 2022), prior infection (yes or no), vaccination status (unvaccinated; 1-dose BNT162b2; 2-dose BNT162b2; 2-dose BNT162b2 plus booster; 1-dose mRNA-1273; 2-dose mRNA-1273; 2-dose mRNA-1273 plus booster; 1-dose Ad26.COV2.S; 1-dose Ad26.COV2.S plus booster), and infection time since vaccination and its square. We imputed the missing event status by generating a binary random variable with success probability estimated from the logistic regression model. We also imputed the missing event status by multiplying the estimated probability by 1.5 for any person who was vaccinated or previously infected. In the second step, we imputed the missing event times by linear regression. (This step was restricted to those who were hospitalized or died, since the event time would be equal to the censoring time otherwise.) The response variable in the linear regression model was $\log(Y+1)$, where Y is the gap time between the SARS-CoV-2 infection and the clinical event. We included the same covariates as in the first step. We repeated the two steps 5 times to create 5 complete datasets and analyzed them separately. We then pooled the 5 sets of estimation results to estimate the hazard ratio function and obtain the variance estimate by using Rubin's formula[5].

We performed the above multiple imputation for missing data on hospitalization and death. The resulting estimates are shown in eFigures 10 and 11. The basic conclusions are the same as those of the complete-case analysis (Figures 1 and 3).

References

1. Cox DR. Regression models and life-tables. J R Stat Soc B 1972;34(2):187-202.

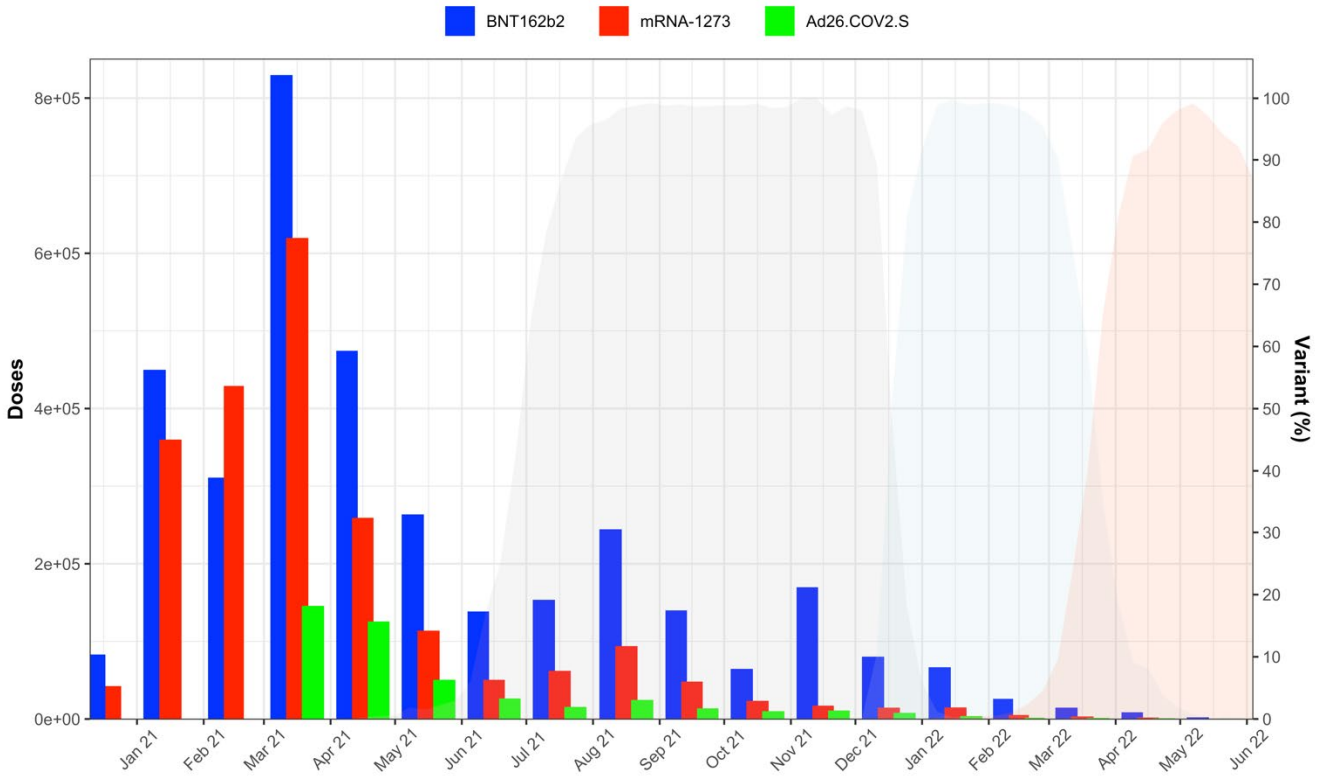
2. Lin DY, Gu Y, Zeng D, Janes HE, Gilbert PB. Evaluating vaccine efficacy against SARS-CoV-2 infection. Clin Infect Dis 2022;74(3):544-52.

3. Lin DY, Gu Y, Wheeler B, et al. Effectiveness of Covid-19 vaccines over a 9-month period in North Carolina. N Engl J Med 2022;386(10):933-41.

4. Andersen PK, Gill RD. Cox's regression model for counting processes: a large sample study. Ann Stat 1982;10(4):1100-20.

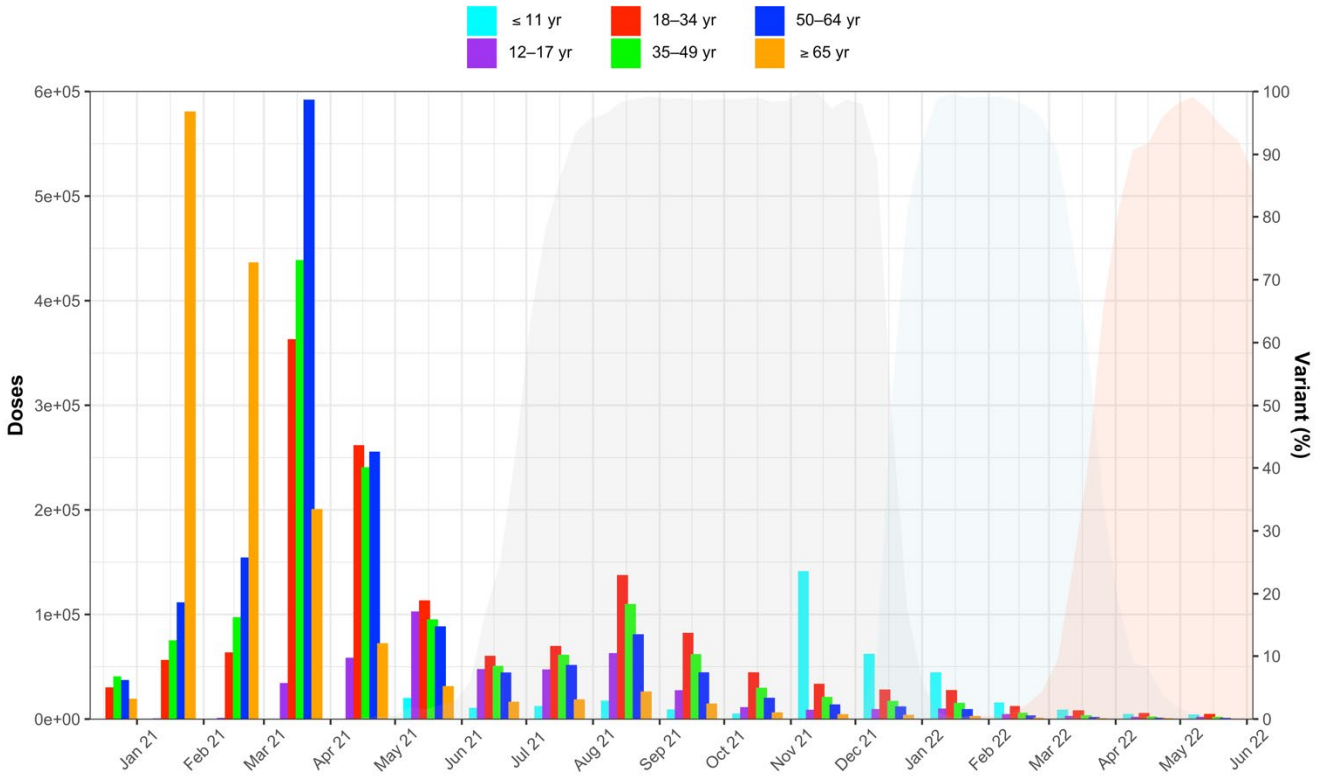
5. Rubin DB. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley, 1987.

eFigure 1. Distribution of primary vaccination products over time



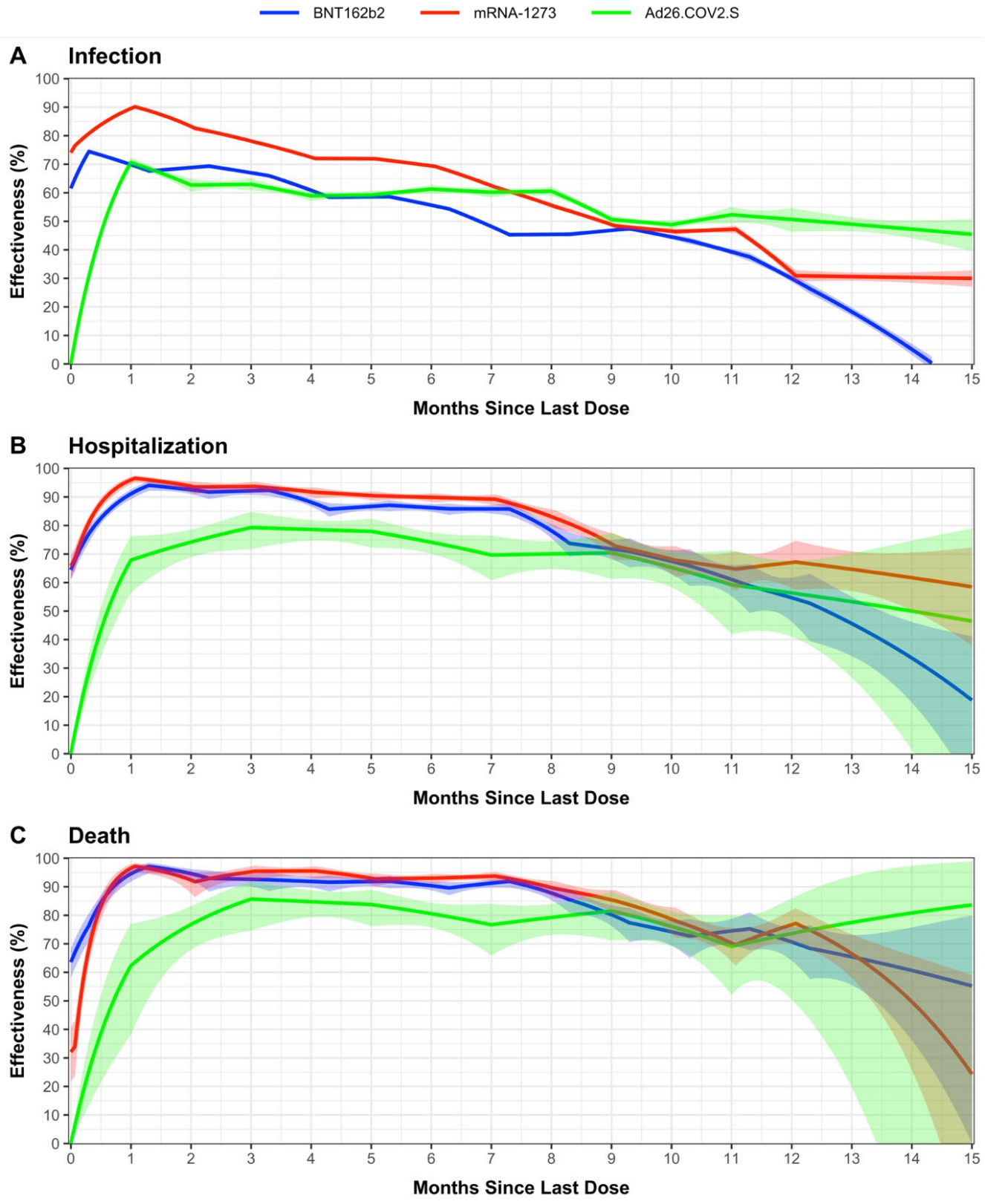
The proportions of delta, omicron BA.1.1/B.1.1.529, and BA.2/BA.2.12.1 variants are indicated by the light gray, blue, and coral areas, respectively.

eFigure 2. Distribution of primary vaccination over time by age group



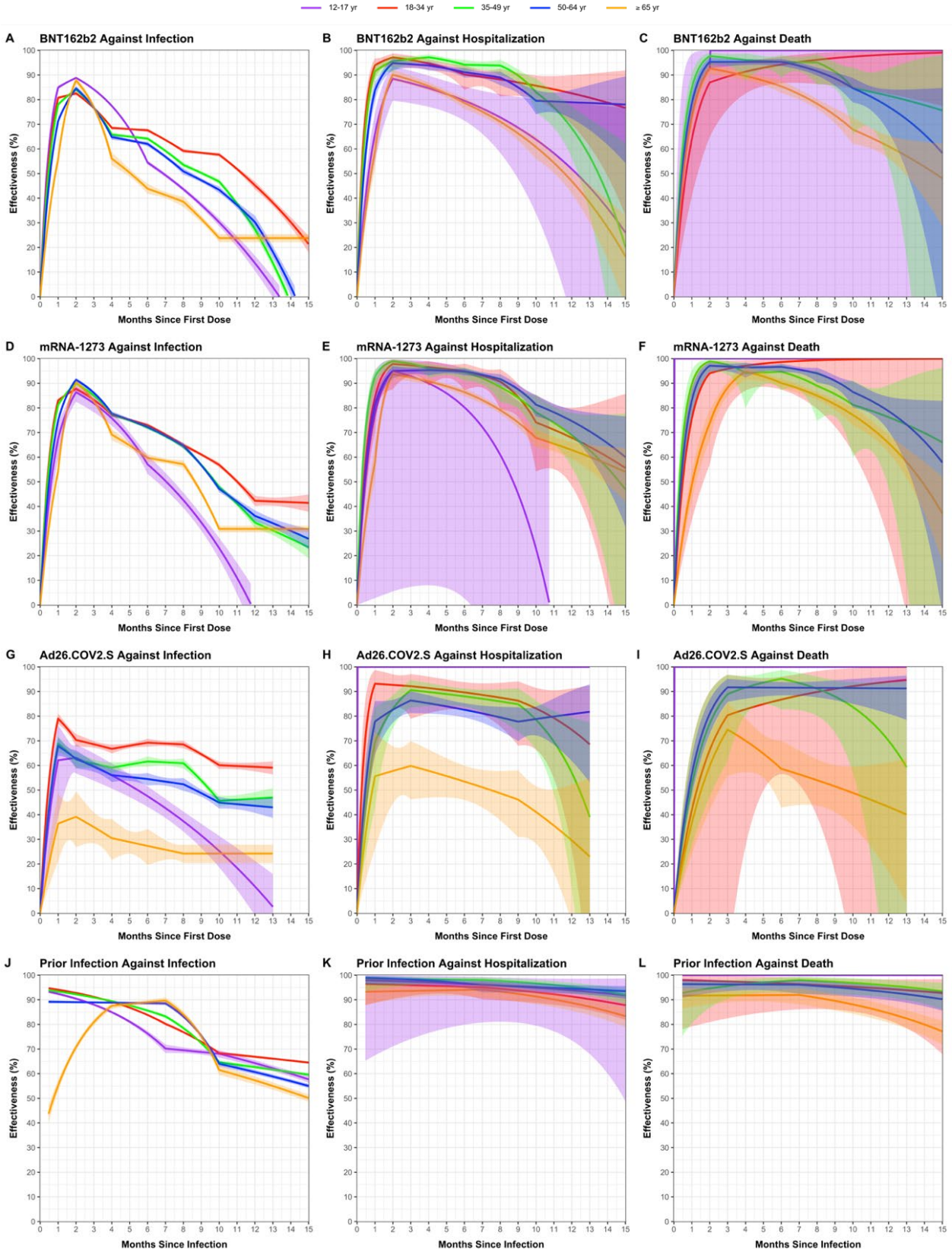
The proportions of delta, omicron BA.1.1/B.1.1.529, and BA.2/BA.2.12.1 variants are indicated by the light gray, blue, and coral areas, respectively.

eFigure 3. Effectiveness of primary vaccination series in reducing the risk of SARS-CoV-2 infection, hospitalization, or death as a function of time since last dose



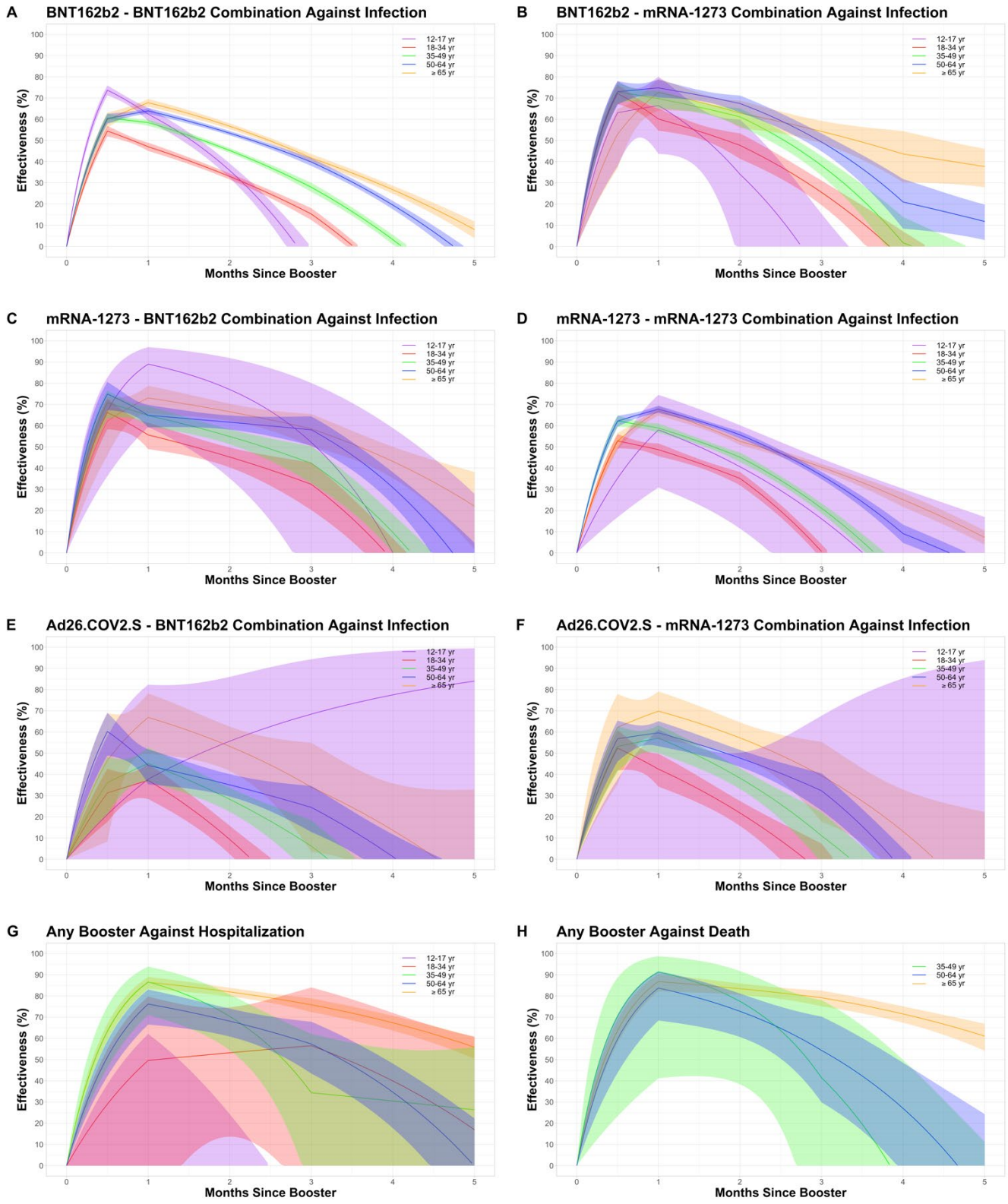
Estimates are shown by solid curves, and 95% confidence intervals are shown by shaded bands.

eFigure 4. Effectiveness of primary vaccination series and prior infection in reducing the risk of SARS-CoV-2 infection, hospitalization, or death by age group



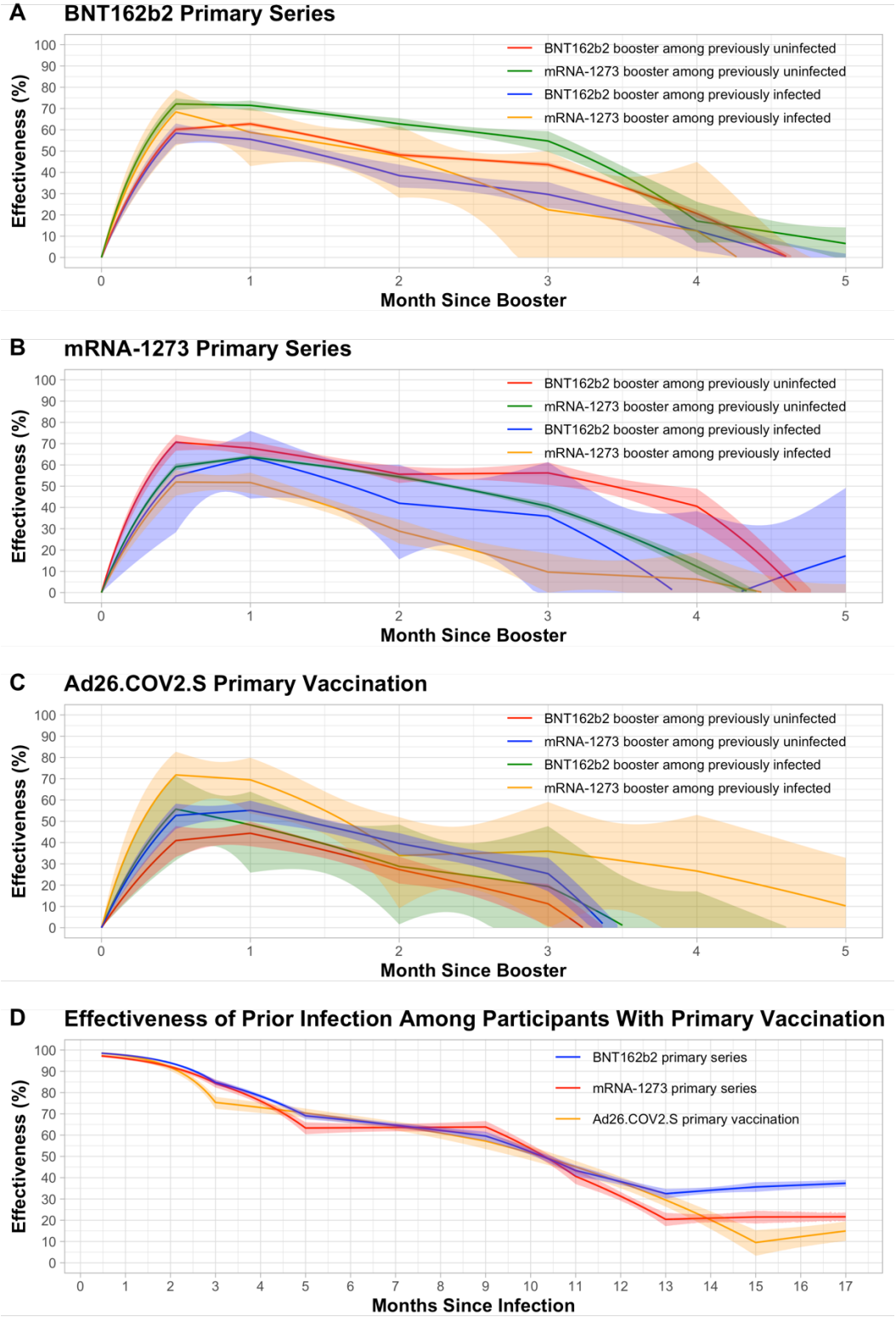
Estimates are shown by solid curves, and 95% confidence intervals are shown by shaded bands.

eFigure 5. Effectiveness of booster vaccination relative to primary vaccination in reducing the risk of SARS-CoV-2 infection, hospitalization, or death by age group



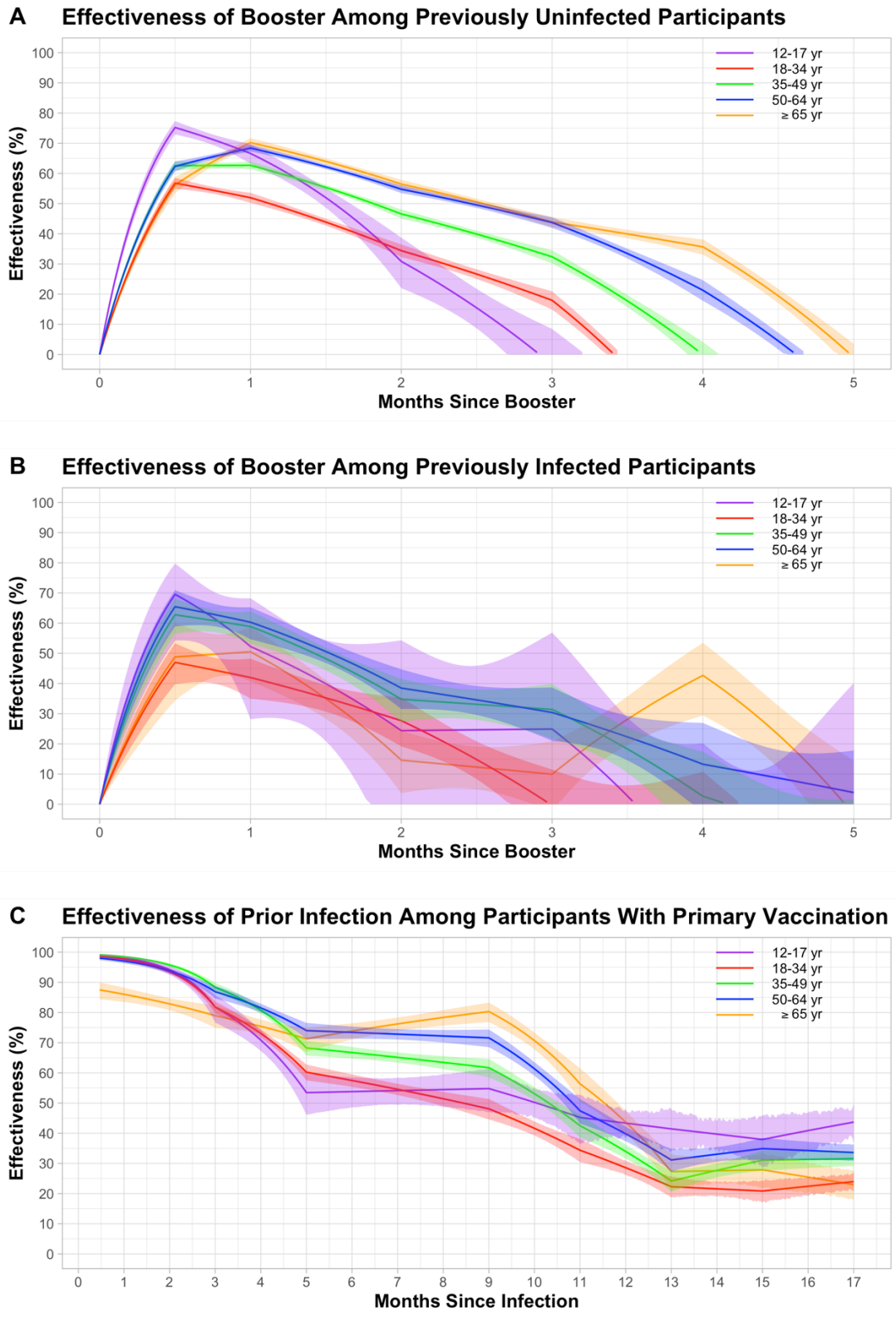
Estimates of effectiveness are shown by solid curves, and 95% confidence intervals are shown by shaded bands.

eFigure 6. Effectiveness of booster vaccination (relative to primary vaccination) and prior infection among persons with primary vaccination in reducing the rate of SARS-CoV-2 infection, by primary and booster combination



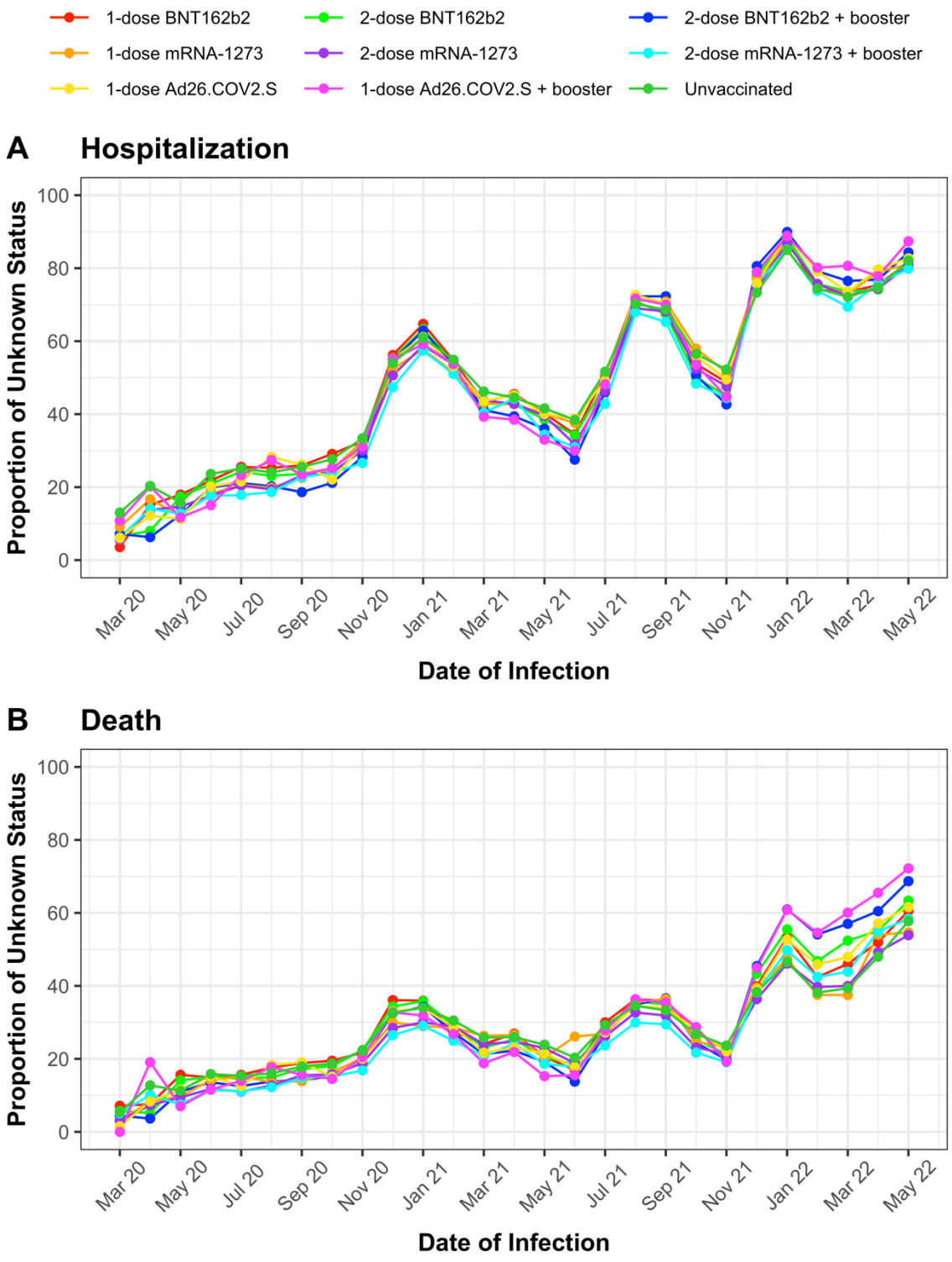
Estimates of effectiveness are shown by solid curves, and 95% confidence intervals are shown by shaded bands.

eFigure 7. Effectiveness of booster vaccination (relative to primary vaccination) and prior infection among persons with primary vaccination in reducing the rate of SARS-CoV-2 infection by age group

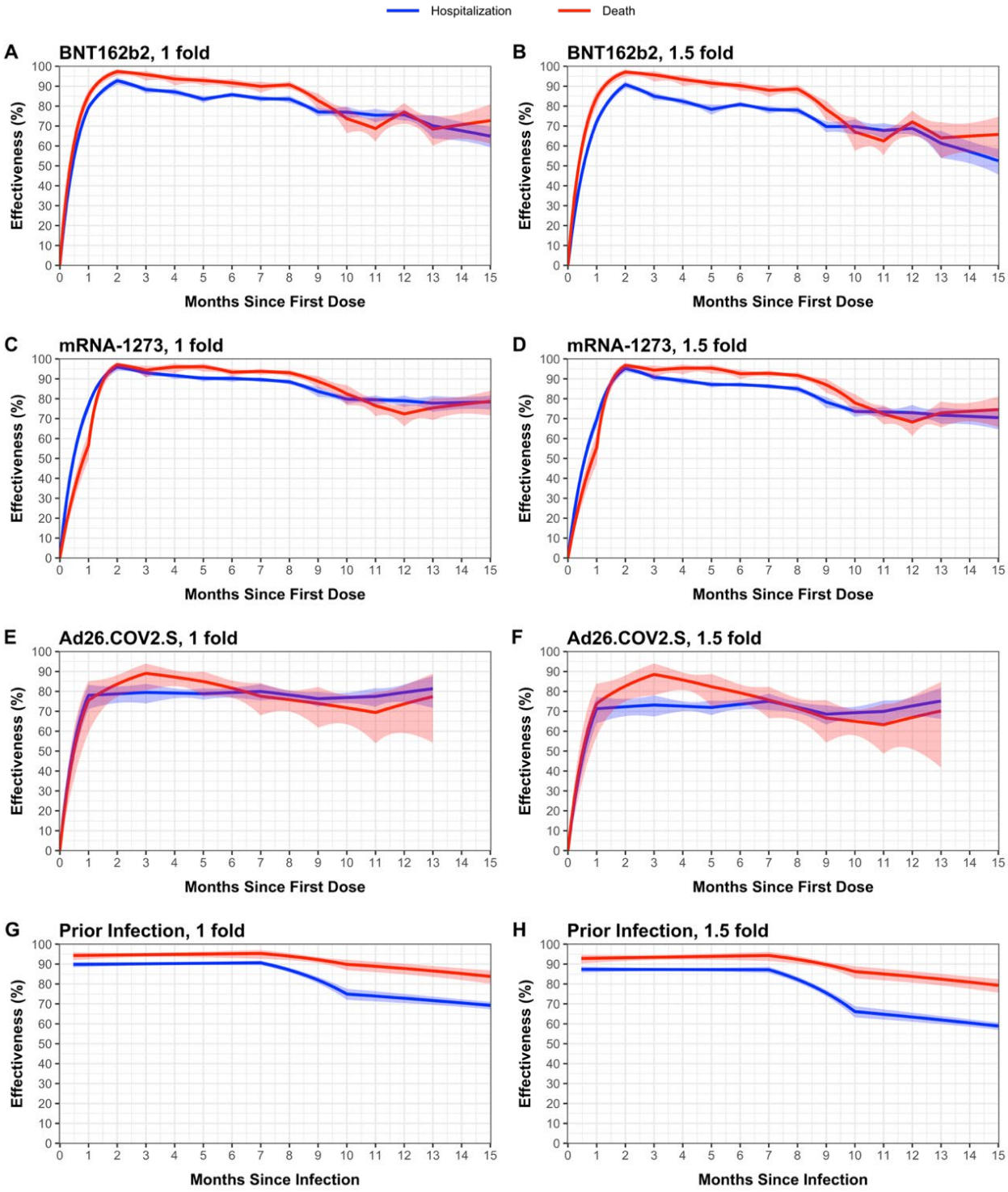


Estimates of effectiveness are shown by solid curves, and 95% confidence intervals are shown by shaded bands.

eFigure 8. Proportions of unknown hospitalization status and unknown survival status according to date of SARS-CoV-2 infection and vaccination status

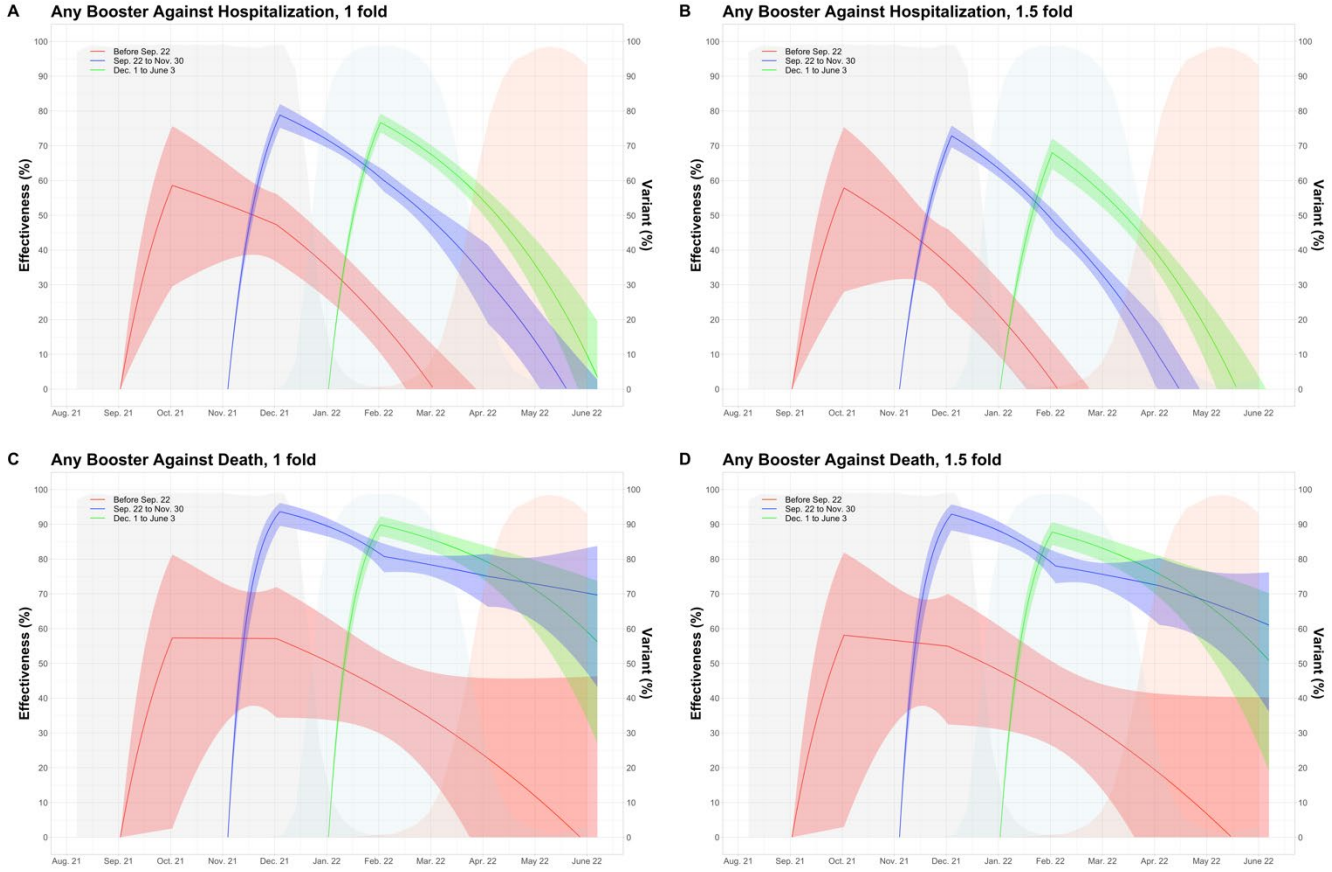


eFigure 9. Effectiveness of primary vaccination series and prior infection in reducing the risk of hospitalization or death under multiple imputation



Estimates are shown by solid curves, and 95% confidence intervals are shown by shaded bands. 1 fold and 1.5 fold mean that the missing hospitalization or death status was imputed with the estimated probability and 1.5 times the estimated probability for any person who was vaccinated or previously infected.

eFigure 10. Effectiveness of booster vaccination (relative to primary vaccination) and prior infection in reducing the risk of hospitalization or death among persons with primary vaccination under multiple imputation



Estimates of effectiveness are shown by solid curves, and 95% confidence intervals are shown by shaded bands. 1 fold and 1.5 fold mean that the missing hospitalization or death status was imputed with the estimated probability and 1.5 times the estimated probability for any person who was vaccinated or previously infected.

eTable 1. Estimates (95% CI) and numbers at risk for the effectiveness of primary vaccination series and prior infection in reducing the risk of SARS-CoV-2 infection, hospitalization, or death

Mos.	Infection		Hospitalization		Death	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
A. BNT162b2						
0	0.0% (0.0, 0.0)	3,521,440	0.0% (0.0, 0.0)	3,066,099	0.0% (0.0, 0.0)	3,245,199
1	74.5% (74.0, 75.0)	3,519,881	77.2% (74.0, 79.9)	3,064,425	76.4% (71.2, 80.6)	3,243,795
2	67.6% (66.9, 68.3)	3,509,554	94.1% (92.2, 95.5)	3,055,710	97.1% (94.7, 98.4)	3,234,460
3	69.3% (68.6, 70.0)	3,494,650	91.8% (89.2, 93.7)	3,043,220	92.9% (88.3, 95.7)	3,220,964
4	66.0% (65.3, 66.6)	3,465,780	92.3% (90.3, 94.0)	3,019,069	92.4% (88.5, 95.1)	3,194,870
5	58.4% (57.8, 59.0)	3,398,495	85.7% (83.1, 87.9)	2,960,624	91.6% (88.3, 94.0)	3,132,672
6	58.6% (58.0, 59.2)	3,301,065	87.1% (85.0, 88.9)	2,875,099	91.9% (89.4, 93.8)	3,042,199
7	54.3% (53.6, 55.0)	3,028,898	85.8% (83.7, 87.7)	2,633,960	89.6% (87.0, 91.6)	2,789,604
8	45.3% (44.5, 46.1)	2,595,997	85.8% (83.4, 87.8)	2,248,009	91.9% (89.7, 93.7)	2,386,249
9	45.4% (44.7, 46.2)	1,887,967	73.7% (69.0, 77.7)	1,617,989	85.5% (80.9, 88.9)	1,726,118
10	47.4% (46.6, 48.2)	1,380,809	70.9% (65.3, 75.6)	1,174,191	77.4% (70.6, 82.6)	1,256,639
11	43.2% (42.0, 44.4)	1,101,712	65.9% (58.8, 71.7)	932,920	72.7% (65.1, 78.7)	999,620
12	37.5% (36.0, 39.0)	954,083	58.8% (49.3, 66.5)	805,224	75.2% (67.7, 81.0)	863,731
13	26.4% (24.6, 28.2)	766,629	52.7% (39.5, 63.1)	645,546	68.4% (57.6, 76.5)	693,224
14	14.5% (13.0, 16.0)	565,229	42.2% (30.7, 51.9)	476,137	64.1% (51.5, 73.4)	511,904
15	0.8% (-1.5, 3.0)	254,722	29.4% (10.3, 44.4)	212,967	59.1% (27.2, 77.0)	230,479
B. mRNA-1273						
0	0.0% (0.0, 0.0)	2,160,179	0.0% (0.0, 0.0)	1,926,815	0.0% (0.0, 0.0)	2,036,313
1	76.5% (75.7, 77.2)	2,160,111	68.3% (63.9, 72.2)	1,926,403	33.9% (23.3, 43.1)	2,036,246
2	90.1% (89.6, 90.7)	2,157,582	96.5% (95.1, 97.6)	1,924,190	97.2% (95.1, 98.4)	2,033,886
3	82.6% (81.8, 83.4)	2,153,383	93.5% (91.0, 95.3)	1,920,653	91.7% (86.2, 95.0)	2,030,017
4	77.7% (77.0, 78.5)	2,146,409	93.7% (91.5, 95.3)	1,914,835	95.4% (92.0, 97.4)	2,023,616
5	72.0% (71.3, 72.7)	2,129,618	91.6% (89.6, 93.3)	1,900,516	95.5% (92.9, 97.2)	2,008,090
6	71.9% (71.3, 72.6)	2,106,376	90.4% (88.6, 91.9)	1,880,254	92.8% (90.3, 94.6)	1,986,434
7	69.2% (68.5, 69.9)	2,060,049	89.8% (88.1, 91.3)	1,839,149	93.0% (91.1, 94.5)	1,942,825
8	61.9% (61.1, 62.7)	1,878,101	89.2% (87.1, 90.9)	1,674,215	93.7% (91.8, 95.2)	1,770,304
9	55.1% (54.3, 55.9)	1,458,630	82.5% (79.1, 85.4)	1,294,751	89.3% (85.9, 91.9)	1,373,279
10	48.4% (47.5, 49.3)	1,045,192	72.7% (67.8, 77.0)	915,843	85.1% (80.1, 88.8)	978,688
11	46.4% (45.3, 47.5)	821,772	67.8% (62.0, 72.8)	714,471	78.0% (72.2, 82.7)	766,578
12	47.2% (45.8, 48.5)	731,059	64.7% (57.2, 70.9)	634,042	69.6% (62.3, 75.5)	681,103
13	30.9% (28.9, 32.9)	645,288	67.2% (57.5, 74.7)	559,517	77.1% (70.1, 82.5)	601,193

14	30.6% (29.1, 32.0)	520,303	64.5% (56.8, 70.8)	451,633	65.6% (56.6, 72.8)	485,435
15	30.3% (28.4, 32.2)	305,513	61.5% (49.6, 70.6)	265,846	48.3% (22.6, 65.4)	285,977
C. Ad26.COV2.S						
0	0.0% (0.0, 0.0)	440,129	0.0% (0.0, 0.0)	380,818	0.0% (0.0, 0.0)	406,132
1	70.6% (68.8, 72.3)	439,221	67.9% (56.5, 76.3)	379,982	62.3% (38.2, 77.0)	405,294
2	62.7% (60.3, 64.9)	437,866	74.2% (68.9, 78.6)	378,858	76.8% (67.9, 83.2)	404,056
3	63.0% (60.8, 65.0)	435,251	79.3% (71.7, 84.8)	376,632	85.7% (74.6, 91.9)	401,641
4	58.9% (57.1, 60.7)	432,038	78.6% (74.7, 81.9)	373,915	84.7% (79.3, 88.7)	398,694
5	59.2% (57.7, 60.7)	425,930	77.9% (72.2, 82.4)	368,705	83.8% (76.1, 89.0)	393,062
6	61.3% (59.6, 62.8)	414,586	74.1% (70.1, 77.6)	358,816	80.5% (75.7, 84.4)	382,498
7	60.2% (58.3, 62.0)	390,458	69.7% (60.8, 76.5)	337,631	76.7% (65.9, 84.0)	359,989
8	60.5% (58.9, 62.1)	338,058	70.0% (64.8, 74.5)	291,736	79.2% (73.1, 84.0)	311,684
9	50.6% (49.1, 52.1)	284,545	70.4% (61.3, 77.4)	245,516	81.5% (71.2, 88.1)	262,524
10	48.8% (47.2, 50.4)	240,794	65.3% (58.3, 71.1)	207,765	76.1% (69.2, 81.4)	222,170
11	52.3% (49.3, 55.1)	218,446	59.2% (41.9, 71.4)	188,515	69.0% (52.1, 80.0)	201,547
12	50.7% (46.3, 54.7)	196,713	56.3% (41.0, 67.7)	169,534	73.6% (50.4, 85.9)	181,301
13	49.0% (46.4, 51.4)	161,203	53.3% (26.7, 70.2)	138,412	77.5% (19.6, 93.7)	148,101
D. Prior Infection						
0	100% (100, 100)	2,483,990	100% (100, 100)	881,844	100% (100, 100)	1,604,620
1	90.9% (90.7, 91.1)	2,406,786	96.3% (94.3, 97.5)	867,648	93.5% (90.6, 95.5)	1,571,853
2	89.6% (89.4, 89.8)	2,362,389	96.2% (94.8, 97.3)	856,368	93.8% (91.7, 95.4)	1,548,583
3	88.1% (88.0, 88.3)	2,335,577	96.2% (95.1, 97.1)	849,036	94.2% (92.5, 95.5)	1,532,666
4	86.5% (86.3, 86.6)	2,249,852	96.2% (95.1, 97.0)	825,919	94.5% (92.8, 95.8)	1,481,239
5	84.6% (84.4, 84.8)	1,717,790	96.2% (94.9, 97.1)	750,271	94.8% (92.8, 96.2)	1,211,979
6	82.5% (82.2, 82.7)	1,484,258	96.1% (94.5, 97.3)	699,530	95.1% (92.5, 96.7)	1,074,813
7	80.0% (79.6, 80.4)	1,426,510	96.1% (93.9, 97.5)	673,394	95.3% (92.2, 97.2)	1,031,374
8	75.8% (75.5, 76.1)	1,370,276	95.2% (93.6, 96.5)	647,753	94.4% (92.0, 96.0)	989,548
9	70.7% (70.4, 71.0)	1,223,352	94.2% (92.7, 95.3)	600,869	93.2% (91.1, 94.7)	889,736
10	64.5% (64.1, 65.0)	1,038,023	92.8% (90.5, 94.6)	549,565	91.7% (88.4, 94.1)	770,673
11	63.4% (63.0, 63.8)	941,826	92.0% (89.7, 93.7)	509,482	90.7% (87.5, 93.0)	702,805
12	62.2% (61.9, 62.6)	897,129	91.0% (88.9, 92.7)	487,367	89.5% (86.5, 91.8)	669,574
13	61.0% (60.7, 61.3)	850,769	89.9% (87.9, 91.6)	462,450	88.1% (85.3, 90.5)	634,298
14	59.8% (59.5, 60.1)	787,949	88.7% (86.7, 90.5)	427,329	86.6% (83.8, 89.0)	586,516
15	58.5% (58.1, 58.8)	731,699	87.4% (85.1, 89.3)	396,343	84.9% (81.8, 87.5)	543,382

eTable 2. Estimates (95% CI) and numbers at risk for the effectiveness of primary vaccination series by date of first dose and of prior infection by type of variant in reducing the risk of SARS-CoV-2 infection, hospitalization, or death

A. BNT162b2 Against Infection

Mos.	Dec 2020–Mar 2021		Apr–May 2021		June–July 2021		Aug–Sep 2021		Oct–Dec 2021		Jan–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	1,629,950	0.0% (0.0, 0.0)	774,272	0.0% (0.0, 0.0)	296,259	0.0% (0.0, 0.0)	383,958	0.0% (0.0, 0.0)	318,279	0.0% (0.0, 0.0)	118,722
1	80.9% (80.0, 81.8)	1,629,942	87.3% (86.0, 88.5)	774,266	85.2% (84.0, 86.3)	296,242	83.0% (82.0, 83.9)	383,898	67.3% (66.1, 68.5)	318,192	72.9% (70.3, 75.3)	117,341
2	95.1% (94.6, 95.6)	1,629,910	90.2% (88.8, 91.4)	774,239	88.6% (87.7, 89.6)	296,113	86.6% (85.3, 87.8)	383,254	42.9% (41.8, 43.9)	317,635	55.2% (47.9, 61.4)	108,403
3	90.1% (89.0, 91.1)	1,629,855	82.6% (81.6, 83.7)	774,176	83.4% (81.9, 84.7)	295,707	69.3% (67.7, 70.9)	382,110	36.7% (35.8, 37.6)	317,080	52.8% (49.0, 56.3)	95,722
4	81.5% (80.4, 82.6)	1,629,825	79.8% (79.0, 80.6)	773,772	83.5% (81.8, 85.0)	295,065	42.2% (41.3, 43.1)	380,577	29.8% (28.7, 30.9)	316,758	50.2% (45.3, 54.8)	69,783
5	73.2% (72.4, 74.1)	1,629,077	78.0% (77.1, 78.9)	772,070	51.1% (48.9, 53.1)	293,806	42.3% (41.6, 42.9)	378,976	22.2% (20.4, 24.0)	316,365		
6	74.2% (73.5, 74.9)	1,621,888	80.1% (79.1, 81.1)	769,397	37.0% (35.8, 38.2)	290,093	42.3% (41.5, 43.0)	372,940	13.8% (11.0, 16.6)	246,747		
7	65.2% (64.3, 66.1)	1,575,216	39.4% (38.3, 40.5)	743,793	37.9% (37.1, 38.7)	270,335	42.3% (41.1, 43.5)	359,661	13.8% (11.0, 16.6)	79,893		
8	65.4% (64.4, 66.4)	1,348,593	40.3% (39.7, 40.9)	632,915	38.7% (37.6, 39.9)	247,919	42.3% (40.6, 44.0)	352,031				
9	43.7% (42.3, 45.1)	923,729	41.2% (40.7, 41.7)	486,418	39.6% (37.7, 41.5)	233,877	42.3% (40.6, 44.0)	243,943				
10	45.7% (44.9, 46.4)	662,253	42.1% (41.2, 43.0)	438,674	39.6% (37.7, 41.5)	229,095						
11	36.5% (35.9, 37.1)	555,453	42.1% (41.2, 43.0)	423,280	39.6% (37.7, 41.5)	122,979						
12	25.8% (25.0, 26.6)	507,117	42.1% (41.2, 43.0)	415,348								
13	13.3% (11.9, 14.7)	484,793	42.1% (41.2, 43.0)	281,836								
14	13.3% (11.9, 14.7)	472,731										
15	13.3% (11.9, 14.7)	254,722										

eTable 2 (cont.)

B. BNT162b2 Against Hospitalization

Mos.	Dec 2020–Mar 2021		Apr–June 2021		July 2021–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	1,439,636	0.0% (0.0, 0.0)	790,948	0.0% (0.0, 0.0)	835,515
1	81.6% (79.0, 83.8)	1,439,426	80.1% (75.1, 84.2)	790,885	79.9% (76.6, 82.8)	834,114
2	96.6% (95.6, 97.4)	1,439,338	96.1% (93.8, 97.5)	790,825	96.0% (94.5, 97.0)	825,547
3	94.9% (94.0, 95.7)	1,439,246	94.8% (93.4, 95.9)	790,611	89.8% (87.9, 91.4)	813,363
4	92.4% (90.2, 94.1)	1,439,188	93.2% (90.8, 95.0)	790,034	74.2% (68.7, 78.8)	789,847
5	90.4% (89.1, 91.5)	1,438,472	91.5% (89.8, 92.8)	788,132	72.8% (68.8, 76.3)	734,020
6	87.9% (86.2, 89.4)	1,432,025	89.3% (85.8, 91.9)	784,941	71.3% (66.9, 75.1)	658,133
7	87.4% (86.4, 88.3)	1,389,622	82.9% (80.2, 85.3)	754,441	69.7% (62.8, 75.3)	489,897
8	86.9% (85.0, 88.5)	1,184,856	72.9% (67.6, 77.2)	640,508	68.0% (57.2, 76.0)	422,645
9	79.5% (77.6, 81.2)	799,071	70.6% (66.5, 74.2)	503,905	66.2% (50.4, 76.9)	315,013
10	67.9% (63.0, 72.1)	564,538	68.1% (62.9, 72.7)	460,142		
11	63.3% (59.9, 66.3)	469,778	65.5% (56.7, 72.5)	445,791		
12	58.0% (51.4, 63.7)	427,307	62.6% (48.7, 72.7)	377,917		
13	49.0% (42.6, 54.7)	408,117	59.5% (38.8, 73.2)	237,429		
14	38.1% (27.4, 47.2)	397,894				
15	24.8% (4.8, 40.7)	212,967				

C. BNT162b2 Against Death

Mos.	Dec 2020–June 2021		July 2021–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	2,350,490	0.0% (0.0, 0.0)	894,709
1	97.5% (96.0, 98.4)	2,350,474	87.9% (83.0, 91.4)	893,321
2	99.9% (99.8, 100.0)	2,350,385	98.5% (97.1, 99.3)	884,075
3	99.3% (98.9, 99.6)	2,350,115	94.3% (91.8, 96.1)	870,849
4	92.8% (89.4, 95.1)	2,349,475	77.8% (68.4, 84.5)	845,395
5	92.5% (90.9, 93.8)	2,346,800	77.8% (72.1, 82.4)	785,872
6	92.2% (90.3, 93.7)	2,336,819	77.8% (72.0, 82.3)	705,380
7	91.4% (90.3, 92.4)	2,261,115	77.7% (68.2, 84.4)	528,489
8	90.5% (88.7, 92.0)	1,930,368	77.7% (62.3, 86.8)	455,881
9	84.1% (82.2, 85.8)	1,386,911	77.7% (54.8, 89.0)	339,207
10	73.3% (67.9, 77.8)	1,096,063		
11	72.4% (69.0, 75.3)	981,100		
12	71.4% (65.6, 76.2)	863,731		
13	67.1% (61.3, 72.0)	693,224		
14	62.0% (49.1, 71.7)	511,904		
15	56.3% (30.5, 72.5)	230,479		

eTable 2 (cont.)

D. mRNA-1273 Against Infection

Mos.	Dec 2020–Mar 2021		Apr–May 2021		June–July 2021		Aug–Sep 2021		Oct–Dec 2021		Jan–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	1,426,385	0.0% (0.0, 0.0)	395,738	0.0% (0.0, 0.0)	113,338	0.0% (0.0, 0.0)	142,207	0.0% (0.0, 0.0)	56,931	0.0% (0.0, 0.0)	25,580
1	74.8% (73.6, 76.0)	1,426,372	90.2% (88.6, 91.5)	395,732	87.0% (85.2, 88.6)	113,337	85.4% (84.0, 86.6)	142,196	78.4% (76.3, 80.3)	56,914	87.3% (84.3, 89.8)	25,560
2	96.1% (95.6, 96.6)	1,426,325	94.1% (92.6, 95.4)	395,722	92.9% (91.6, 93.9)	113,284	91.9% (90.3, 93.3)	141,948	68.3% (65.7, 70.8)	56,740	73.3% (61.2, 81.7)	23,563
3	93.4% (92.4, 94.2)	1,426,284	89.0% (87.7, 90.1)	395,699	88.8% (86.9, 90.5)	113,043	78.8% (76.5, 80.9)	141,295	59.9% (57.4, 62.2)	56,421	71.2% (65.1, 76.2)	20,641
4	88.7% (87.6, 89.7)	1,426,221	87.2% (86.3, 88.1)	395,443	88.5% (86.2, 90.4)	112,589	60.3% (58.6, 62.1)	140,468	58.6% (56.7, 60.5)	56,257	68.9% (60.9, 75.2)	15,431
5	82.4% (81.6, 83.1)	1,425,802	84.4% (83.4, 85.4)	394,598	66.0% (63.3, 68.5)	111,789	51.8% (50.7, 52.9)	139,675	57.3% (54.6, 60.0)	56,035		
6	79.9% (79.3, 80.6)	1,420,961	81.4% (79.9, 82.8)	393,218	51.4% (49.8, 53.0)	110,504	51.8% (50.7, 52.9)	138,546	56.0% (51.5, 60.1)	43,147		
7	75.4% (74.6, 76.2)	1,409,709	70.8% (69.1, 72.5)	386,343	51.8% (50.7, 52.8)	104,730	51.8% (50.7, 52.9)	133,122	56.0% (51.5, 60.1)	26,145		
8	74.6% (73.7, 75.5)	1,320,054	50.1% (49.1, 51.2)	328,328	52.1% (50.5, 53.7)	94,445	51.8% (50.7, 52.9)	129,286				
9	59.0% (57.7, 60.3)	1,019,504	50.1% (49.5, 50.7)	260,290	52.5% (49.9, 55.0)	87,978	51.8% (50.7, 52.9)	90,858				
10	42.5% (41.4, 43.6)	704,075	50.1% (49.1, 51.0)	235,683	52.5% (49.9, 55.0)	86,127						
11	44.6% (43.4, 45.7)	549,134	50.1% (48.5, 51.6)	227,711	52.5% (49.9, 55.0)	44,927						
12	38.8% (37.5, 40.2)	496,541	50.1% (48.5, 51.6)	223,625								
13	34.0% (33.0, 35.1)	477,563	50.1% (48.5, 51.6)	167,725								
14	28.9% (27.4, 30.3)	467,194										
15	23.3% (20.8, 25.6)	305,513										

eTable 2 (cont.)

E. mRNA-1273 Against Hospitalization

Mos.	Dec 2020–Mar 2021		Apr–June 2021		July 2021–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	1,287,637	0.0% (0.0, 0.0)	392,182	0.0% (0.0, 0.0)	246,996
1	81.0% (78.5, 83.2)	1,287,354	83.7% (77.8, 88.1)	392,145	83.7% (79.1, 87.3)	246,904
2	96.4% (95.4, 97.2)	1,287,243	97.3% (95.1, 98.6)	392,116	97.3% (95.6, 98.4)	244,831
3	95.6% (94.7, 96.3)	1,287,173	96.0% (94.4, 97.1)	392,000	93.5% (91.5, 95.1)	241,480
4	94.5% (92.7, 95.9)	1,287,090	93.9% (91.1, 95.8)	391,670	84.3% (78.8, 88.3)	236,075
5	93.2% (92.1, 94.1)	1,286,650	91.9% (90.0, 93.4)	390,672	80.0% (75.2, 83.9)	223,194
6	91.4% (90.1, 92.6)	1,282,226	89.3% (84.9, 92.4)	388,902	74.6% (69.3, 79.0)	209,126
7	91.2% (90.4, 91.9)	1,271,650	84.1% (80.9, 86.8)	380,880	67.7% (59.0, 74.6)	186,619
8	90.9% (89.5, 92.1)	1,189,209	76.5% (71.0, 81.0)	322,402	59.0% (42.9, 70.5)	162,604
9	84.4% (83.0, 85.7)	913,782	72.9% (68.3, 76.8)	259,251	47.8% (19.1, 66.3)	121,718
10	73.2% (69.4, 76.6)	620,352	68.7% (62.7, 73.7)	236,509		
11	68.4% (65.7, 70.8)	478,589	63.9% (53.5, 71.9)	229,088		
12	62.6% (57.2, 67.4)	431,348	58.3% (40.8, 70.6)	202,694		
13	62.1% (57.3, 66.3)	414,661	51.9% (24.0, 69.5)	144,856		
14	61.5% (54.0, 67.9)	405,831				
15	61.0% (48.8, 70.3)	265,846				

F. mRNA-1273 Against Death

Mos.	Dec 2020–June 2021		July 2021–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	1,770,106	0.0% (0.0, 0.0)	266,207
1	92.2% (89.6, 94.1)	1,770,085	87.3% (80.5, 91.7)	266,161
2	99.4% (98.9, 99.7)	1,769,988	98.4% (96.2, 99.3)	263,898
3	98.2% (97.5, 98.7)	1,769,824	95.5% (92.7, 97.2)	260,193
4	94.9% (92.1, 96.7)	1,769,409	87.3% (78.1, 92.6)	254,207
5	94.2% (92.8, 95.4)	1,767,942	85.3% (79.0, 89.7)	240,148
6	93.4% (91.7, 94.8)	1,761,510	83.0% (76.9, 87.5)	224,924
7	93.3% (92.4, 94.1)	1,742,234	80.3% (69.4, 87.4)	200,591
8	93.1% (91.7, 94.3)	1,595,650	77.2% (56.0, 88.2)	174,654
9	88.9% (87.5, 90.1)	1,242,742	73.7% (35.4, 89.3)	130,537
10	82.1% (78.2, 85.3)	915,463		
11	77.2% (74.5, 79.6)	759,293		
12	71.0% (65.9, 75.3)	681,103		
13	67.4% (62.6, 71.6)	601,193		
14	63.4% (53.2, 71.4)	485,435		
15	58.9% (39.3, 72.2)	285,977		

eTable 2 (cont.)

G. Ad26.COV2.S Against Infection

Mos.	Dec 2020–Mar 2021		Apr–May 2021		June–July 2021		Aug–Sep 2021		Oct–Dec 2021		Jan–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	135,902	0.0% (0.0, 0.0)	184,726	0.0% (0.0, 0.0)	43,155	0.0% (0.0, 0.0)	38,067	0.0% (0.0, 0.0)	29,430	0.0% (0.0, 0.0)	8,849
1	78.1% (74.6, 81.2)	135,843	85.3% (82.6, 87.6)	184,672	68.5% (62.9, 73.3)	43,115	66.4% (61.9, 70.4)	37,966	64.3% (60.4, 67.8)	29,393	64.6% (52.7, 73.5)	8,232
2	79.1% (74.0, 83.1)	135,793	68.4% (62.4, 73.5)	184,628	73.1% (69.0, 76.7)	43,092	54.0% (45.3, 61.3)	37,916	54.9% (50.6, 58.8)	29,299	51.8% (38.4, 62.4)	7,138
3	70.6% (61.7, 77.5)	135,766	71.7% (68.6, 74.5)	184,598	72.8% (68.4, 76.7)	43,051	50.8% (43.6, 57.2)	37,494	52.6% (47.5, 57.2)	28,627	51.8% (38.4, 62.4)	5,715
4	58.2% (52.7, 63.1)	135,737	64.5% (62.1, 66.7)	184,539	75.6% (70.0, 80.2)	42,792	50.9% (46.8, 54.6)	36,783	45.7% (34.4, 55.0)	28,200	51.8% (38.4, 62.4)	3,987
5	51.6% (48.3, 54.6)	135,588	70.7% (68.8, 72.5)	184,406	64.4% (58.6, 69.4)	41,699	55.1% (51.7, 58.3)	35,760	57.1% (51.0, 62.4)	27,984		
6	66.6% (64.2, 68.7)	135,306	66.7% (63.8, 69.3)	182,964	57.8% (54.1, 61.3)	39,763	55.6% (48.9, 61.4)	34,863	57.1% (51.0, 62.4)	21,690		
7	59.1% (55.2, 62.6)	134,813	60.5% (57.1, 63.6)	172,316	60.8% (57.8, 63.7)	37,163	59.3% (54.3, 63.7)	34,474	57.1% (51.0, 62.4)	11,692		
8	53.0% (47.6, 57.9)	112,810	59.9% (57.9, 61.8)	153,425	57.8% (51.9, 62.9)	35,834	59.3% (54.3, 63.7)	34,248				
9	37.3% (32.9, 41.5)	90,875	47.6% (45.8, 49.4)	134,819	65.5% (61.1, 69.5)	35,217	59.3% (54.3, 63.7)	23,634				
10	40.8% (38.4, 43.1)	75,317	54.4% (51.9, 56.8)	126,314	65.5% (61.1, 69.5)	34,781						
11	48.8% (45.0, 52.3)	70,018	52.0% (49.3, 54.6)	123,459	65.5% (61.1, 69.5)	24,969						
12	32.8% (17.6, 45.2)	68,396	52.0% (49.3, 54.6)	121,833								
13	38.8% (34.3, 43.1)	67,483	52.0% (49.3, 54.6)	93,720								
14	38.8% (34.3, 43.1)	66,486	52.0% (49.3, 54.6)	52,003								
15	38.8% (34.3, 43.1)	13,595										

eTable 2 (cont.)

H. Ad26.COV2.S Against Hospitalization

Mos.	Dec 2020–Apr 2021		May 2021–June 2022	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	233,079	0.0% (0.0, 0.0)	147,739
1	62.6% (51.6, 71.2)	232,955	56.0% (46.6, 63.7)	147,027
2	86.0% (76.5, 91.7)	232,887	80.6% (71.5, 86.8)	145,971
3	83.0% (77.2, 87.3)	232,838	78.2% (72.5, 82.7)	143,794
4	79.2% (70.5, 85.4)	232,756	75.4% (64.2, 83.1)	141,159
5	79.8% (75.7, 83.2)	232,505	65.5% (56.6, 72.5)	136,200
6	80.4% (73.7, 85.3)	232,096	51.5% (29.3, 66.8)	126,720
7	75.4% (70.1, 79.8)	224,937	61.8% (51.2, 70.0)	112,694
8	69.2% (56.9, 78.0)	192,374	69.8% (53.8, 80.3)	99,362
9	66.4% (59.8, 72.0)	158,840	71.3% (58.1, 80.4)	86,676
10	63.4% (52.5, 71.7)	138,765	72.7% (49.8, 85.2)	69,000
11	58.7% (48.8, 66.7)	132,290	74.1% (34.1, 89.8)	56,225
12	53.4% (37.2, 65.3)	130,102		
13	47.4% (18.2, 66.1)	128,440		
14	40.6% (-8.5, 67.5)	101,342		

I. Ad26.COV2.S Against Death

Mos.	Overall	
	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	406,132
1	55.6% (42.8, 65.6)	405,294
2	80.3% (67.3, 88.2)	404,056
3	82.1% (75.5, 86.9)	401,641
4	83.7% (73.6, 89.9)	398,694
5	80.5% (75.0, 84.8)	393,062
6	76.7% (67.2, 83.5)	382,498
7	77.8% (71.7, 82.7)	359,989
8	78.9% (66.8, 86.6)	311,684
9	75.2% (68.1, 80.8)	262,524
10	70.9% (58.0, 79.9)	222,170
11	70.4% (59.7, 78.2)	201,547
12	69.8% (46.7, 82.9)	181,301
13	69.2% (23.8, 87.6)	148,101
14	68.6% (-10.6, 91.1)	108,783

eTable 2 (cont.)

J. Prior Infection Against Infection

Mos.	Pre-delta		Delta		Omicron	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	100% (100, 100)	1,000,834	100% (100, 100)	568,586	100% (100, 100)	914,570
1	82.2% (81.5, 82.8)	1,000,833	95.0% (94.7, 95.2)	565,387	95.4% (95.1, 95.6)	840,566
2	94.1% (93.8, 94.4)	1,000,825	91.5% (91.2, 91.8)	557,184	92.1% (91.8, 92.4)	804,380
3	98.1% (97.9, 98.2)	1,000,807	85.6% (85.3, 85.8)	545,663	86.5% (86.0, 86.9)	789,107
4	99.4% (99.3, 99.4)	1,000,671	75.5% (75.0, 76.1)	529,135	76.8% (75.7, 78.0)	720,046
5	98.6% (98.5, 98.7)	1,000,380	71.8% (71.4, 72.2)	519,727		
6	96.9% (96.7, 97.0)	999,792	67.5% (66.8, 68.3)	484,466		
7	93.1% (92.8, 93.4)	998,546	62.6% (61.2, 64.0)	427,964		
8	87.8% (87.5, 88.1)	994,990	60.9% (59.8, 62.0)	375,286		
9	78.5% (78.2, 78.8)	986,121	59.1% (57.4, 60.7)	237,231		
10	62.2% (61.7, 62.7)	967,387				
11	61.3% (60.8, 61.7)	937,554				
12	60.3% (59.9, 60.7)	897,129				
13	59.3% (59.0, 59.7)	850,769				
14	58.3% (58.0, 58.6)	787,949				
15	57.3% (57.0, 57.6)	731,699				
16	56.2% (55.8, 56.6)	666,941				
17	55.2% (54.7, 55.6)	532,422				

eTable 2 (cont.)

K. Prior Infection Against Hospitalization

Mos.	Pre-delta		Delta/Omicron	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	100% (100, 100)	536,537	100% (100, 100)	345,307
1	96.9% (93.7, 98.4)	536,532	94.7% (91.0, 96.9)	331,116
2	97.8% (96.4, 98.7)	536,523	93.5% (90.1, 95.8)	319,845
3	98.5% (97.2, 99.2)	536,512	92.1% (88.7, 94.4)	312,524
4	99.0% (97.3, 99.6)	536,419	90.3% (86.5, 93.0)	289,500
5	98.4% (96.9, 99.1)	536,234	88.1% (82.9, 91.7)	214,037
6	97.4% (96.3, 98.2)	535,882	85.4% (77.2, 90.6)	163,648
7	95.9% (94.3, 97.0)	535,163		
8	95.3% (93.7, 96.4)	533,318		
9	94.6% (93.0, 95.8)	528,975		
10	93.8% (92.2, 95.0)	520,615		
11	92.8% (91.3, 94.1)	507,180		
12	91.8% (90.2, 93.1)	487,367		
13	90.6% (89.0, 92.0)	462,450		
14	89.2% (87.4, 90.8)	427,329		
15	87.7% (85.5, 89.5)	396,343		
16	85.8% (83.2, 88.1)	363,667		
17	83.8% (80.4, 86.6)	310,830		
18	81.4% (77.0, 85.0)	242,587		

L. Prior Infection Against Death

Mos.	Pre-delta		Delta/Omicron	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	100% (100, 100)	746,004	100% (100, 100)	858,616
1	91.6% (84.9, 95.3)	745,996	93.6% (89.9, 96.0)	825,857
2	97.4% (94.5, 98.7)	745,984	92.4% (89.0, 94.7)	802,599
3	99.2% (97.0, 99.8)	745,970	90.9% (87.7, 93.3)	786,696
4	99.7% (98.2, 100.0)	745,848	89.1% (85.4, 91.9)	735,391
5	99.3% (97.5, 99.8)	745,605	87.0% (81.6, 90.9)	466,374
6	98.2% (96.4, 99.1)	745,125		
7	95.2% (92.9, 96.7)	744,129		
8	94.4% (92.1, 96.0)	741,387		
9	93.5% (91.2, 95.2)	734,754		
10	92.5% (90.2, 94.3)	721,146		
11	91.3% (89.0, 93.2)	699,556		
12	90.0% (87.6, 91.9)	669,574		
13	88.4% (85.9, 90.4)	634,298		
14	86.5% (83.8, 88.7)	586,516		
15	84.4% (81.3, 87.0)	543,382		
16	81.9% (78.0, 85.1)	495,131		

17	79.0% (74.0, 83.1)	404,092		

eTable 3. Estimates (95% CI) and numbers at risk for the effectiveness of booster vaccination (relative to primary vaccination) by date of booster in reducing the risk of SARS-CoV-2 infection, hospitalization, or death

A. BNT162b2 − BNT162b2 Combination Against Infection

Mos.	Before Sep. 22		Sep. 22 to Nov. 30		Dec. 1 to Dec. 31		Jan. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	56,717	0.0% (0.0, 0.0)	755,623	0.0% (0.0, 0.0)	350,229	0.0% (0.0, 0.0)	388,421
1	60.1% (64.3, 70.4)	56,701	66.8% (65.0, 68.5)	755,509	61.2% (60.0, 62.4)	350,198	51.6% (48.9, 54.1)	356,354
2	53.1% (50.2, 55.9)	56,692	48.2% (46.9, 49.4)	755,467	33.0% (30.4, 35.5)	350,185	36.4% (34.0, 38.7)	323,406
3	42.3% (39.6, 45.0)	56,683	39.3% (38.4, 40.3)	755,432	16.2% (13.9, 18.3)	350,171	16.5% (14.1, 18.8)	284,594
4	29.1% (26.5, 31.6)	56,671	21.0% (20.0, 22.0)	755,369				
5	12.8% (10.2, 15.3)	56,621						

B. BNT162b2 − mRNA-1273 Combination Against Infection

Mos.	Before Dec. 1		Dec. 1 to Dec. 31		Jan. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	42,758	0.0% (0.0, 0.0)	45,873	0.0% (0.0, 0.0)	32,032
1	68.2% (62.4, 73.1)	42,747	68.4% (66.2, 70.5)	45,867	60.4% (51.7, 67.5)	29,530
2	64.1% (60.8, 67.2)	42,736	56.7% (54.4, 58.8)	45,864	50.3% (43.1, 56.6)	26,163
3	43.1% (37.5, 48.2)	42,730	40.5% (37.7, 43.2)	45,860	37.7% (31.0, 43.8)	23,215
4	28.6% (23.6, 33.3)	42,720	18.3% (13.8, 22.6)	45,827	21.8% (11.2, 31.2)	19,026
5	10.4% (5.2, 15.4)	42,391			2.0% (0.0, 18.8)	

C. mRNA-1273 − BNT162b2 Combination Against Infection

Mos.	Before Dec. 1		Dec. 1 to Dec. 31		Jan. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	32,553	0.0% (0.0, 0.0)	28,497	0.0% (0.0, 0.0)	27,315
1	66.8% (64.1, 69.3)	32,530	66.1% (61.9, 70.0)	28,494	61.3% (55.9, 66.1)	24,936
2	58.3% (55.8, 60.7)	32,516	43.7% (35.5, 51.0)	28,493	50.0% (44.5, 54.9)	21,915
3	47.8% (45.2, 50.2)	32,505	27.0% (19.6, 33.7)	28,492	35.3% (27.4, 42.4)	18,682
4	34.5% (31.1, 37.8)	32,495	5.3% (0.0, 12.4)	28,479	16.4% (2.1, 28.6)	13,928
5	17.9% (12.4, 23.0)	32,231				

eTable 3 (cont.)

D. mRNA-1273 − mRNA-1273 Combination Against Infection

Mos.	Before Sep. 22		Sep. 22 to Nov. 30		Dec. 1 to Dec. 31		Jan. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	31,205	0.0% (0.0, 0.0)	550,101	0.0% (0.0, 0.0)	304,533	0.0% (0.0, 0.0)	227,085
1	61.6% (57.4, 65.5)	31,195	67.8% (65.8, 69.6)	549,954	62.1% (60.7, 63.5)	304,463	55.3% (51.7, 58.6)	213,793
2	52.8% (48.7, 56.6)	31,190	54.5% (53.3, 55.7)	549,896	33.1% (30.2, 35.9)	304,432	41.1% (37.9, 44.1)	193,733
3	41.9% (38.0, 45.6)	31,175	31.8% (30.0, 33.6)	549,847	14.7% (12.1, 17.3)	304,404	22.3% (19.0, 25.4)	173,330
4	28.6% (25.0, 32.0)	31,169	10.5% (8.7, 12.4)	549,736				
5	12.1% (8.5, 15.6)	31,136						

E. Ad26.COV2.S − BNT162b2 Combination Against Infection

Mos.	On or before Dec. 15		After Dec. 15	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	30,653	0.0% (0.0, 0.0)	27,956
1	46.0% (38.8, 52.3)	30,583	38.2% (29.8, 45.5)	26,237
2	23.4% (18.5, 28.0)	30,549	20.7% (13.0, 27.8)	24,305
3	5.1% (0.4, 9.7)	30,524		

F. Ad26.COV2.S − mRNA-1273 Combination Against Infection

Mos.	On or before Dec. 15		After Dec. 15	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	39,756	0.0% (0.0, 0.0)	29,281
1	60.4% (54.9, 65.2)	39,681	46.4% (39.1, 52.9)	28,086
2	34.7% (30.8, 38.4)	39,631	28.6% (21.5, 35.0)	26,662
3	16.4% (12.4, 20.1)	39,608	4.8% (0.0, 12.4)	25,309

G. Booster Against Hospitalization

Mos.	Before Sep. 22		Sep. 22 to Nov. 30		Dec. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	91,615	0.0% (0.0, 0.0)	1,440,499	0.0% (0.0, 0.0)	1,491,449
1	45.7% (0.0, 71.9)	91,548	85.8% (81.6, 89.1)	1,439,998	80.8% (76.7, 84.2)	1,437,877
2	39.3% (14.6, 56.8)	91,505	81.0% (78.3, 83.3)	1,439,717	73.3% (69.0, 77.0)	1,374,765
3	32.1% (11.1, 48.1)	91,455	74.5% (70.2, 78.3)	1,439,381	62.8% (56.7, 68.0)	1,305,825
4	17.3% (0.0, 32.1)	91,388	68.6% (64.2, 72.5)	1,438,997	48.1% (36.6, 57.5)	1,189,358
5			61.3% (50.3, 69.9)	1,429,515	27.6% (5.0, 44.8)	837,020

eTable 3 (cont.)

H. Booster Against Death

Mos.	Before Sep. 22		Sep. 22 to Nov. 30		Dec. 1 to June 3	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	91,647	0.0% (0.0, 0.0)	1,440,888	0.0% (0.0, 0.0)	1,492,345
1	29.8% (0.0, 68.9)	91,587	90.2% (84.3, 93.9)	1,440,437	85.7% (80.6, 89.5)	1,438,800
2	39.0% (5.0, 60.8)	91,546	84.3% (80.2, 87.5)	1,440,197	80.3% (75.5, 84.2)	1,375,634
3	46.9% (16.2, 66.4)	91,499	74.7% (68.9, 79.4)	1,439,953	72.8% (64.1, 79.5)	1,306,606
4	32.9% (8.1, 51.0)	91,449	73.5% (69.0, 77.4)	1,439,603	62.6% (42.4, 75.6)	1,190,024
5	15.1% (0.0, 31.9)	91,300	72.3% (62.3, 79.6)	1,430,110	48.4% (5.1, 71.9)	837,437

eTable 4. Estimates (95% CI) and numbers at risk for the effectiveness of booster vaccination compared with no vaccination in reducing the risk of SARS-CoV-2 infection for receipt of the first dose in April – May 2021 and receipt of booster dose between September 22, 2021 and November 30, 2021, by primary and booster combination

Mos.	BNT162b2 – BNT162b2		BNT162b2 – mRNA-1273		mRNA-1273 – BNT162b2		mRNA-1273 – mRNA-1273	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	76.1% (75.0, 77.0)	755,623	77.8% (76.7, 78.7)	42,758	74.9% (73.7, 76.0)	32,553	74.1% (72.9, 75.3)	550,101
1	79.9% (78.8, 81.0)	755,509	80.7% (77.2, 83.7)	42,747	86.1% (81.9, 89.4)	32,530	86.1% (83.5, 88.2)	549,954
2	69.1% (68.3, 69.9)	755,467	78.6% (77.1, 80.0)	42,736	79.2% (77.8, 80.5)	32,516	77.3% (75.7, 78.8)	549,896
3	64.4% (63.8, 65.1)	755,432	66.6% (63.9, 69.1)	42,730	73.9% (72.6, 75.2)	32,505	66.0% (63.2, 68.5)	549,847
4	54.3% (53.4, 55.1)	755,369	58.7% (56.2, 61.0)	42,720	67.3% (66.0, 68.5)	32,495	55.3% (52.5, 58.0)	549,736
5	40.5% (39.5, 41.4)	752,908	48.1% (45.4, 50.8)	42,391	59.0% (57.6, 60.3)	32,231	41.4% (38.1, 44.5)	543,575

eTable 5. Estimates (95% CI) and numbers at risk for the effectiveness of booster vaccination and prior infection in reducing the risk of SARS-CoV-2 infection, hospitalization, or death among persons with primary vaccination

A. Booster Without Prior Infection

Mos.	Infection		Hospitalization		Death	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	2,640,161	0.0% (0.0, 0.0)	2,648,112	0.0% (0.0, 0.0)	2,640,218
1	62.9% (62.3, 63.6)	2,597,013	82.7% (77.6, 86.7)	2,604,604	87.7% (80.9, 92.1)	2,597,020
2	50.8% (50.1, 51.5)	2,545,773	80.9% (76.6, 84.4)	2,553,024	80.0% (73.6, 84.9)	2,545,720
3	40.6% (39.7, 41.6)	2,491,929	73.3% (68.0, 77.7)	2,498,713	77.8% (71.8, 82.5)	2,491,761
4	11.7% (9.9, 13.5)	2,400,924	69.4% (63.1, 74.6)	2,407,135	74.1% (66.2, 80.1)	2,400,626
5			61.2% (55.3, 66.2)	2,098,807	74.1% (62.0, 82.3)	2,093,329

B. Booster With Prior Infection

Mos.	Infection		Hospitalization	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	0.0% (0.0, 0.0)	296,002	0.0% (0.0, 0.0)	286,759
1	53.9% (50.8, 56.8)	285,203	49.7% (16.2, 69.8)	276,194
2	32.3% (28.5, 35.9)	273,094	46.8% (21.1, 64.2)	264,380
3	20.3% (15.2, 25.2)	257,778	43.8% (19.4, 60.9)	249,414
4	12.4% (4.6, 19.5)	231,975	40.7% (9.0, 61.3)	224,139
5			37.3% (0.0, 64.2)	170,640

eTable 5 (cont.)

C. Prior Infection

Mos.	Infection		Hospitalization	
	Est. (95% CI)	No. at risk	Est. (95% CI)	No. at risk
0	100.0% (100.0, 100.0)	1,145,737	100.0% (100.0, 100.0)	1,123,348
1	97.1% (96.8, 97.3)	1,096,735	81.4% (70.5, 88.3)	1,074,575
2	93.2% (92.8, 93.6)	1,070,024	80.0% (71.9, 85.8)	1,048,010
3	84.2% (83.2, 85.2)	1,061,423	78.6% (71.7, 83.7)	1,039,521
4	77.2% (76.4, 77.9)	1,024,715	77.0% (68.6, 83.1)	1,003,267
5	66.9% (65.5, 68.2)	769,393	75.3% (62.4, 83.7)	749,436
6	65.7% (64.6, 66.7)	642,123	75.3% (65.7, 82.3)	623,031
7	64.4% (63.5, 65.3)	621,535	75.4% (68.1, 81.1)	602,872
8	63.1% (61.9, 64.2)	603,094	75.5% (69.3, 80.4)	584,846
9	61.7% (60.0, 63.2)	559,799	75.5% (69.1, 80.7)	542,413
10	53.1% (51.9, 54.2)	500,393	75.6% (67.3, 81.8)	484,217
11	42.6% (40.6, 44.6)	474,919	73.8% (66.2, 79.7)	459,439
12	35.3% (34.1, 36.5)	470,828	71.8% (64.9, 77.4)	455,548
13	27.1% (25.3, 28.9)	464,846	69.7% (62.9, 75.3)	449,860
14	28.3% (27.1, 29.5)	448,210	67.4% (60.6, 73.0)	433,769
15	29.5% (27.7, 31.3)	426,640	65.0% (57.3, 71.2)	412,801
16	29.9% (28.4, 31.4)	396,500	62.3% (53.2, 69.7)	383,365
17	30.3% (29.0, 31.6)	320,720	59.5% (48.2, 68.3)	309,120