

Supplementary Appendix

Supplement to: Mehta HB, Li S, Goodwin JS. Effectiveness of COVID-19 Booster on the Risk of Hospitalization among Medicare Beneficiaries. This appendix has been provided by the authors to give readers additional information about the work.

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SUPPLEMENTAL METHODS

Data source

We used the Medicare Beneficiary Summary File for demographic and enrollment information, the Carrier File for physician claims, the Outpatient Standard Analytic File (SAF) for outpatient claims, the Hospital SAF for hospitalization, skilled nursing facility (SNF) SAF, and the Minimum Data Set. More details on these files can be found at Research Data Assistance Center.¹

Target trial approach

We emulated a target trial of COVID-19 booster for the prevention of COVID-19 hospitalization.^{2,3,4} We designed a hypothetical trial and emulated using Medicare claims data. Use of target trial clearly specifies inclusion/exclusion criteria and defines intervention and outcome. Thus, it reduces the risk of selection bias, immortal time bias, clearly assigns time zero and avoids common methodological pitfalls of observational studies.^{5,6,7} In observational studies of comparing booster to no booster, it is straightforward to assign time zero booster group – the day they receive a booster. However, there are multiple time points when individuals become eligible to be assigned to no booster group. We emulated target trial each week and assigned eligible individuals to booster vs. no booster treatment strategy each week. This helped us clearly assign time zero to non-boosted people and avoided possibility of introducing immortal time bias.² In contrast to a traditional matching where we use future information (after time zero) to identify and match individual who receive booster to those who do not receive boosters, the target trial approach avoids using future information and adheres to the principles of hypothetical randomized trial emulation. By matching individuals on the type and date of original

vaccination, and other demographic and clinical characteristics, we explicitly controlled for confounding and selection bias due to these factors. We additionally controlled confounding by controlling for all demographic and clinical characteristics. However, by design, the target trial cannot control for selection bias and confounding if important variables are not measured and controlled in the analysis.⁸

We first specified the target trial protocol (**Table**). We emulated target trial each week. First, we included individuals who met the *eligibility criteria*. We included Medicare beneficiaries who received two doses of Pfizer or two doses of Moderna as the primary vaccination series from 12/11/2020 through 12/31/2021. Consistent with the protocol, we included beneficiaries if the duration between the first and second dose was between 17 to 41 days. We limited the cohort to individuals who were continuously enrolled in Medicare Parts A and B with no enrollment in health maintenance organization in the year prior the *original vaccination date* and those who were residing in 50 states or District of Columbia. The *original vaccination date* was defined as the date when individuals received 2nd dose of Pfizer or Moderna. We assigned individuals to two *treatment strategies*: booster vs. no booster. For *treatment assignment*, we identified individuals who received boosters starting 8/12/2021 to 11/30/2021. All individuals who did not receive booster that week or prior were eligible to become unboosted controls. We assigned the index date of boosted individual to the matched unboosted controls. To mimic randomization, we matched one unboosted control to one boosted case based on the week and type of original vaccine, age (+/- 2 years), sex, race (Non-Hispanic White, Non-Hispanic Black, Asian, Hispanic and others), Medicaid eligibility, number of prior COVID-19 hospitalizations, prior COVID-19 infection, residence (community vs. nursing facility) and tertile of summary Elixhauser

comorbidity score (**Supplemental Figure 1**). For example, 10,656 individuals received boosters between 8/12/2021 (Thursday) and 8/15/2021 (Sunday). Of 9,207,784 individuals who did not receive boosters by 8/15/2021, we matched 10,656 unboosted controls to 10,367 boosted cases. We followed boosted cases and controls for hospitalization due to COVID-19 *outcome*. The *follow-up* started 10 days after the booster receipt. We used a 10-day lag time because it would take 7 to 10 days for boosters to build immunity.⁹

Table. Target trial protocol specification and emulation

Protocol component	Target trial specification	Target trial emulation
Eligibility criteria	<ul style="list-style-type: none"> • Fee-for-service Medicare beneficiaries who received 2 doses of Pfizer or 2 doses of Modernavaccine between 12/11/2020 and 12/31/2021. • The duration between 1st and 2nd dose of the vaccine (only applicable to Pfizer and Moderna) should be between 17 and 41 days. • Residing in 50 states or DC • Individuals with at least 10 days of follow-up after the treatment receipt 	Same as for the target trial
Treatment strategies	<ol style="list-style-type: none"> 1. Receipt of Pfizer or Moderna booster 90 days after the original vaccination 2. No receipt of booster 	Same as for the target trial
Treatment assignment	Random assignment of treatment strategy	We attempted to emulate randomization by matching (1:1 ratio) individuals who received boosters to those who did not receive boosters by week and type of the original vaccination, and demographic and clinical characteristics
Outcome	Hospitalization due to COVID-19	Same as for the target trial
Follow-up	For each person, follow-up starts 10 days after treatment (booster and no booster) and ends on the day of the outcome of interest, death, disenroll from fee-for-service Medicare plan or the end of the study period (December 31, 2021), or 180 days after booster whichever occurs first. We performed symmetric censoring and censored both unboosted and boosted individual of the matched pair at the same date when the unboosted individual received a booster.	Same as for the target trial

Causal contrast	Per-protocol effect	Observational analogue of per-protocol effect
Statistical analysis	<ul style="list-style-type: none"> • Cumulative incidence curves • Unadjusted hospitalization rates and risk differences • Estimates of hazard ratio and vaccine effectiveness comparing booster group to non-booster group • Estimates of hazard ratio and vaccine effectiveness comparing booster group to non-booster group for different intervals between vaccination and receipt of boosters • Subgroup analyses by baseline demographic and clinical characteristics 	Same as for the target trial

Traditional matching approach

In the target trial approach, unboosted controls were censored when they received a booster. Nearly 44.39% of unboosted controls eventually received boosters and were censored. This may introduce selection bias if the reason for censoring is affected by booster receipt and shares common causes with hospitalization. To address these issues, we used a traditional matching approach as a sensitivity analysis,¹⁰ where we matched boosted cases to unboosted controls based on the week and type of original vaccine, age +/- 2 years, sex, race (Non-Hispanic White, Non-Hispanic Black, Asian, Hispanic and others), Medicaid eligibility, number of prior COVID-19 hospitalizations, prior COVID-19 infection, residence (community vs. nursing facility) and tertile of summary Elixhauser comorbidity score (**Supplemental Figure 2**). Boosted group included individuals who received boosters from 8/12/2021 through 11/30/2021. Unboosted group included individuals who did not receive boosters from 8/12/2021 through 12/31/2021. Unboosted individuals were assigned the same index date as the matched boosted individual. Of 4,731,607 boosted individuals, 2,293,887 (48.5%) were matched to controls on all characteristics.

Covariates

Using a previously validated approach, we identified residence (community vs. nursing facility/institution) in the 90 days before the original vaccination date.¹¹ Using all claim files, we identified if an individual had a COVID-19 diagnosis before 08/12/2021. If an individual was diagnosed with COVID-19 before April 1, 2020, we used ICD-10-CM codes of J12.89, J20.8, J40, J22 J98.8, J80 combined with B97.29, or U07.1 to identify COVID-19 diagnosis.¹² We used Agency for Healthcare Research and Quality's Elixhauser comorbidity index of 38 comorbidities and combined comorbidities in some analyses.¹³ We used AHRQ weights to derive summary Elixhauser comorbidity score. We considered patients having comorbidity if they had at least one claim in Hospital SAF or SNF SAF or two claims in Outpatient SAF or Carrier File that were at least 30 days apart.¹⁴

Statistical analysis

We constructed Cox proportional hazards regression models to determine the association of booster receipt with the risk of COVID-19 hospitalization, controlling for the prior vaccine and patient characteristics. All individuals were censored when they died, disenrolled from fee-for-service Medicare plan or at the end of the study period (December 31, 2021). We performed symmetric censoring and censored both the unboosted and boosted individuals of the matched pair at the same date when the unboosted individual received a booster. We estimated vaccine effectiveness as $(1 - \text{hazard ratio}) * 100$. We tested proportional hazard assumption in these Cox models by determining that the logarithm of the baseline cumulative hazard rates and the Schoenfeld residuals were proportional to follow-up time. The residual plots and the Supremum tests for all covariates suggested that the proportional hazard assumption was not violated.¹⁵

In the main Cox regression models, we performed an interaction of patient characteristics with a booster. For each interaction term, we created a separate Cox model while controlling for all the other patient characteristics. If the interaction term was significant, we performed stratified analyses to assess booster's effectiveness on the risk of COVID-19 hospitalization.

We used risk difference from the primary target trial cohort analysis, i.e., difference in number of individuals hospitalized among boosted vs. non-boosted individuals and multiplied with 130 to obtain risk difference over 130 days per million persons. As per the most recent CDC data, nearly 15 million people over 65 years of age are eligible to receive boosters.¹⁶ We multiplied calculated risk difference with 15 to estimate how many hospitalizations will be prevented if all age 65+ unboosted individuals received COVID-19 booster.

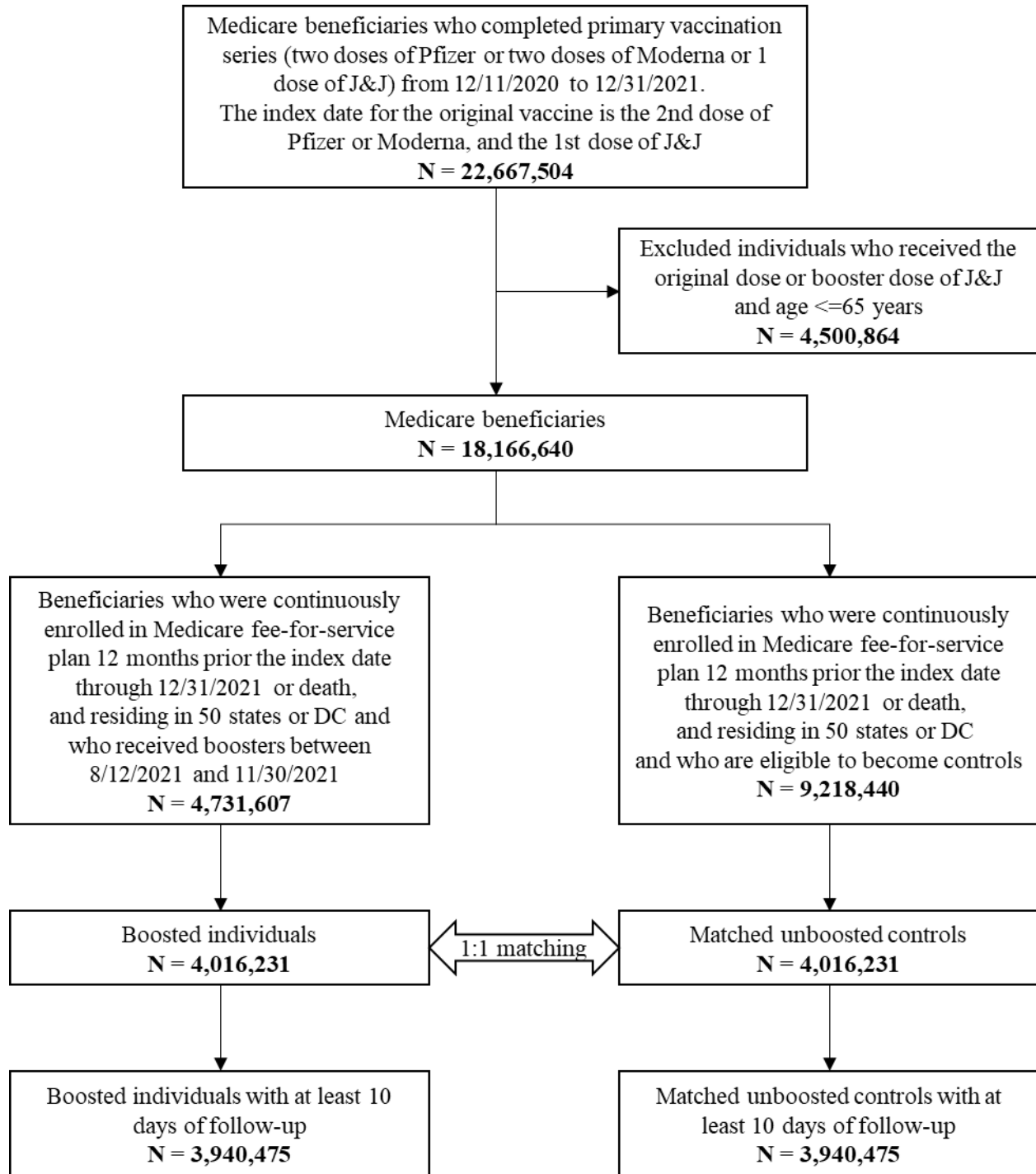
We also used Cox regression model to estimate the risk of hospitalization for boosted cases compared to unboosted controls for different intervals between vaccination and receipt of boosters, controlling for all patient characteristics, original vaccination type and the type of booster.

Sensitivity analyses

We performed all the above analyses using the target trial cohort and repeated them for the traditionally matched cohort. We addressed “hospitalized *with* COVID-19 versus hospitalized *because of* COVID-19” issue¹⁷ by identifying the outcome of COVID-19 hospitalization as those with a primary admitting COVID-19 diagnosis in sensitivity analyses.

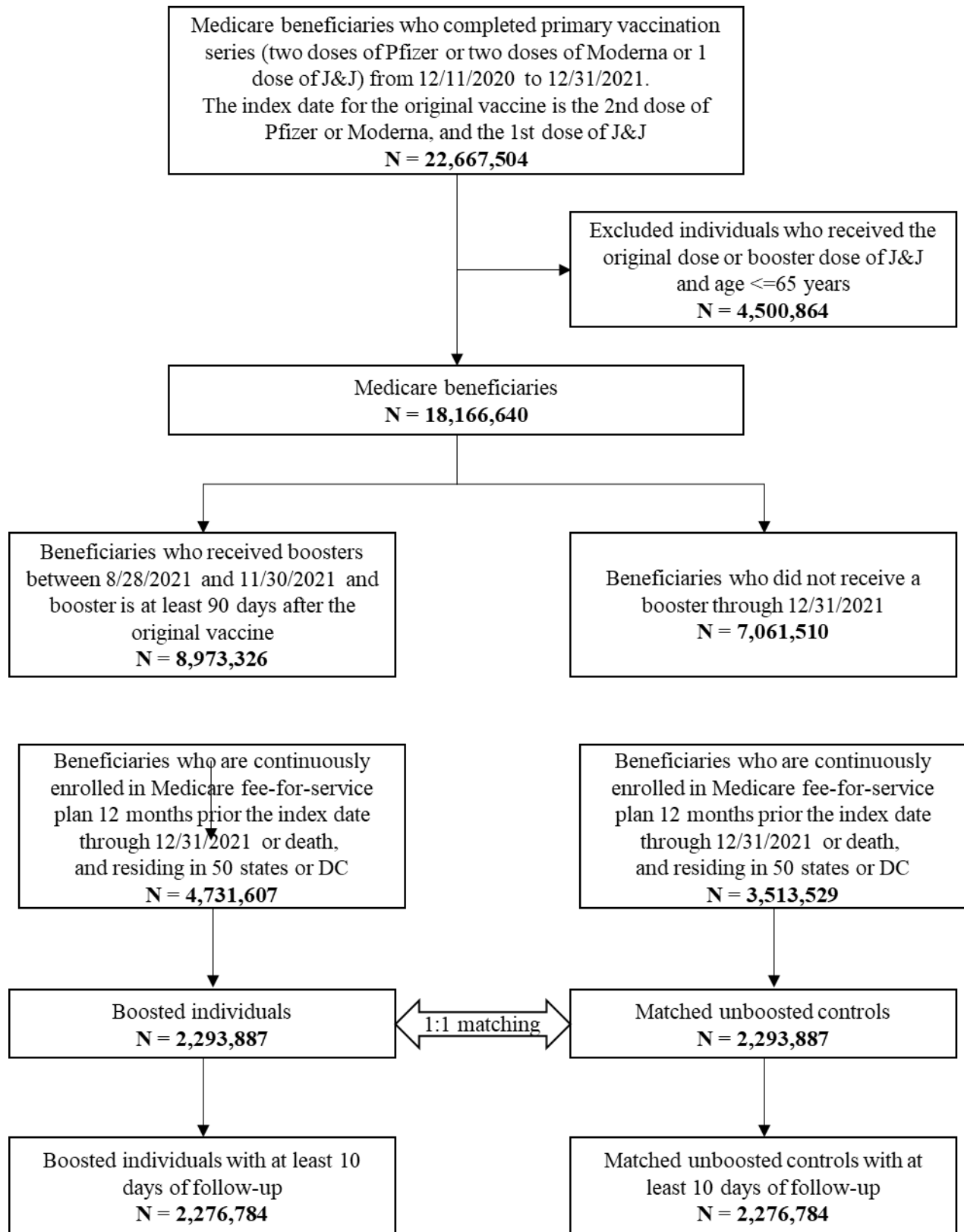
All analyses were performed with SAS Enterprise, version 7.1 (SAS Institute Inc), at the Centers for Medicare & Medicaid Services Virtual Research Data Center.

Supplemental Figure 1. Cohort derivation, target trial method.

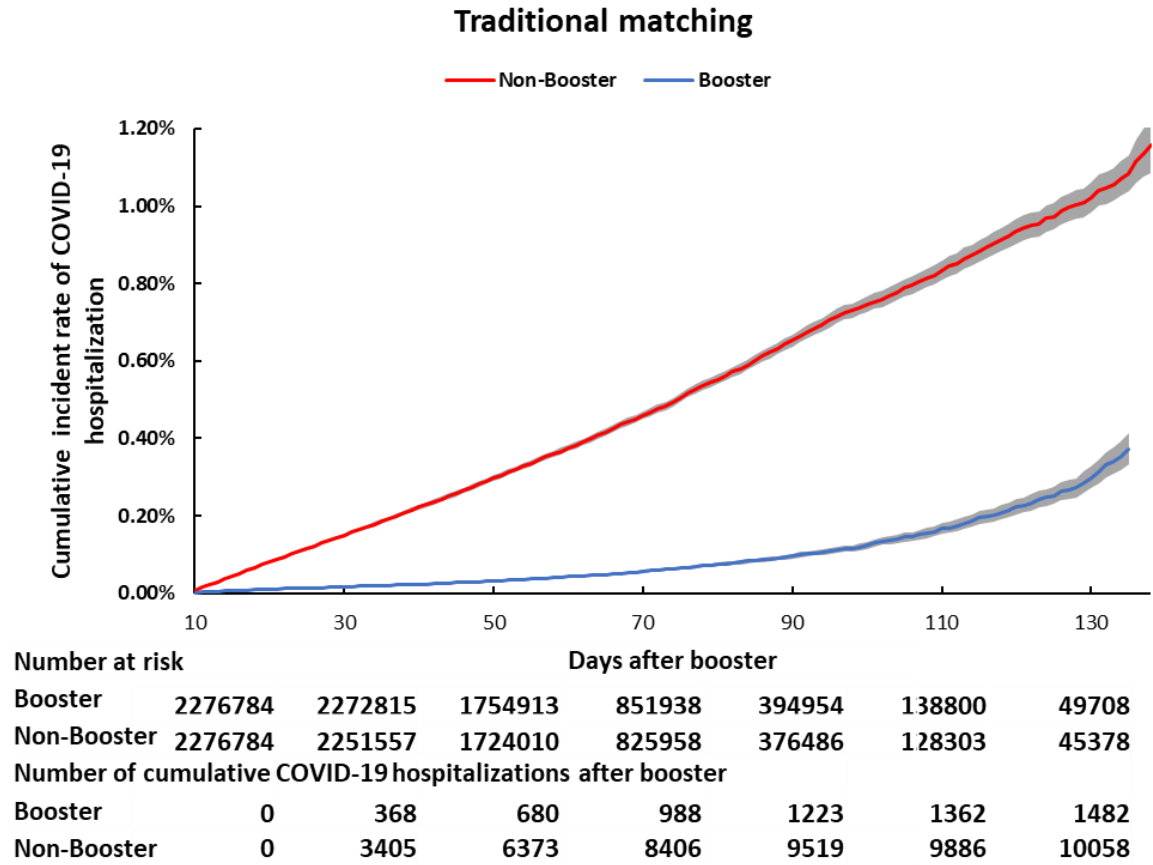


While the cohort initially included all those who completed their original vaccination by 12/31/21 after subsequent exclusions and matching, only those with an original vaccination date between 1/2/21 and 9/1/21 were studied.

Supplemental Figure 2. Cohort derivation, traditional matching method.



Supplemental Figure 3. Cumulative incidence curve of COVID-19 hospitalization among individuals who received boosters vs. those who did not receive boosters, traditional matching method. Joinpoint analyses of the curves found no significant changes in slope.



Supplemental Table 1. Unadjusted COVID-19 hospitalization rates for boosted individuals and unboosted controls, and adjusted booster vaccine effectiveness, stratified by all individual patient characteristics.^a

	All N (%)	Hospitalization rate per 1,000,000 person days among boosted individuals	Hospitalization rate per 1,000,000 person days among unboosted controls	Hospitalization rate difference (95% CI), boosted individuals vs. unboosted controls	Booster vaccine effectiveness, percent (95% CI) ^b
All	7,880,950	8.20 (7.81, 8.60)	43.70 (42.79, 44.64)	35.51 (24.50, 36.51)	81 (80, 82)
COVID-19 vaccine original					
Pfizer	4,035,158 (51.20%)	9.69 (9.13, 10.29)	50.14 (48.83, 51.47)	40.44 (39.00, 41.88)	81 (79, 82)
Moderna	3,845,792 (48.80%)	6.30 (5.79, 6.84)	35.56 (34.33, 36.83)	29.26 (27.91, 30.62)	82 (81, 83)
Age					
66-70	2,248,536 (28.53%)	4.89 (4.35, 5.50)	22.27 (21.06, 23.55)	17.38 (16.01, 18.75)	79 (76, 81)
71-75	2,169,531 (27.53%)	6.21 (5.59, 6.91)	32.83 (31.35, 34.39)	26.62 (24.96, 28.27)	81 (79, 83)
76-80	1,526,810 (19.37%)	8.36 (7.50, 9.33)	50.42 (48.24, 52.70)	42.06 (39.65, 44.47)	83 (81, 85)
81-85	1,006,481 (12.77%)	12.38 (11.07, 13.83)	65.49 (62.43, 68.71)	53.11 (49.69, 56.54)	81 (79, 83)
86+	929,592 (11.80%)	16.22 (14.66, 17.95)	84.50 (80.86, 88.30)	68.28 (64.21, 72.35)	81 (79, 83)
Race					
Non-Hispanic White	6,807,760 (86.38%)	8.21 (7.80, 8.65)	45.37 (44.37, 46.40)	37.16 (36.06, 38.26)	82 (81, 83)
Non-Hispanic Black	337,824 (4.29%)	10.94 (8.92, 13.41)	44.39 (40.12, 49.11)	33.45 (28.44, 38.46)	76 (70, 81)
Asian	225,590 (2.86%)	3.96 (2.61, 6.02)	17.71 (14.53, 21.59)	13.75 (9.87, 17.63)	79 (66, 87)
Hispanic	218,912 (2.78%)	10.80 (8.40, 13.88)	37.31 (32.59, 42.71)	26.51 (20.78, 32.24)	72 (63, 79)
Other	290,864 (3.69%)	5.82 (4.31, 7.85)	28.65 (25.03, 32.79)	22.83 (18.59, 27.07)	80 (72, 85)
Medicaid eligibility					
No	7,388,256 (93.75%)	7.66 (7.28, 8.07)	42.18 (41.25, 43.12)	34.52 (33.50, 35.53)	82 (81, 83)
Yes	492,694 (6.25%)	16.03 (13.97, 18.40)	66.16 (61.81, 70.81)	50.12 (45.12, 55.13)	76 (72, 79)
Number of prior hospitalizations					
0	6,986,464 (88.65%)	6.05 (5.70, 6.43)	36.43 (35.54, 37.34)	30.38 (29.41, 31.35)	83 (82, 84)
1	675,388 (8.57%)	19.39 (17.44, 21.56)	82.57 (78.41, 86.94)	63.18 (58.45, 67.91)	76 (73, 79)
2 and above	219,098 (2.78%)	38.34 (33.66, 43.66)	144.92 (135.46, 155.03)	106.60 (95.61, 117.60)	73 (69, 77)
Prior COVID-19					
No	7,398,502 (93.88%)	8.07 (7.67, 8.49)	44.64 (43.96, 33.02)	36.57 (35.53, 37.62)	82 (81, 83)

Yes	482,448 (6.12%)	10.07 (8.46, 11.98)	29.84 (26.96, 33.02)	19.77 (16.28, 23.27)	67 (60, 73)
Residence prior to original vaccination					
Community	7,754,612 (98.40%)	8.03 (7.64, 8.44)	43.66 (42.74, 44.60)	35.63 (34.62, 36.64)	82 (81, 82)
Nursing facility	126,338 (1.60%)	17.59 (13.68, 22.60)	45.99 (39.36, 53.76)	28.41 (19.99, 36.83)	62 (49, 72)
Comorbidity status					
Deficiency anemia					
No	7,052,259 (89.48%)	6.23 (5.87, 6.61)	36.91 (36.03, 37.82)	30.68 (29.71, 31.65)	83 (82, 84)
Yes	828,691 (10.52%)	24.20 (22.22, 26.36)	99.59 (95.45, 103.91)	75.39 (70.68, 80.10)	76 (74, 78)
Auto immune					
No	7,560,335 (95.93%)	7.49 (7.11, 7.89)	42.21 (41.30, 43.14)	34.72 (33.71, 35.72)	82 (81, 83)
Yes	320,615 (4.07%)	21.93 (19.17, 25.09)	81.16 (74.99, 87.83)	59.23 (52.17, 66.29)	73 (68, 77)
Leukemia					
No	7,830,656 (99.36%)	7.72 (7.34, 8.11)	43.17 (42.26, 44.10)	35.45 (36.45, 34.46)	82 (81, 83)
Yes	50,294 (0.64%)	62.29 (51.63, 75.15)	137.21 (117.16, 160.68)	74.92 (50.30, 99.54)	57 (44, 66)
Lymphoma					
No	7,796,030 (98.92%)	7.60 (7.23, 8.00)	53.24 (42.33, 44.17)	35.64 (34.64, 36.64)	82 (81, 83)
Yes	84,920 (1.08%)	48.48 (41.08, 57.22)	90.81 (78.27, 105.35)	42.32 (26.62, 58.02)	50 (37, 60)
Metastatic cancer					
No	7,794,663 (98.91%)	7.99 (7.60, 8.40)	43.34 (42.43, 44.27)	35.35 (34.35, 36.35)	81 (80, 82)
Yes	86,287 (1.09%)	22.49 (17.57, 28.79)	77.80 (66.69, 90.75)	55.31 (42.10, 68.51)	73 (63, 79)
Solid tumor without metastasis, malignant					
No	7,237,444 (91.83%)	7.81 (7.41, 8.23)	42.72 (41.78, 43.68)	34.91 (33.88, 35.94)	82 (80, 83)
Yes	643,506 (8.17%)	12.09 (10.58, 13.82)	55.05 (51.51, 58.84)	42.96 (38.95, 46.96)	79 (75, 82)
Solid tumor without metastasis, in situ					
No	7,815,409 (99.17%)	8.13 (7.74, 8.54)	43.61 (42.70, 44.55)	35.48 (34.48, 36.49)	82 (80, 83)
Yes	65,541 (0.83%)	15.44 (10.66, 22.36)	55.49 (44.86, 68.63)	40.05 (26.94, 53.16)	72 (58, 82)

Congestive heart failure					
No	7,338,605 (93.12%)	6.83 (6.47, 7.22)	36.88 (36.01, 37.77)	30.05 (29.09, 31.00)	82 (80, 83)
Yes	542,345 (6.88%)	26.94 (24.31, 29.86)	128.50 (122.83, 134.42)	101.60 (95.13, 108.01)	79 (77, 81)
Coagulopathy					
No	7,697,984 (97.68%)	7.53 (7.16, 7.93)	42.15 (41.25, 43.08)	34.62 (33.63, 35.61)	82 (81, 83)
Yes	182,966 (2.32%)	32.97 (28.38, 38.30)	108.98 (99.83, 118.96)	76.01 (65.25, 86.76)	71 (66, 76)
Dementia					
No	7,496,063 (95.12%)	7.55 (7.17, 7.95)	40.79 (39.88, 41.72)	33.24 (32.24, 34.24)	82 (81, 83)
Yes	384,887 (4.88%)	22.81 (19.81, 26.27)	89.41 (84.19, 94.96)	66.60 (60.33, 72.87)	73 (68, 77)
Depression					
No	7,173,168 (91.02%)	7.46 (7.08, 7.87)	40.57 (39.65, 41.52)	33.11 (32.09, 34.12)	82 (81, 83)
Yes	707,782 (8.98%)	15.74 (13.99, 17.70)	72.97 (69.24, 76.90)	57.23 (52.98, 61.49)	78 (75, 81)
Diabetes, complicated					
No	6,872,668 (87.21%)	6.46 (6.09, 6.84)	35.86 (34.97, 36.77)	29.40 (28.43, 30.37)	82 (81, 83)
Yes	1,008,282 (12.79%)	20.31 (18.61, 22.16)	94.09 (90.47, 97.85)	73.78 (69.70, 77.87)	79 (77, 81)
Hypertension, complicated					
No	7,112,705 (90.25%)	6.16 (5.80, 6.53)	36.20 (35.32, 37.09)	30.01 (29.08, 31.00)	83 (82, 84)
Yes	768,245 (9.75%)	26.86 (24.66, 29.25)	109.58 (105.11, 114.24)	82.72 (77.62, 87.83)	76 (73, 78)
Hypertension, uncomplicated					
No	4,278,042 (54.28%)	8.47 (7.93, 9.03)	41.15 (39.95, 42.38)	32.68 (31.34, 34.02)	79 (78, 81)
Yes	3,602,908 (45.72%)	7.88 (7.32, 8.48)	46.70 (45.32, 48.13)	38.83 (37.31, 40.34)	83 (82, 84)
Liver disease, moderate to severe					
No	7,858,514 (99.72%)	8.09 (7.70, 8.50)	43.46 (42.55, 44.39)	35.37 (34.37, 36.38)	81 (80, 82)
Yes	22,436 (0.28%)	36.31 (24.90, 52.95)	127.42 (101.14, 160.53)	91.11 (58.65, 123.60)	74 (60, 83)
Other neurological disorders					

No	7,724,657 (98.02%)	7.76 (7.38, 8.16)	42.15 (41.25, 43.08)	34.39 (33.39, 35.38)	82 (81, 83)
Yes	156,293 (1.98%)	29.75 (24.82, 35.66)	111.38 (101.98, 121.65)	81.63 (70.43, 92.84)	72 (66, 77)
Renal failure, severe					
No	7,732,380 (98.11%)	7.17 (6.80, 7.56)	41.06 (40.17, 41.98)	33.89 (32.92, 34.87)	81 (80, 82)
Yes	148,570 (1.89%)	56.92 (50.07, 64.72)	180.02 (166.95, 194.11)	123.10 (107.71, 138.51)	74 (60, 83)
Peptic ulcer with bleeding					
No	7,840,474 (99.49%)	8.11 (7.73, 8.52)	43.49 (42.58, 44.42)	35.38 (34.37, 36.38)	81 (80, 82)
Yes	40,476 (0.51%)	23.81 (16.09, 35.23)	83.55 (67.80, 102.97)	59.75 (39.95, 79.54)	73 (59, 83)
Valvular disease					
No	7,337,313 (93.10%)	7.59 (7.20, 8.00)	40.84 (39.93, 41.77)	33.25 (32.24, 34.25)	81 (80, 82)
Yes	543,637 (6.90%)	16.00 (14.05, 18.21)	82.79 (78.07, 87.79)	66.79 (61.51, 72.07)	80 (78, 83)
Weight loss					
No	7,714,023 (97.88%)	7.83 (7.45, 8.24)	42.74 (41.83, 43.67)	34.91 (33.91, 35.91)	82 (81, 83)
Yes	166,927 (2.12%)	24.64 (20.37, 29.80)	84.61 (76.57, 93.50)	59.98 (50.31, 69.64)	72 (65, 77)

^aOnly characteristics for which there was a significant interaction with receipt of booster in the analyses in **Table 2** are presented. This is similar to **Table 3**, but in **Table 3** we combined some comorbidities for simplicity of presentation.

^bBooster vaccine effectiveness was computed as $(1 - HR) \times 100$.

Supplemental Table 2. Unadjusted COVID-19 hospitalization rate, adjusted hazard of hospitalization, and vaccine effectiveness for boosted enrollees vs non-boosted controls, by interval between primary vaccine and booster dose. The Target trial method was used for derivation of the cohorts.

Months between primary vaccine and booster dose	Booster	Patients, N (%), N=7,880,650	Hospitalized individuals, N	Rate of hospitalization, per 1,000,000 person-day	Adjusted HR (95% CI) ^a	Booster vaccine effectiveness, percent (95% CI) ^b
4 to <5 months	Unboosted	28,006 (0.36%)	116	44.26 (36.89, 53.09)	Ref	Ref
	Boosted	28,006 (0.36%)	69	26.23 (20.72, 33.21)	0.42 (0.32, 0.59)	58 (41, 68)
5 to <6 months	Unboosted	116,174 (1.47%)	341	37.49 (33.72, 41.69)	Ref	Ref
	Boosted	116,174 (1.47%)	156	17.08 (14.60, 19.99)	0.38 (0.32, 0.47)	62 (53, 68)
6 to <7 months	Unboosted	882,501 (11.20%)	2,150	42.67 (40.90, 44.51)	Ref	Ref
	Boosted	882,501 (11.28%)	379	7.48 (6.77, 8.28)	0.17 (0.15, 0.19)	83 (81, 85)
7 to <8 months	Unboosted	1,648,115 (20.91%)	3,327	41.97 (40.56, 43.42)	Ref	Ref
	Boosted	1,648,115 (20.91%)	482	6.05 (5.53, 6.62)	0.15 (0.14, 0.17)	85 (83, 86)
8 to <9 months	Unboosted	1,102,838 (13.99%)	2,314	46.93 (45.06, 48.88)	Ref	Ref
	Boosted	1,102,838 (13.99%)	418	8.43 (7.66, 9.28)	0.19 (0.17, 0.21)	81 (79, 83)
≥9 months	Unboosted	162,841 (2.07%)	389	56.13 (50.82, 61.99)	Ref	Ref
	Boosted	162,841 (2.07%)	124	17.79 (14.92, 21.21)	0.32 (0.26, 0.39)	68 (61, 74)

^aAdjusted for individual's age, gender, race, Medicaid status, the type of booster and original vaccination type, prior COVID-19 infection, residence and 38 comorbidities.

^bVaccine effectiveness was computed as $(1 - HR) * 10$.

Supplemental Table 3. Characteristics of the study cohort derived using traditional matching method.

	All N (%) ^a	Boosted All patients, N (%) ^b N=2,276,784	Non-Boosted All patients, N (%) ^b N=2,276,784	Standardized Difference
Follow up time				0.0426
Median (p25 p75)	64 (50, 81)	64 (51, 81)	63 (50, 80)	
Min, Max	[10, 141]	[10,141]	[10,141]	
Age, year				-0.0217
Median (p25 p75)	74 (69, 81)	74 (69, 80)	75 (70, 81)	
COVID-19 vaccine original				0
Pfizer	2,255,330 (49.53%)	1,127,665 (50.00%)	1,127,665 (50.00%)	
Moderna	2,298,238 (50.47%)	1,149,119 (50.00%)	1,149,119 (50.00%)	
Age				0
66-70	1,457,106 (32.00%)	833,171 (57.18%)	623,935 (42.82%)	
71-75	1,137,888 (24.99%)	544,691 (47.87%)	593,197 (52.13%)	
76-80	815,910 (17.92%)	385,640 (47.27%)	430,270 (52.73%)	
81-85	570,487 (12.53%)	264,980 (46.45%)	305,507 (53.55%)	
86+	572,177 (12.57%)	248,302 (43.40%)	323,875 (56.60%)	
Gender				0
Male	1,856,786 (40.78%)	928,393 (50.00%)	928,393 (50.00%)	
Female	2,696,782 (59.22%)	1,348,391 (50.00%)	1,348,391 (50.00%)	
Race				0
Non-Hispanic White	3,872,602 (85.05%)	1,936,301 (50.00%)	1,936,301 (50.00%)	
Non-Hispanic Black	242,278 (5.32%)	121,139 (50.00%)	121,139 (50.00%)	
Asian	122,198 (2.68%)	61,099 (50.00%)	61,099 (50.00%)	
Hispanic	166,582 (3.66%)	83,291 (50.00%)	83,291 (50.00%)	
Other	149,908 (3.29%)	74,954 (50.00%)	74,954 (50.00%)	
Medicaid eligibility				0
No	4,130,228 (90.70%)	2,065,114 (50.00%)	2,065,114 (50.00%)	
Yes	423,340 (9.30%)	211,670 (50.00%)	211,670 (50.00%)	
Number of prior hospitalizations				0
0	3,961,834 (87.01%)	1,980,917 (50.00%)	1,980,917 (50.00%)	
1	437,178 (9.60%)	218,589 (50.00%)	218,589 (50.00%)	
2 and above	154,556 (3.39%)	77,278 (50.00%)	77,278 (50.00%)	
Prior COVID-19				0
No	4,189,400 (92.00%)	2,094,700 (50.00%)	2,094,700 (50.00%)	

Yes	364,168 (8.00%)	182,084 (50.00%)	182,084 (50.00%)	
Residence prior to original vaccination				0
Community	4,441,404 (97.54%)	2,220,702 (50.00%)	2,220,702 (50.00%)	
Nursing facility	112,164 (2.46%)	56,082 (50.00%)	56,082 (50.00%)	
Comorbidity status				
AIDS/HIV	6,127 (0.13%)	3,724 (60.75%)	2,406 (39.25%)	0.0158
Alcohol abuse	36,469 (0.80%)	17,858 (48.97%)	18,611 (51.03%)	-0.0037
Deficiency anemia	528,747 (11.61%)	257,183 (48.64%)	271,564 (51.36%)	-0.0197
Auto immune	189,550 (4.16%)	100,400 (52.97%)	89,150 (47.03%)	0.0247
Blood loss anemia	38,733 (0.85%)	18,993 (49.04%)	19,740 (50.96%)	-0.0036
Leukemia	29,637 (0.65%)	16,526 (55.76%)	13,111 (44.24%)	0.0187
Lymphoma	49,913 (1.10%)	27,918 (55.93%)	21,995 (44.07%)	0.0250
Metastatic cancer	54,302 (1.19%)	28,665 (52.79%)	25,637 (47.21%)	0.0123
Solid tumor without metastasis, malignant	367,393 (8.07%)	243,472 (66.27%)	196,355 (33.73%)	0.0408
Solid tumor without metastasis, in situ	34,597 (0.76%)	18,172 (52.52%)	16,425 (47.48%)	0.0088
Cerebrovascular disease	282,310 (6.20%)	135,314 (47.93%)	146,996 (52.07%)	-0.0213
Congestive heart failure	356,103 (7.82%)	166,736 (46.82%)	189,367 (53.18%)	-0.0370
Coagulopathy	115,730 (2.54%)	60,266 (52.07%)	55,464 (47.93%)	0.0134
Dementia	280,135 (6.15%)	112,532 (40.17%)	167,603 (59.83%)	-0.1008
Depression	459,883 (10.10%)	220,016 (47.84%)	239,867 (52.16%)	-0.0289
Diabetes, complicated	622,866 (13.68%)	299,712 (48.12%)	323,154 (51.88%)	-0.0300
Diabetes, uncomplicated	395,136 (8.68%)	194,142 (49.13%)	200,994 (50.87%)	-0.0107
Drug abuse	30,671 (0.67%)	14,263 (46.50%)	16,408 (53.50%)	-0.0115
Hypertension, complicated	490,506 (10.77%)	237,135 (48.34%)	253,371 (51.66%)	-0.0230
Hypertension, uncomplicated	2,084,461 (45.78%)	1,034,099 (49.61%)	1,050,362 (50.39%)	-0.0143
Liver disease, mild	101,027 (2.22%)	53,429 (52.89%)	47,598 (47.11%)	0.0174
Liver disease, moderate to severe	15,217 (0.33%)	8,133 (53.45%)	7,084 (46.55%)	0.0080
Chronic pulmonary disease	538,917 (11.84%)	265,124 (49.20%)	273,793 (50.80%)	-0.0118
Neurological disorders affecting movement	128,287 (2.82%)	59,645 (46.49%)	68,642 (53.51%)	-0.0239
Seizures and epilepsy	70,887 (1.56%)	33,614 (47.42%)	37,273 (52.58%)	-0.0130
Other neurological disorders	111,769 (2.45%)	52,395 (46.88%)	59,374 (53.12%)	-0.0198

Obesity	515,693 (11.33%)	259,505 (50.32%)	256,188 (49.68%)	0.0046
Paralysis	65,254 (1.43%)	29,718 (45.54%)	35,536 (54.46%)	-0.0215
Peripheral vascular disease	501,662 (11.02%)	243,727 (48.58%)	257,935 (51.42%)	-0.0199
Psychoses	147,591 (3.24%)	71,737 (48.61%)	75,854 (51.39%)	-0.0102
Pulmonary circulation disease	79,484 (1.75%)	38,948 (49.00%)	40,536 (51.00%)	-0.0053
Renal failure, moderate	410,262 (9.01%)	196,878 (47.99%)	213,384 (52.01%)	-0.0253
Renal failure, severe	98,053 (2.15%)	49,313 (50.29%)	48,740 (49.71%)	0.0017
Hypothyroidism	745,029 (16.36%)	369,655 (49.62%)	375,374 (50.38%)	-0.0068
Other thyroid disorders	129,354 (2.84%)	68,142 (52.68%)	61,212 (47.32%)	0.0183
Peptic ulcer with bleeding	25,912 (0.57%)	12,763 (49.26%)	13,149 (50.74%)	-0.0023
Valvular disease	318,354 (6.99%)	159,361 (50.06%)	158,993 (49.94%)	0.0006
Weight loss	117,125 (2.57%)	55,600 (47.47%)	61,525 (52.53%)	-0.0164

^aColumn percents are presented.

^bRow percents are presented.

Supplemental Table 4. Unadjusted COVID-19 hospitalization rates and adjusted hazards of hospitalization from a Cox proportional hazards regression model including booster and all patient characteristics: sensitivity analysis results for the study cohort derived using the traditional matching method.

	All N (%)	Hospitalization rate per 1,000,000 person day	Adjusted HR (95% CI)
COVID-19 vaccine original			
Pfizer	2,255,330 (49.53%)	49.71 (48.57, 50.87)	Ref
Moderna	2,298,238 (50.47%)	38.60 (37.48, 39.76)	0.82 (0.79, 0.86)
Booster			
No	2,276,784 (50.00%)	11.58 (11.01, 12.17)	Ref
Yes	2,276,784 (50.00%)	78.65 (77.13, 80.20)	0.16 (0.15, 0.16)
Age			
66-70	1,457,106 (32.00%)	21.22 (20.25, 22.24)	Ref
71-75	1,137,888 (24.99%)	35.27 (33.86, 36.74)	1.32 (1.24, 1.40)
76-80	815,910 (17.92%)	53.15 (51.10, 55.27)	1.80 (1.69, 1.92)
81-85	570,487 (12.53%)	71.03 (68.19, 74.06)	2.32 (2.17, 2.47)
86+	572,177 (12.57%)	87.10 (83.90, 90.42)	2.91 (2.73, 3.11)
Gender			
Male	1,856,786 (40.78%)	53.62 (52.24, 55.03)	Ref
Female	2,696,782 (59.22%)	38.67 (37.70, 39.68)	0.71 (0.68, 0.74)
Race			
Non-Hispanic White	3,872,602 (85.05%)	46.28 (45.39, 47.19)	Ref
Non-Hispanic Black	242,278 (5.32%)	45.01 (41.53, 48.78)	0.82 (0.75, 0.89)
Asian	122,198 (2.68%)	20.80 (17.64, 24.52)	0.41 (0.35, 0.48)
Hispanic	166,582 (3.66%)	38.23 (34.42, 42.46)	0.74 (0.66, 0.83)
Other	149,908 (3.29%)	33.31 (29.10, 37.34)	0.91 (0.81, 1.02)
Medicaid eligibility			
No	4,130,228 (90.70%)	43.12 (42.29, 43.96)	Ref
Yes	423,340 (9.30%)	62.76 (59.57, 66.13)	1.41 (1.33, 1.50)
Number of prior hospitalizations			
0	3,961,834 (87.01%)	36.97 (36.18, 37.77)	Ref
1	437,178 (9.60%)	80.51 (77.08, 84.08)	1.11 (1.04, 1.17)
2 and above	154,556 (3.39%)	140.07 (132.57, 147.99)	1.17 (1.08, 1.27)
Prior COVID-19			
No	4,189,400 (92.00%)	46.07 (45.21, 46.94)	Ref
Yes	364,168 (8.00%)	30.08 (27.78, 32.56)	0.38 (0.34, 0.41)

Residence prior to original vaccination			
Community	4,441,404 (97.54%)	44.90 (44.08, 45.73)	Ref
Nursing facility	112,164 (2.46%)	41.59 (36.78, 47.03)	0.49 (0.43, 0.56)
Comorbidity status			
AIDS/HIV	6,127 (0.13%)	29.20 (16.59, 51.42)	0.78 (0.44, 1.37)
Alcohol abuse	36,469 (0.80%)	65.01 (54.91, 76.95)	0.88 (0.74, 1.04)
Deficiency anemia	528,747 (11.61%)	102.13 (98.60, 105.79)	1.19 (1.13, 1.25)
Auto immune	189,550 (4.16%)	80.23 (75.27, 85.52)	1.72 (1.61, 1.84)
Blood loss anemia	38,733 (0.85%)	123.57 (109.84, 139.01)	1.11 (0.98, 1.25)
Leukemia	29,637 (0.65%)	146.14 (130.28, 163.93)	2.53 (2.25, 2.85)
Lymphoma	49,913 (1.10%)	106.77 (96.22, 118.47)	1.88 (1.69, 2.10)
Metastatic cancer	54,302 (1.19%)	73.47 (65.04, 82.98)	1.36 (1.20, 1.54)
Solid tumor without metastasis, malignant	367,393 (8.07%)	55.95 (52.92, 59.16)	1.03 (0.97, 1.10)
Solid tumor without metastasis, in situ	34,597 (0.76%)	56.48 (47.09, 67.76)	1.08 (0.90, 1.29)
Cerebrovascular disease	282,310 (6.20%)	81.05 (76.78, 85.55)	0.98 (0.92, 1.05)
Congestive heart failure	356,103 (7.82%)	131.44 (126.55, 136.54)	1.37 (1.30, 1.45)
Coagulopathy	115,730 (2.54%)	116.76 (108.99, 125.08)	1.21 (1.12, 1.31)
Dementia	280,135 (6.15%)	93.40 (88.72, 98.33)	1.21 (1.14, 1.29)
Depression	459,883 (10.10%)	71.56 (68.40, 74.88)	1.07 (1.02, 1.13)
Diabetes, complicated	622,866 (13.68%)	98.17 (94.95, 101.49)	1.65 (1.57, 1.73)
Diabetes, uncomplicated	395,136 (8.68%)	51.30 (48.41, 54.37)	1.37 (1.28, 1.46)
Drug abuse	30,671 (0.67%)	78.88 (66.72, 93.26)	1.06 (0.90, 1.26)
Hypertension, complicated	490,506 (10.77%)	113.45 (109.57, 117.46)	1.16 (1.08, 1.25)
Hypertension, uncomplicated	2,084,461 (45.78%)	47.02 (45.81, 48.27)	1.22 (1.17, 1.28)
Liver disease, mild	101,027 (2.22%)	69.86 (63.45, 76.92)	1.17 (1.06, 1.29)
Liver disease, moderate to severe	15,217 (0.33%)	125.06 (105.02, 148.91)	1.78 (1.49, 2.13)
Chronic pulmonary disease	538,917 (11.84%)	93.55 (90.20, 97.01)	1.57 (1.50, 1.64)
Neurological disorders affecting movement	128,287 (2.82%)	82.04 (75.75, 88.85)	1.15 (1.06, 1.25)
Seizures and epilepsy	70,887 (1.56%)	90.79 (81.93, 100.62)	1.34 (1.20, 1.50)
Other neurological disorders	111,769 (2.45%)	111.42 (103.57, 119.87)	1.07 (0.98, 1.17)
Obesity	515,693 (11.33%)	76.49 (73.38, 79.72)	1.28 (1.22, 1.34)
Paralysis	65,254 (1.43%)	94.37 (84.93, 104.85)	1.11 (0.98, 1.25)
Peripheral vascular disease	501,662 (11.02%)	90.86 (87.44, 94.41)	1.23 (1.17, 1.29)

Psychoses	147,591 (3.24%)	72.76 (67.19, 78.79)	1.26 (1.15, 1.37)
Pulmonary circulation disease	79,484 (1.75%)	144.67 (134.05, 156.12)	1.23 (1.13, 1.34)
Renal failure, moderate	410,262 (9.01%)	97.40 (93.49, 101.47)	1.34 (1.27, 1.42)
Renal failure, severe	98,053 (2.15%)	192.37 (181.30, 204.12)	2.35 (2.18, 2.54)
Hypothyroidism	745,029 (16.36%)	58.64 (56.39, 60.98)	1.00 (0.96, 1.05)
Other thyroid disorders	129,354 (2.84%)	50.79 (45.95, 56.15)	1.01 (0.91, 1.12)
Peptic ulcer with bleeding	25,912 (0.57%)	87.75 (73.94, 104.14)	0.88 (0.74, 1.05)
Valvular disease	318,354 (6.99%)	84.09 (80.00, 88.38)	0.95 (0.90, 1.01)
Weight loss	117,125 (2.57%)	86.56 (79.61, 93.68)	0.92 (0.84, 1.01)

Supplemental Table 5. Unadjusted COVID-19 hospitalization rates and adjusted hazards of hospitalization from a Cox proportional hazards regression model including booster and all patient characteristics: sensitivity analysis restricting the outcome to those with an admitting diagnosis of COVID-19 and excluding individuals with prior COVID-19 infection in the study cohort derived using target trial method.

	All N (%)	Hospitalization rate 1,000,000 per person day	Adjusted HR (95% CI)
All	7,398,502 (100%)		
COVID-19 vaccine original			
Pfizer	3,742,898 (50.59%)	14.56 (14.04, 15.09)	Ref
Moderna	3,655,604 (49.41%)	10.05 (9.58, 10.55)	0.79 (0.74, 0.84)
Booster			
No	3,699,251 (50.00%)	3.65 (3.39, 3.94)	Ref
Yes	3,699,251 (50.00%)	21.47 (20.82, 22.15)	0.17 (0.16, 0.19)
Age			
66-70	2,132,749 (28.83%)	6.78 (6.30, 7.29)	Ref
71-75	2,052,429 (27.74%)	9.46 (8.88, 10.07)	1.26 (1.15, 1.39)
76-80	1,435,494 (19.40%)	14.20 (13.36, 15.10)	1.72 (1.56, 1.89)
81-85	938,186 (12.68%)	18.80 (17.60, 20.09)	2.19 (1.97, 2.42)
86+	839,644 (11.35%)	24.82 (23.35, 26.37)	2.96 (2.68, 3.28)
Gender			
Male	3,093,166 (41.81%)	15.13 (14.53, 15.75)	Ref
Female	4,605,336 (62.25%)	10.66 (10.24, 11.11)	0.70 (0.66, 0.74)
Race			
Non-Hispanic White	6,391,306 (86.39%)	13.04 (12.65, 13.44)	Ref
Non-Hispanic Black	311,520 (4.21%)	10.50 (9.01, 12.24)	0.65 (0.56, 0.77)
Asian	217,552 (2.94%)	4.97 (3.80, 6.51)	0.35 (0.26, 0.46)
Hispanic	200,148 (2.71%)	11.97 (10.04, 14.29)	0.77 (0.64, 0.92)
Other	277,976 (3.76%)	9.67 (8.18, 11.44)	0.95 (0.80, 1.12)
Medicaid eligibility			
No	6,987,528 (94.45%)	11.97 (11.61, 12.34)	Ref
Yes	410,974 (5.55%)	22.18 (20.25, 24.30)	1.64 (1.47, 1.82)
Number of prior hospitalizations			
0	6,651,950 (89.91%)	10.20 (9.86, 10.54)	Ref
1	574,532 (7.77%)	27.57 (25.75, 29.52)	1.25 (1.14, 1.45)
2 and above	172,020 (2.33%)	48.41 (44.12, 53.11)	1.27 (1.11, 1.45)
Residence prior to original vaccination			
Community	7,339,662 (99.20%)	12.45 (12.09, 12.81)	Ref

Nursing facility	58,840 (0.80%)	23.75 (18.97, 29.74)	0.60 (0.47, 0.76)
Comorbidity status			
AIDS/HIV	8,075 (0.11%)	10.65 (4.43, 25.59)	0.91 (0.38, 2.20)
Alcohol abuse	47,924 (0.65%)	18.93 (14.22, 25.19)	0.81 (0.60, 1.08)
Deficiency anemia	716,872 (9.69%)	29.74 (28.04, 31.54)	1.07 (0.99, 1.16)
Auto immune	294,373 (3.98%)	23.89 (21.60, 26.42)	1.78 (1.60, 1.98)
Blood loss anemia	54,261 (0.73%)	36.44 (30.04, 44.20)	1.12 (0.91, 1.37)
Leukemia	46,467 (0.63%)	50.08 (42.25, 59.35)	3.02 (2.53, 3.61)
Lymphoma	78,740 (1.06%)	35.06 (29.97, 41.01)	2.14 (1.81, 2.52)
Metastatic cancer	80,524 (1.09%)	18.87 (15.28, 23.31)	1.15 (0.93, 1.43)
Solid tumor without metastasis, malignant	601,510 (8.13%)	15.89 (14.56, 17.35)	1.02 (0.93, 1.12)
Solid tumor without metastasis, in situ	61,710 (0.83%)	15.89 (12.04, 20.96)	1.08 (0.82, 1.43)
Cerebrovascular disease	395,484 (5.35%)	24.15 (22.11, 26.37)	0.97 (0.88, 1.08)
Congestive heart failure	467,231 (6.32%)	41.32 (38.83, 43.95)	1.34 (1.22, 1.46)
Coagulopathy	157,710 (2.13%)	34.41 (30.67, 38.60)	1.14 (1.01, 1.30)
Dementia	286,208 (3.87%)	33.98 (31.16, 37.06)	1.29 (1.17, 1.44)
Depression	597,266 (8.07%)	23.39 (21.74, 25.16)	1.13 (1.03, 1.23)
Diabetes, complicated	911,464 (12.32%)	29.21 (27.70, 30.81)	1.68 (1.56, 1.81)
Diabetes, uncomplicated	619,206 (8.37%)	14.67 (13.38, 16.08)	1.38 (1.25, 1.53)
Drug abuse	40,788 (0.55%)	19.76 (15.69, 24.90)	0.94 (0.70, 1.26)
Hypertension, complicated	671,223 (9.07%)	35.26 (33.34, 37.29)	1.14 (1.02, 1.28)
Hypertension, uncomplicated	3,354,447 (45.34%)	13.18 (12.64, 13.74)	1.17 (1.09, 1.26)
Liver disease, mild	147,417 (1.99%)	23.02 (19.87, 26.68)	1.29 (1.04, 1.50)
Liver disease, moderate to severe	20,147 (0.27%)	60.38 (54.60, 66.38)	1.25 (0.87, 1.78)
Chronic pulmonary disease	764,601 (10.33%)	30.05 (28.39, 31.80)	1.74 (1.62, 1.87)
Neurological disorders affecting movement	181,527 (2.45%)	25.71 (22.66, 29.17)	1.20 (1.05, 1.37)
Seizures and epilepsy	83,949 (1.13%)	30.92 (26.12, 36.60)	1.40 (1.17, 1.67)
Other neurological disorders	119,002 (1.61%)	37.99 (33.49, 43.09)	1.03 (0.89, 1.19)
Obesity	767,200 (10.37%)	24.24 (22.74, 25.84)	1.39 (1.29, 1.51)
Paralysis	67,927 (0.92%)	32.91 (27.48, 39.42)	1.09 (0.89, 1.33)
Peripheral vascular disease	712,834 (9.63%)	26.44 (24.83, 28.16)	1.17 (1.08, 1.26)
Psychoses	176,832 (2.39%)	23.57 (20.62, 26.94)	1.23 (1.06, 1.42)
Pulmonary circulation disease	109,683 (1.48%)	48.05 (42.69, 54.09)	1.37 (1.20, 1.56)
Renal failure, moderate	610,559 (8.25%)	28.54 (26.73, 30.47)	1.35 (1.24, 1.47)
Renal failure, severe	131,115 (1.77%)	60.31 (54.80, 66.38)	2.52 (2.23, 2.84)

Hypothyroidism	1,147,787 (15.51%)	17.30 (16.27, 18.40)	1.05 (0.97, 1.13)
Other thyroid disorders	207,976 (2.81%)	13.17 (11.15, 15.55)	0.92 (0.77, 1.09)
Peptic ulcer with bleeding	37,979 (0.51%)	24.78 (18.50, 33.19)	0.83 (0.62, 1.12)
Valvular disease	498,420 (6.74%)	23.49 (21.68, 25.45)	0.92 (0.84, 1.02)
Weight loss	129,999 (1.76%)	28.36 (24.65, 32.64)	0.92 (0.79, 1.07)

Supplemental Table 6. Unadjusted COVID-19 hospitalization rates and adjusted hazards of hospitalization from a Cox proportional hazards regression models including booster and all patient characteristics: sensitivity analysis restricting the outcome to those with an admitting diagnosis of COVID-19 and excluding individuals with prior COVID-19 infection in the study cohort derived using the traditional matching method.

	All N (%)	Hospitalization rate per 1,000,000 person day	Adjusted HR (95% CI)
COVID-19 vaccine original			
Pfizer	2,038,992 (48.67%)	24.91 (24.07, 25.78)	Ref
Moderna	2,150,408 (51.33%)	18.91 (24.07, 25.78)	0.79 (0.75, 0.84)
Booster			
No	2,094,700 (50.00%)	4.94 (4.56, 5.36)	Ref
Yes	2,094,700 (50.00%)	39.69 (38.58, 40.85)	0.13 (0.12, 0.14)
Age			
66-70	1,364,894 (32.58%)	10.38 (9.68, 11.12)	Ref
71-75	1,055,430 (25.19%)	17.46 (16.44, 18.54)	1.32 (1.20, 1.44)
76-80	750,146 (17.91%)	26.25 (24.77, 27.82)	1.80 (1.64, 1.97)
81-85	518,226 (12.37%)	36.70 (34.58, 38.96)	2.41 (2.19, 2.65)
86+	500,704 (11.95%)	43.74 (41.34, 46.27)	2.89 (2.62, 2.65)
Gender			
Male	1,717,182 (40.99%)	27.19 (26.18, 28.23)	Ref
Female	2,472,218 (59.01%)	18.65 (17.95, 19.38)	0.67 (0.63, 0.71)
Race			
Non-Hispanic White	3,557,572 (84.92%)	23.12 (22.47, 23.79)	Ref
Non-Hispanic Black	221,522 (5.29%)	17.50 (15.29, 20.02)	0.64 (0.55, 0.73)
Asian	117,260 (2.80%)	10.39 (8.19, 13.18)	0.41 (0.33, 0.53)
Hispanic	151,226 (3.61%)	19.58 (16.78, 22.84)	0.75 (0.64, 0.88)
Other	141,820 (3.39%)	17.70 (15.07, 20.80)	0.97 (0.82, 1.14)
Medicaid			
No	3,839,076 (91.64%)	21.23 (20.63, 21.84)	Ref
Yes	350,324 (8.36%)	33.47 (30.93, 36.21)	1.47 (1.34, 1.61)
Number of prior hospitalizations			
0	3,715,352 (88.68%)	18.13 (17.56, 18.71)	Ref
1	357,842 (8.54%)	45.14 (42.35, 48.11)	1.20 (1.11, 1.31)
2 and above	116,206 (2.77%)	76.32 (70.08, 83.11)	1.22 (1.08, 1.37)
Residence prior to original vaccination			
Community	4,138,566 (98.79%)	22.02 (21.43, 22.63)	Ref
Nursing facility	50,834 (1.21%)	35.57 (29.21, 43.31)	0.66 (0.53, 0.81)

Comorbidity status			
AIDS/HIV	5,508 (0.13%)	18.84 (8.98, 39.52)	1.08 (0.51, 2.27)
Alcohol abuse	30,737 (0.73%)	31.82 (24.49, 41.35)	0.85 (0.65, 1.11)
Deficiency anemia	438,785 (10.47%)	50.94 (48.24, 53.79)	1.07 (0.99, 1.15)
Auto immune	169,397 (4.04%)	41.35 (37.65, 45.42)	1.81 (1.64, 2.00)
Blood loss anemia	33,001 (0.79%)	61.32 (51.20, 73.44)	1.09 (0.91, 1.32)
Leukemia	26,751 (0.64%)	84.45 (72.07, 98.95)	2.96 (2.51, 3.49)
Lymphoma	45,213 (1.08%)	59.81 (51.70, 69.19)	2.16 (1.85, 2.52)
Metastatic cancer	49,796 (1.19%)	32.97 (27.28, 39.85)	1.22 (1.01, 1.49)
Solid tumor without metastasis, malignant	336,268 (8.03%)	27.19 (25.02, 29.55)	1.01 (0.92, 1.10)
Solid tumor without metastasis, in situ	31,914 (0.76%)	29.50 (22.70, 38.33)	1.12 (0.86, 1.46)
Cerebrovascular disease	237,178 (5.66%)	40.71 (37.46, 44.23)	0.93 (0.84, 1.03)
Congestive heart failure	294,785 (7.04%)	70.19 (66.31, 74.30)	1.37 (1.26, 1.49)
Coagulopathy	95,771 (2.29%)	58.39 (52.50, 64.93)	1.16 (1.03, 1.30)
Dementia	196,140 (4.68%)	53.79 (49.63, 58.31)	1.18 (1.07, 1.30)
Depression	36,485 (8.80%)	37.54 (35.03, 40.24)	1.06 (0.97, 1.14)
Diabetes, complicated	546,407 (13.04%)	51.27 (48.82, 53.85)	1.74 (1.62, 1.86)
Diabetes, uncomplicated	358,661 (8.56%)	26.54 (24.39, 28.88)	1.44 (1.31, 1.58)
Drug abuse	26,901 (0.64%)	42.54 (33.36, 54.24)	1.15 (0.90, 1.48)
Hypertension, complicated	413,015 (9.86%)	58.84 (55.83, 61.99)	1.11 (0.99, 1.23)
Hypertension, uncomplicated	1,896,475 (45.27%)	23.58 (22.69, 24.52)	1.19 (1.11, 1.28)
Liver disease, mild	89,531 (2.14%)	34.37 (29.72, 39.74)	1.14 (0.98, 1.33)
Liver disease, moderate to severe	13,301 (0.32%)	48.14 (35.70, 64.91)	1.37 (1.01, 1.86)
Chronic pulmonary disease	463,784 (11.07%)	49.87 (47.27, 52.61)	1.66 (1.55, 1.77)
Neurological disorders affecting movement	107,375 (2.56%)	44.39 (39.45, 49.95)	1.20 (1.06, 1.35)
Seizures and epilepsy	54,628 (1.30%)	45.09 (38.23, 53.18)	1.23 (1.03, 1.46)
Other neurological disorders	80,505 (1.92%)	62.89 (56.14, 70.45)	1.10 (0.96, 1.25)
Obesity	455,572 (10.87%)	40.65 (38.27, 43.17)	1.35 (1.26, 1.46)
Paralysis	47,108 (1.12%)	54.77 (46.60, 64.38)	1.16 (0.97, 1.39)
Peripheral vascular disease	421,410 (10.06%)	46.95 (44.30, 49.75)	1.21 (1.12, 1.29)
Psychoses	112,883 (2.69%)	37.13 (32.71, 42.15)	1.17 (1.02, 1.34)
Pulmonary circulation disease	68,108 (1.63%)	78.33 (70.07, 87.57)	1.30 (1.15, 1.47)
Renal failure, moderate	358,276 (8.55%)	48.57 (45.67, 51.67)	1.31 (1.21, 1.42)
Renal failure, severe	83,961 (2.00%)	101.61 (93.07, 110.92)	2.51 (2.24, 2.86)
Hypothyroidism	660,296 (15.76%)	30.64 (28.93, 32.45)	1.06 (0.99, 1.14)

Other thyroid disorders	117,446 (2.80%)	24.10 (20.69, 28.07)	0.97 (0.83, 1.13)
Peptic ulcer with bleeding	21,601 (0.52%)	45.42 (35.04, 58.89)	0.90 (0.69, 1.18)
Valvular disease	284,109 (6.78%)	42.55 (39.51, 45.81)	0.96 (0.88, 1.05)
Weight loss	86,086 (2.05%)	46.48 (40.88, 52.84)	0.91 (0.79, 1.04)

Supplemental Table 7. Unadjusted COVID-19 hospitalization rates, adjusted hazards of hospitalization and vaccine effectiveness for booster vs non-booster, by interval between primary vaccine and booster dose in the study cohort derived using traditional matching method.

Months between primary vaccine and booster dose	Booster	Patients, N (%), N=4,553,568	Hospitalized individuals, N	Rate of hospitalization, per 1,000,000 person-day	Adjusted HR (95% CI) ^a	Booster vaccine effectiveness, percent (95% CI) ^b
4 to <5 months	Unboosted	22,910 (0.50%) ^c	197	82.23 (71.51, 95.55)	Ref	Ref
	Boosted	22,910 (0.50%)	90	36.37 (29.58, 44.72)	0.32 (0.25, 0.42)	68 (58, 75)
5 to <6 months	Unboosted	65,528 (1.44%)	607	96.34 (88.97, 104.31)	Ref	Ref
	Boosted	65,528 (1.44%)	179	27.14 (23.44, 31.42)	0.24 (0.21, 0.29)	76 (71, 79)
6 to <7 months	Unboosted	558,943 (12.27%)	3,131	84.40 (81.50, 87.41)	Ref	Ref
	Boosted	558,943 (12.27%)	411	10.84 (9.84, 11.94)	0.14 (0.12, 0.15)	86 (85, 88)
7 to <8 months	Unboosted	874,273 (19.20%)	3,596	74.49 (72.09, 76.96)	Ref	Ref
	Boosted	874,273 (19.20%)	421	8.60 (7.82, 9.46)	0.13 (0.12, 0.14)	87 (86, 88)
8 to <9 months	Unboosted	611,391 (13.43%)	2,153	74.22 (71.15, 77.42)	Ref	Ref
	Boosted	611,391 (13.43%)	303	10.32 (9.22, 11.55)	0.15 (0.13, 0.17)	85 (83, 87)
≥9 months	Unboosted	143,739 (3.16%)	404	77.84 (70.61, 85.81)	Ref	Ref
	Boosted	143,739 (3.16%)	107	20.44 (16.91, 24.70)	0.27 (0.22, 0.34)	73 (66, 78)

^aAdjusted for individual's age, gender, race, Medicaid status, the type of booster and original vaccination type, prior COVID-19 infection, residence and 38 comorbidities.

^bVaccine effectiveness was computed as $(1 - HR) * 10$.

^cColumn percent.

Supplemental Table 8. Association of interval between original vaccination and booster with risk of hospitalization for COVID-19: adjusted hazards ratio from a fully adjusted Cox proportional hazards regression model in the study cohort derived using the traditional matching method.

	Adjusted HR (95% CI)
Months between primary vaccine and booster dose ^a	
4 to <5 months	1.21 (0.91, 1.61)
5 to <6 months	Ref
6 to <7 months	0.82 (0.67, 0.99)
7 to <8 months	0.88 (0.72, 1.07)
8 to <9 months	1.18 (0.96, 1.44)
>=9 months	1.90 (1.46, 2.49)
Age	
66-70	Ref
71-75	1.16 (0.99, 1.35)
76-80	1.35 (1.14, 1.59)
81-85	1.85 (1.56, 2.19)
86+	2.38 (2.01, 2.83)
Gender	
Male	Ref
Female	0.66 (0.60, 0.74)
Race	
Non-Hispanic White	Ref
Non-Hispanic Black	1.01 (0.81, 1.24)
Asian	0.46 (0.30, 0.70)
Hispanic	1.06 (0.81, 1.38)
Other	0.87 (0.64, 1.18)
Medicaid eligibility	
No	Ref
Yes	1.50 (1.27, 1.77)
Booster and Original Vaccination ^a	
Homologous:	
Pfizer-Pfizer	Ref
Moderna-Moderna	0.71 (0.63, 0.79)
Heterologous:	
Pfizer-Moderna	1.22 (0.99, 1.35)
Moderna-Pfizer	0.82 (0.54, 1.23)
Number of prior hospitalizations	
0	Ref
1	1.38 (1.19, 1.59)
2 and above	1.43 (1.17, 1.74)
Prior COVID-19 infection	
No	Ref
Yes	0.51 (0.41, 0.63)
Residence	
Community	Ref
Nursing facility	0.63 (0.47, 0.86)
Comorbidity ^b	
AIDS/HIV	0.74 (0.24, 2.29)

Alcohol abuse	0.87 (0.55, 1.37)
Deficiency anemia	1.17 (1.03, 1.33)
Auto immune disease	2.34 (2.02, 2.72)
Blood loss anemia	0.95 (0.69, 1.31)
Leukemia	4.13 (3.36, 5.08)
Lymphoma	3.21 (2.66, 3.86)
Metastatic cancer	1.60 (1.24, 2.08)
Solid tumor without metastasis	1.07 (0.93, 1.24)
Solid tumor in situ	1.44 (0.99, 2.10)
Cerebrovascular disease	0.92 (0.78, 1.10)
Congestive heart failure	1.12 (0.97, 1.31)
Coagulopathy	1.19 (0.99, 1.42)
Dementia	1.43 (1.20, 1.71)
Depression	1.10 (0.95, 1.27)
Diabetes, complicated	1.67 (1.48, 1.89)
Diabetes, uncomplicated	1.27 (1.06, 1.52)
Drug abuse	0.73 (0.42, 1.27)
Hypertension, complicated	1.22 (1.01, 1.48)
Hypertension, uncomplicated	1.14 (1.01, 1.30)
Liver disease, mild	1.32 (1.05, 1.66)
Liver disease, moderate to severe	1.79 (1.21, 2.65)
Chronic pulmonary disease	1.60 (1.42, 1.80)
Neurological disorders affecting movement	1.20 (0.96, 1.50)
Seizures and epilepsy	1.28 (0.95, 1.71)
Other neurological disorders	1.13 (0.91, 1.40)
Obesity	1.12 (0.98, 1.29)
Paralysis	0.98 (0.70, 1.37)
Peripheral vascular disease	1.30 (1.15, 1.47)
Psychoses	1.25 (0.99, 1.57)
Pulmonary circulation disease	1.24 (0.99, 1.55)
Renal failure, moderate	1.50 (1.29, 1.73)
Renal failure, severe	3.34 (2.79, 4.01)
Hypothyroidism	1.03 (0.91, 1.16)
Other thyroid disorders	0.87 (0.66, 1.15)
Peptic ulcer with bleeding	1.02 (0.68, 1.53)
Valvular disease	0.88 (0.75, 1.03)
Weight loss	0.96 (0.78, 1.19)

^aIn this analysis the hospitalization rates for boosted enrollees are compared across different intervals between original vaccination and booster. In the other analyses of booster effectiveness by interval (**Figure 1, eTable 2, eTable 8**), hospitalization rates for boosted individuals were compared to non-boosted controls within each time interval.

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