## **Supplemental Online Content**

Kelly JD, Leonard S, Hoggatt KJ, et al. Incidence of severe COVID-19 illness following vaccination and booster with BNT162b2, mRNA-1273, and Ad26.COV2.S vaccines. *JAMA*. Published online September 26, 2022. doi:10.1001/jama.2022.17985

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**eFigure 1.** Cohort Selection in a Study of U.S. Veterans Who Received Booster Vaccination for COVID-19

eFigure 2. Map of VA Regions

**eTable 1.** Incidence of Hospitalization With COVID-19 Pneumonia/Death Following Vaccination and Boosters With Follow-up Time Ending on Date of 4<sup>th</sup> Dose, by Overall Cohort and Immunocompromised Subgroup

**eTable 2.** Characteristics of the Boosted Cohort by Combination of Vaccination Series

eTable 3. Characteristics of Cohort by Outcome

**eTable 4.** Incidence of Outcomes Following Vaccination and Booster With mRNA-1273 x3, BNT162b2 x3, and Ad26.COV2.S x2 by Delta Variant vs Omicron Variant Eras

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

### eAppendix 1. COVID-19 Pneumonia Ascertainment Using a Combination Text-Processing Facilitated Chart Review and ICD Codes

To develop a text processing algorithm for rapid chart review, we stratified hospitalizations by the ICD code J12.82 and the presence of the word pneumonia in the medical record. We searched the VA medical record during the hospitalization period for the word "pneumonia" using a text processing tool available on the VA Informatics and Computing Infrastructure. Using the text processing tool and the ICD coded J12.82, we stratified a sample of hospitalizations into 4 groups: A) those with a discharge diagnosis of J12.82 and the word pneumonia in their notes B) those without a discharge diagnosis of J12.82 but who had the word pneumonia in their notes C) those with a discharge diagnosis of J12.82 but no note containing the word pneumonia and D) those with neither the code J12.82 nor the word pneumonia in their notes.

Algorithm to identify patients admitted with COVID pneumonia (Total Reviewed to Develop Algorithm N=594)					
Discharge diagnosis J12.82 Discharge diagnosis J12.82 present absent					
Discharge summary or another note contains the word "pneumonia"	A=222	B=202			
No note contains "pneumonia"	C=3	D=167			

A: There were 222 patients who were discharged with the ICD code J12.82 and had the word pneumonia in hospital notes or in the discharge summary. We reviewed a random sample of 25 cases. All 25 cases had documented COVID pneumonia.

B: There were 202 patients who did not have a discharge diagnosis of J12.82 but had the word pneumonia in hospital notes or in the discharge summary. We reviewed <u>all</u> 202 cases. Among the 202 cases review, 34 were identified by the care team as having COVID-19 pneumonia.

C: There were 3 hospitalizations with a discharge diagnosis of J12.82 but no note containing the word pneumonia. We reviewed all 3 cases. Among the 3 cases, two cases were identified by the care team as having COVID-19 pneumonia.

D: There were 167 cases with neither the code J12.82 nor the word pneumonia in their notes. We reviewed a random sample of 50 charts in this category. No patient was identified as having COVID-19 pneumonia in this group.

This algorithm demonstrated that all cases randomly sampled in Box A (cases with both the diagnosis code and the word pneumonia in the chart) were COVID-19 pneumonia and in Box B (cases without the code J12.82 and without the word pneumonia in the chart) were not COVID-19 pneumonia. Therefore, we did not conduct any further chart review of cases identified in Boxes A and B. This algorithm further demonstrated the presence of inconsistences among cases identified in Boxes B and C. For example, some cases were COVID-19 pneumonia even though the discharge diagnosis of J12.82 was absent. Therefore, we decided to conduct chart review of all cases identified in these Boxes (B and C). This algorithm was then applied to all patients who were hospitalized in the follow-up period.

## eAppendix 2. Reasons for Hospitalization

We reviewed a random sample of 50 charts of patients who were hospitalized within 30 days post breakthrough infection who did not have COVID-19 pneumonia. Among these 50 patients, 15 patients (30%) were diagnosed by the care team as having COVID-related hospitalizations.

Reasons for hospitalization	COVID-related (yes/no)
Admitted for nephrectomy due to cancer (right renal mass s/p open right radical	No
nephrectomy)	
Bacterial pneumonia, COPD exacerbation	Yes
Musculoskeletal pain, Cough d/t covid or heavy lifting from work	Yes
COVID-19 associated nausea/vomiting	Yes
Atrial fibrillation, asymptomatic COVID-19 screening test during planned admission for cardioversion	No
Alcohol withdrawal, asymptomatic covid	No
Chest pain during dialysis, no mention of COVID, tested positive 12 days prior to hospitalization	No
Alcohol withdrawal, COVID-19 outside window of isolation	No
Proximal humeral fracture, screened positive	No
Fall and syncope likely secondary to polypharmacy	No
Alcohol Detoxification, mild URI symptoms	No
Bilateral Ureteral stones, right flank pain, tested positive for COVID-19 18 days before	No
admission. COVID not mentioned in hospitalizations	NO
Malaise, shortness of breath, mild COVID-19 infection	Yes
Cervical myelopathy, status-post C3 to C5 laminoplasty, asymptomatic COVID-19 infection, discovered during screening.	No
COVID-19 infection, malaise	Yes
Recurrent urinary tract infection and COVID-19 related diarrhea	Yes
Alcohol use disorder, moderate, asymptomatic COVID-19 infection	No
Cord compression from multiple myeloma, asymptomatic COVID-19 infection	No
Tension pneumothorax in setting of metastatic esophageal cancer, asymptomatic COVID-19 infection	No
COVID-19 infection, syncope, diarrhea	Yes
Dyspnea on exertion and chest pain concerning for unstable angina or pulmonary, COVID-19 positive one month before	No
Head trauma secondary to mechanical fall, asymptomatic COVID-19, alcohol abuse	No
Presenting from Community Living Center for altered mental status, found to have urinary tract infection and hypernatremia, COVID-19 one month ago	No
Nausea, vomiting, diarrhea likely secondary to COVID-19 and uremia	Yes
Patient admitted with diabetes; right-sided weakness and fatigue, found to be hypoglycemic, negative stroke work up; labeled as incidental COVID-19 infection by care team	No
Iron deficiency anemia secondary to recurrent gastrointestinal bleeding	No
Bipolar Type I disorder, depressed episode (severe), incidental COVID-19 with mild symptoms	Yes
COVID-19 illness and mild acute kidney injury	Yes
Chest pain, palpitations, and pain in left leg after running out of hydrocodone, asymptomatic COVID-19	No
COVID-19 with resolved acute hypoxic respiratory failure	Yes
Referred to Emergency Department for admission for pacemaker placement	No
Acute kidney injury on chronic kidney disease stage III, hyperkalemia, asymptomatic pyuria,	No
fevers, asymptomatic COVID-19 found 2 days before discharge	
Infarct left cerebellar region, COVID-19 with bilateral interstitial opacities on chest x-ray requiring O2 supplementation	Yes
Orthostatic hypotension, incidental COVID-19	No
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Right obstructing ureteral stone 2mm, acute kidney injury, resolved urinary tract infection,	No
proximal atrial fibrillation, asymptomatic COVID-19	
History of severe chronic obstructive pulmonary disease and chronic kidney disease stage V	Yes
who presents with COVID-19 infection	
Acute on chronic anemia, shortness of breath and difficulty swallowing, incidental COVID-19	No
Abdominal pain, constipation, light headache, poor appetite	No
Hyponatremia and concern for gastrointestinal bleed, mild symptoms/asymptomatic COVID-19	No
Nausea and dizziness in patient who reports drinking 5-6 shots of scotch a day but recently had a binge, incidental COVID-19	No
3 days of acute worsening of chronic vertigo possibly exacerbated by acute COVID-19 infection	Yes
Work up and management of recurring chest pain, shortness of breath, nausea, and diaphoresis, incidental COVID-19	No
Osteomyelitis of left lower extremity, COVID-19 asymptomatic	No
COVID-19 with gastrointestinal symptoms	Yes
Left hilar mass and mediastinal left anterior descending artery, COVID-19 asymptomatic	No
Multifocal intracerebral brain hemorrhage and large epidural hematoma without MLS, fracture of parietal bone, COVID-19 positive 6 weeks into 4-month hospitalization	No
Homicidal ideation with auditory hallucinations, incidental COVID-19	No
Symptomatic anemia, incidental COVID-19	No
Alzheimer's dementia admitted for now resolving acute encephalopathy and found to have urinary tract infection, prior COVID-19 infection noted	No
Chronic obstructive pulmonary disease with acute exacerbation, likely precipitated by COVID-19	Yes

# eAppendix 3. Variable Definitions

Variable	Definition	
Hypertension	Two outpatient one inpatient code in past 2 years	110, 111, 111.0, 111.9, 112.0, 112.9, 113, 113.0, 113.1, 113.10
Heart Failure	Two outpatient one inpatient code in past 2 years	109.81, 111.0, 113.0, 113.2, 150.1, 150.20, 150.21, 150.22, 150.23, 150.30, 150.31, 150.32, 150.33, 150.40, 150.41, 150.42, 150.43, 150.814, 150.82, 150.83, 150.84, 150.89, 150.9
Ischemic Heart Disease  Two outpatient one inpatient code in past 2 years		120.0, 120.8, 120.9, 121.01, 121.02, 121.09, 121.11, 121.19, 121.21, 121.29, 121.A9, 122.0, 122.1, 122.2, 122.8, 122.9, 123.0, 123.1, 123.2, 123.3, 123.4, 123.5, 123.6, 123.7, 123.8, 124.0, 124.1, 124.8, 124.9, 125.10, 125.110, 125.118, 125.119, 125.2, 125.3, 125.4, 125.5, 125.6, 125.7, 125.700, 125.708, 125.709, 125.710, 125.718, 125.719, 125.720, 125.728, 125.729, 125.730, 125.738, 125.739, 125.750, 125.758, 125.759, 125.760, 125.768, 125.769, 125.790, 125.790, 125.790, 125.790, 125.790, 125.810, 125.811, 125.812, 125.82, 125.83, 125.84, 125.89, 125.9, 151.2, Z98.61
	Two outpatient one inpatient code in past 2 years	E08, E08.0, E08.00, E08.01, E08.1, E08.10, E08.11, E08.2, E08.21, E08.22, E08.29, E08.3, E08.31, E08.311, E08.319, E08.32, E08.321, E08.3211, E08.3212, E08.3213, E08.3219, E08.3202, E08.3203, E08.3203, E08.3203, E08.3203
Diabetes		E08.329, E08.3291, E08.3292, E08.3293, E08.3299, E08.33, E08.331, E08.3311, E08.3312, E08.3313, E08.3319, E08.3391, E08.3391, E08.3392, E08.3393, E08.3399, E08.34, E08.341, E08.3411, E08.3412, E08.3413, E08.3419, E08.349, E08.3491, E08.3492, E08.3493, E08.3519, E08.3552, E08.3511, E08.3512, E08.3513, E08.3519, E08.3521, E08.3521, E08.3522, E08.3523, E08.3529, E08.3523, E08.3531, E08.3531, E08.3531, E08.3531, E08.3531, E08.3531, E08.3531, E08.3531, E08.3532, E08.3533, E08.3539, E08.3531, E08.3541, E08.3542, E08.3543, E08.3549, E08.3554, E08.3551, E08.3552, E08.3553, E08.3559, E08.3591, E08.3592, E08.3593, E08.3599, E08.36, E08.37, E08.37X1, E08.37X2, E08.37X3, E08.37X9, E08.39, E08.44, E08.49, E08.5, E08.60, E08.41, E08.42, E08.43, E08.44, E08.49, E08.5, E08.51, E08.52, E08.59, E08.6, E08.610, E08.610, E08.618, E08.62, E08.620, E08.621, E08.622, E08.628, E08.63, E08.630, E08.638, E08.64, E08.641, E08.649, E08.65, E08.69, E08.8, E08.9, E09, E09.0, E09.00, E09.01, E09.1, E09.10, E09.11, E09.21, E09.22, E09.22, E09.29, E09.3, E09.311, E09.3213, E09.3213, E09.3219, E09.3292, E09.3293, E09.3293, E09.3293, E09.3293, E09.3393, E09.3391, E09.3312, E09.3313, E09.3319, E09.3399, E09.341, E09.3411, E09.3412, E09.3413, E09.3319, E09.339, E09.3391, E09.3492, E09.3493, E09.3499, E09.352, E09.3511, E09.3512, E09.3513, E09.3519, E09.352, E09.3511, E09.3512, E09.3513, E09.3519, E09.3522, E09.3533, E09.3531, E09.3514, E09.3542, E09.3543, E09.3549, E09.3559, E09.3551, E09.3552, E09.3553, E09.3559, E09.3559, E09.3551, E09.3551, E09.3552, E09.3553, E09.3559, E09.3599, E09.3591, E09.3592, E09.3593, E09.3599, E09.3599, E09.3591, E09.3592, E09.3593, E09.3599, E09.3594, E09.377X1, E09.37X2, E09.3593, E09.3599, E09.36, E09.37, E09.37X1, E09.37X2, E09.3593, E09.3599, E09.36, E09.44, E09.40,

E09.41, E09.42, E09.43, E09.44, E09.49, E09.5, E09.51, E09.52, E09.59, E09.6, E09.61, E09.610, E09.618, E09.62, E09.620, E09.621, E09.622, E09.628, E09.63, E09.630, E09.638, E09.64, E09.641, E09.649, E09.65, E09.69, E09.8, E09.9, E10, E10.1, E10.10, E10.11, E10.2, E10.21, E10.22, E10.29, E10.3, E10.31, E10.311, E10.319, E10.32, E10.321, E10.3211, E10.3212, E10.3213, E10.3219, E10.329, E10.3291, E10.3292, E10.3293, E10.3299, E10.33, E10.331, E10.3311, E10.3312, E10.3313, E10.3319, E10.339, E10.3391, E10.3392, E10.3393, E10.3399, E10.34, E10.341, E10.3411, E10.3412, E10.3413, E10.3419, E10.349, E10.3491, E10.3492, E10.3493, E10.3499, E10.35, E10.351, E10.3511, E10.3512, E10.3513, E10.3519, E10.352, E10.3521, E10.3522, E10.3523, E10.3529, E10.353, E10.3531, E10.3532, E10.3533, E10.3539, E10.354, E10.3541, E10.3542, E10.3543, E10.3549, E10.355, E10.3551, E10.3552, E10.3553, E10.3559, E10.359, E10.3591, E10.3592, E10.3593, E10.3599, E10.36, E10.37, E10.37X1, E10.37X2, E10.37X3, E10.37X9, E10.39, E10.4, E10.40, E10.41, E10.42, E10.43, E10.44, E10.49, E10.5, E10.51, E10.52, E10.59, E10.6, E10.61, E10.610, E10.618, E10.62, E10.620, E10.621, E10.622, E10.628, E10.63, E10.630, E10.638, E10.64, E10.641, E10.649, E10.65, E10.69, E10.8, E10.9, E11, E11.0, E11.00, E11.01, E11.1, E11.10, E11.11, E11.2, E11.21, E11.22, E11.29, E11.3, E11.31, E11.311, E11.319, E11.32, E11.321, E11.3211, E11.3212, E11.3213, E11.3219, E11.329, E11.3291, E11.3292, E11.3293, E11.3299, E11.33, E11.331, E11.3311, E11.3312, E11.3313, E11.3319, E11.339, E11.3391, E11.3392, E11.3393, E11.3399, E11.34, E11.341 E11.3411, E11.3412, E11.3413, E11.3419, E11.349, E11.3491, E11.3492, E11.3493, E11.3499, E11.35, E11.351, E11.3511, E11.3512, E11.3513, E11.3519, E11.352, E11.3521, E11.3522, E11.3523, E11.3529, E11.353, E11.3531, E11.3532, E11.3533, E11.3539, E11.354, E11.3541, E11.3542, E11.3543, E11.3549, E11.355, E11.3551, E11.3552, E11.3553, E11.3559, E11.359, E11.3591, E11.3592, E11.3593, E11.3599, E11.36, E11.37, E11.37X1, E11.37X2, E11.37X3, E11.37X9, E11.39, E11.4, E11.40, E11.41, E11.42, E11.43, E11.44, E11.49, E11.5, E11.51, E11.52, E11.59, E11.6, E11.61, E11.610, E11.618, E11.62, E11.620, E11.621, E11.622, E11.628, E11.63, E11.630, E11.638, E11.64, E11.641, E11.649, E11.65, E11.69, E11.8, E11.9, E13, E13.0, E13.00, E13.01, E13.1, E13.10, E13.11, E13.2, E13.21, E13.22, E13.29, E13.3, E13.31, E13.311, E13.319, E13.32, E13.321, E13.3211, E13.3212, E13.3213, E13.3219, E13.329, E13.3291, E13.3292, E13.3293, E13.3299, E13.33, E13.331, E13.3311, E13.3312, E13.3313, E13.3319, E13.339, E13.3391, E13.3392, E13.3393, E13.3399, E13.34, E13.341, E13.3411, E13.3412, E13.3413, E13.3419, E13.349, E13.3491, E13.3492, E13.3493, E13.3499, E13.35, E13.351, E13.3511, E13.3512, E13.3513, E13.3519, E13.352, E13.3521, E13.3522, E13.3523, E13.3529, E13.353, E13.3531, E13.3532, E13.3533, E13.3539, E13.354, E13.3541, E13.3542, E13.3543, E13.3549, E13.355, E13.3551, E13.3552, E13.3553,

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Stroke or Transient Ischemic Attack (TIA)  COPD or Bronchiectasis Cirrhosis	Two outpatient one inpatient code in past 2 years  Two outpatient one inpatient code in past 2 years  Two outpatient one inpatient code in past 2 years	E13.3559, E13.359, E13.3591, E13.3592, E13.3593, E13.3599, E13.36, E13.37, E13.37X1, E13.37X2, E13.37X3, E13.37X9, E13.39, E13.4, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.5, E13.51, E13.52, E13.59, E13.6, E13.61, E13.610, E13.618, E13.62, E13.620, E13.621, E13.622, E13.628, E13.63, E13.630, E13.638, E13.64, E13.641, E13.649, E13.65, E13.69, E13.8, E13.9  G45, G45.1, G45.3, G45.8, G45.9  J41, J41.0, J41.1, J41.8, J42, J43, J43.0, J43.1, J43.2, J43.8, J43.9, J44, J44.0, J44.1, J44.9  B19.0, B19.11, B19.21, K65.2, K70.11, K70.2, K70.3, K70.30, K70.31, K70.41, K70.9, K71.11, K71.51, K71.7, K72.01, K72.11, K72.91, K74, K74.00, K74.01, K74.02, K74.1, K74.2, K74.3, K74.4, K74.5, K74.6, K74.60, K74.69, K76.6, K76.7, K76.81, I85, I85.0, I85.00, I85.01, I85.1, I85.10, I85.11, R18.8
Dialysis	Any single code in prior 6 months	VA algorithm, code available upon request
Chronic Kidney Disease	Most recent GFR prior to booster dose	Severe CKD was defined as GFR<30
Dementia Disease	Two outpatient one inpatient code in past 2 years	F01, F01.5, F01.50, F01.51, F02, F02.8, F02.80, F02.81, F03, F03.9, F03.90, F03.91, F10.27, F10.97, F13.27, F13.97, F18.17, F18.27, F18.97, F19.17, F19.27, F19.97, G30, G30.0, G30.1, G30.8, G30.9, G31.0, G31.01, G31.09, G31.83
Immunocompromised	Receipt IV chemotherapy in the 90 days before vaccination completion     Receipt of immunosuppressant drugs     Receipt of antiretroviral drugs	See table below for complete list of drugs
Solid Organ Tumor	Head and Neck Cancer Lung Cancer/respiratory tract GI Tract Cancer Other GI Cancer Endocrine cancer Genitourinary tract Cancer Prostate cancer CNS cancer Bone/limb/connective tissue cancers Other cancer	C00, C00.0, C00.1, C00.2, C00.3, C00.4, C00.5, C00.6, C00.8, C00.9, C43.0, C4A.0, C44.00, C44.01, C44.02, C44.09, C01, C02, C02.0, C02.1, C02.2, C02.3, C02.4, C02.8, C02.9, C03, C03.0, C03.1, C03.9, C04, C04.0, C04.1, C04.8, C04.9, C05, C05.0, C05.1, C05.2, C05.8, C05.9, C06, C06.0, C06.1, C06.2, C06.8, C06.80, C06.89, C06.9, C07, C08, C08.0, C08.1, C08.9, C09, C09.0, C09.1, C09.8, C09.9, C10, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C11, C11.0, C11.1, C11.2, C11.3, C11.8, C11.9, C12, C13, C13.0, C13.1, C13.2, C13.8, C13.9, C14, C14.0, C14.2, C14.8, C30, C30.0, C30.1, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C33, C34.00, C34.01, C34.02, C34.10, C34.11, C34.12, C34.2, C34.30, C34.31, C34.32, C34.80, C34.81, C34.82, C34.90, C34.91, C34.92, C37, C38.0, C38.1, C38.2, C38.3,

C38.4, C38.8, C39.0, C39.9, C31, C31.0, C31.1, C31.2, C31.3, C31.8, C31.9, C37, C69, C69.0, C69.00, C69.01, C69.02, C69.1, C69.10, C69.11, C69.12, C69.2, C69.20, C69.21, C69.22, C69.3, C69.30, C69.31, C69.32, C69.4, C69.40, C69.41, C69.42, C69.5, C69.50, C69.51, C69.52, C69.6, C69.60, C69.61, C69.62, C69.8, C69.80, C69.81, C69.82, C69.9, C69.90, C69.91, C69.92, C32, C32.0, C32.1, C32.2, C32.3, C32.8, C32.9, C33, C34, C34.0, C34.00, C34.01, C34.02, C34.1, C34.10, C34.11, C34.12, C34.2, C34.3, C34.30, C34.31, C34.32, C34.8, C34.80, C34.81, C34.82, C34.9, C34.90, C34.91, C34.92, C38, C38.0, C38.1, C38.2, C38.3, C38.4, C38.8, C39, C39.0, C39.9, C45, C45.0, C45.1, C45.2, C45.7, C45.9, C15, C15.3, C15.4, C15.5, C15.8, C15.9, C16, C16.0, C16.1, C16.2, C16.3, C16.4, C16.5, C16.6, C16.8, C16.9, C17, C17.0, C17.1, C17.2, C17.3, C17.8, C17.9, C18, C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19, C20, C21, C21.0, C21.1, C21.2, C21.8, C22, C22.0, C22.1, C22.2, C22.3, C22.4, C22.7, C22.8, C22.9, C23, C24, C24.0, C24.1, C24.8, C24.9, C25, C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C26, C26.0, C26.1, C46.4, C26.9, C48, C48.0, C48.1, C48.2, C48.8, C73, C74, C74.0, C74.00, C74.01, C74.02, C74.1, C74.10, C74.11, C74.12, C74.9, C74.90, C74.91, C74.92, C7A, C7A. 0, C7A.00, C7A.01, C7A.010, C7A.011, C7A.012, C7A.019, C7A.02, C7A.020, C7A.021, C7A.022, C7A.023, C7A.024, C7A.025, C7A.026, C7A.029, C7A.09, C7A.090, C7A.091, C7A.092, C7A.093, C7A.094, C7A.095, C7A.096, C7A.098, C7A.1, C7A.8, C7B, C7B.0, C7B.00, C7B.01, C7B.02, C7B.03, C7B.04, C7B.09, C7B.1, C7B.8, C75, C75.0, C75.1, C75.2, C75.3, C75.4, C75.5, C75.8, C75.9, C62, C62.0, C62.00, C62.01, C62.02, C62.1, C62.10, C62.11, C62.12, C62.9, C62.90, C62.91, C62.92, C63, C63.0, C63.00, C63.01, C63.02, C63.1, C63.10, C63.11, C63.12, C63.2, C63.7, C63.8, C63.9, C64, C64.1, C64.2, C64.9, C65, C65.1, C65.2, C65.9, C67, C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.7, C67.8, C67.9, C66, C66.1, C66.2, C66.9, C68, C68.0, C68.1, C68.8, C68.9, C61, C70, C70.0, C70.1, C70.9, C71, C71.0, C71.1, C71.2, C71.3, C71.4, C71.5, C71.6, C71.7, C71.8, C71.9, C72, C72.0, C72.1, C72.2, C72.20, C72.21, C72.22, C72.3, C72.30, C72.31, C72.32, C72.4, C72.40, C72.41, C72.42, C72.5, C72.50, C72.59, C72.9, C40, C40.0, C40.00, C40.01, C40.02, C40.1, C40.10, C40.11, C40.12, C40.2, C40.20, C40.21, C40.22, C40.3, C40.30, C40.31, C40.32, C40.8, C40.80, C40.81, C40.82, C40.9, C40.90, C40.91, C40.92, C41, C41.0, C41.1, C41.2, C41.3, C41.4, C41.9, C46, C46.0, C46.1, C46.2, C46.3, C46.4,

		C46.5, C46.50, C46.51, C46.52, C46.7, C46.9, C47, C47.0,
		C47.1, C47.10, C47.11, C47.12,
		C47.2, C47.20, C47.21, C47.22, C47.3, C47.4,
		C47.5, C47.6, C47.8, C47.9, C49,
		C49.0, C49.1, C49.10, C49.11, C49.12, C49.2,
		C49.20, C49.21, C49.22, C49.3, C49.4, C49.5,
		C49.6, C49.8, C49.9, C49.A, C49.A0, C49.A1, C49.A2,
		C49.A3, C49.A4, C49.A5, C49.A9, C76,
		C76.0, C76.1, C76.2, C76.3, C76.4, C76.40, C76.41, C76.42,
		C76.5, C76.50, C76.51, C76.52,
		C76.8, C79, C79.0, C79.00, C79.01, C79.02,
		C79.1, C79.10, C79.11, C79.19, C79.2, C79.3,
		C79.31, C79.32, C79.4, C79.40, C79.49, C79.5,
		C79.51, C79.52, C79.4, C79.40, C79.49, C79.5, C79.51, C79.52, C79.6, C79.60, C79.61, C79.62,
		C79.7, C79.70, C79.71, C79.72, C79.8, C79.81,
		C79.82, C79.89, C79.9, C78, C78.0, C78.00,
		C78.01, C78.02, C78.1, C78.2, C78.3, C78.30,
		C78.39, C78.4, C78.5, C78.6, C78.7, C78.8,
		C78.80, C78.89, C77, C77.0, C77.1, C77.2, C77.3,
		C77.4, C77.5, C77.8, C77.9, C80, C80.0, C80.1,
		C80.2
Hematologic malignancy	Hodgkin lymphoma	C81, C81.0, C81.00, C81.01, C81.02, C81.03,
	Follicular lymphoma	C81.04, C81.05, C81.06, C81.07, C81.08, C81.09,
	Non follicular lymphoma	C81.1, C81.10, C81.11, C81.12, C81.13, C81.14,
	TNK cell lymphoma	C81.15, C81.16, C81.17, C81.18, C81.19, C81.2,
	Other non-Hodgkin's lymphoma	C81.20, C81.21, C81.22, C81.23, C81.24, C81.25,
	Other specified TNK lymphoma	C81.26, C81.27, C81.28, C81.29, C81.3, C81.30,
	Immunoproliferative and b cell	C81.31, C81.32, C81.33, C81.34, C81.35, C81.36,
	lymphoma	C81.37, C81.38, C81.39, C81.4, C81.40, C81.41,
	Multiple myeloma and plasma cell	C81.42, C81.43, C81.44, C81.45, C81.46, C81.47,
	Lymphoid leukemia	C81.48, C81.49, C81.7, C81.70, C81.71, C81.72,
	Myeloid leukemia	C81.73, C81.74, C81.75, C81.76, C81.77, C81.78,
	Monocytic leukemia	C81.79, C81.9, C81.90, C81.91, C81.92, C81.93,
	Leukemia & Specified Cell Type	C81.94, C81.95, C81.96, C81.97, C81.98, C81.99, C82,
		C82.0, C82.00, C82.01, C82.02, C82.03,
	Leukemia of unspecified cell	
	Unspecified malignant neoplasm	C82.04, C82.05, C82.06, C82.07, C82.08, C82.09,
		C82.1, C82.10, C82.11, C82.12, C82.13, C82.14,
		C82.15, C82.16, C82.17, C82.18, C82.19, C82.2,
		C82.20, C82.21, C82.22, C82.23, C82.24, C82.25,
		C82.26, C82.27, C82.28, C82.29, C82.3, C82.30,
		C82.31, C82.32, C82.33, C82.34, C82.35, C82.36,
		C82.37, C82.38, C82.39, C82.4, C82.40, C82.41,
		C82.42, C82.43, C82.44, C82.45, C82.46, C82.47,
		C82.48, C82.49, C82.5, C82.50, C82.51, C82.52,
		C82.53, C82.54, C82.55, C82.56, C82.57, C82.58,
		C82.59, C82.6, C82.60, C82.61, C82.62, C82.63,
		C82.64, C82.65, C82.66, C82.67, C82.68, C82.69,
		C82.8, C82.80, C82.81, C82.82, C82.83, C82.84,
		C82.85, C82.86, C82.87, C82.88, C82.89, C82.9,
		C82.90, C82.91, C82.92, C82.93, C82.94, C82.95,
		C82.96, C82.97, C82.98, C82.99, C83, C83.0,
		C83.00, C83.01, C83.02, C83.03, C83.04, C83.05,
		C83.06, C83.07, C83.08, C83.09, C83.1, C83.10,
		C83.11, C83.12, C83.13, C83.14, C83.15, C83.16,
		C83.17, C83.18, C83.19, C83.3, C83.30, C83.31,
	1	C83.32, C83.33, C83.34, C83.35, C83.36, C83.37,

C83.38, C83.39, C83.5, C83.50, C83.51, C83.52, C83.53, C83.54, C83.55, C83.56, C83.57, C83.58, C83.59, C83.7, C83.70, C83.71, C83.72, C83.73, C83.74, C83.75, C83.76, C83.77, C83.78, C83.79, C83.8, C83.80, C83.81, C83.82, C83.83, C83.84, C83.85, C83.86, C83.87, C83.88, C83.89, C83.9, C83.90, C83.91, C83.92, C83.93, C83.94, C83.95, C83.96, C83.97, C83.98, C83.99, C84, C84.0, C84.00, C84.01, C84.02, C84.03, C84.04, C84.05, C84.06, C84.07, C84.08, C84.09, C84.1, C84.10, C84.11, C84.12, C84.13, C84.14, C84.15, C84.16, C84.17, C84.18, C84.19, C84.4, C84.40, C84.41, C84.42, C84.43, C84.44, C84.45, C84.46, C84.47, C84.48, C84.49, C84.6, C84.60, C84.61, C84.62, C84.63, C84.64, C84.65, C84.66, C84.67, C84.68, C84.69, C84.7, C84.70, C84.71, C84.72, C84.73, C84.74, C84.75, C84.76, C84.77, C84.78, C84.79, C84.A, C84.A0, C84.A1, C84.A2, C84.A3, C84.A4, C84.A5, C84.A6, C84.A7, C84.A8, C84.A9, C84.Z, C84.Z0, C84.Z1, C84.Z2, C84.Z3, C84.Z4, C84.Z5, C84.Z6, C84.Z7, C84.Z8, C84.Z9, C84.9, C84.90, C84.91, C84.92, C84.93, C84.94, C84.95, C84.96, C84.97, C84.98, C84.99, C85, C85.1, C85.10, C85.11, C85.12, C85.13, C85.14, C85.15, C85.16, C85.17, C85.18, C85.19, C85.2, C85.20, C85.21, C85.22, C85.23, C85.24, C85.25, C85.26, C85.27, C85.28, C85.29, C85.8, C85.80, C85.81, C85.82, C85.83, C85.84, C85.85, C85.86, C85.87, C85.88, C85.89, C85.9, C85.90, C85.91, C85.92, C85.93, C85.94, C85.95, C85.96, C85.97, C85.98, C85.99. C86, C86.0, C86.1, C86.2, C86.3, C86.4, C86.5, C86.6, C88, C88.0, C88.2, C88.3, C88.4, C88.8, C88.9, C90, C90.0, C90.00, C90.01, C90.02, C90.1, C90.10, C90.11, C90.12, C90.2, C90.20, C90.21, C90.22, C90.3, C90.30, C90.31, C90.32, C91, C91.0, C91.00, C91.01, C91.02, C91.1, C91.10, C91.11, C91.12, C91.3, C91.30, C91.31, C91.32, C91.4, C91.40, C91.41, C91.42, C91.5, C91.50, C91.51, C91.52, C91.6, C91.60, C91.61, C91.62, C91.A, C91.A0, C91.A1, C91.A2, C91.Z, C91.Z0, C91.Z1, C91.Z2, C91.9, C91.90, C91.91, C91.92, C92 C92.0, C92.00, C92.01, C92.02, C92.1, C92.10, C92.11, C92.12, C92.2, C92.20, C92.21, C92.22, C92.3, C92.30, C92.31, C92.32, C92.4, C92.40, C92.41, C92.42, C92.5, C92.50, C92.51, C92.52, C92.6, C92.60, C92.61, C92.62, C92.A, C92.A0, C92.A1, C92.A2, C92.Z, C92.Z0, C92.Z1, C92.Z2, C92.9, C92.90, C92.91, C92.92, C93, C93.0, C93.00, C93.01, C93.02, C93.1, C93.10, C93.11, C93.12, C93.3, C93.30, C93.31, C93.32, C93.Z, C93.Z0, C93.Z1, C93.Z2, C93.9, C93.90, C93.91, C93.92, C94, C94.0, C94.00, C94.01, C94.02, C94.2, C94.20, C94.21, C94.22, C94.3, C94.30, C94.31, C94.32, C94.4, C94.40, C94.41, C94.42, C94.6, C94.8, C94.80, C94.81, C94.82, C95, C95.0, C95.00, C95.01, C95.02,

		C95.1, C95.10, C95.11, C95.12, C95.9, C95.90, C95.91, C95.92, C96, C96.0, C96.2, C96.20, C96.21, C96.22, C96.29, C96.4, C96.5, C96.6, C96.A
Current smoker	Corporate Data Warehouse health factors file and existing algorithm	ICD-10 codes, at least one code in the past year F17.200, F17.210, F17.290, Z72.0  Tobacco use CPT code, at least one code in the past year: 99406, 99407, S9075, S9453, G0436, G0437  Clinic stop code, at least one code in the past year: 707, 708  OR  Most recent health factor within past year indicates current smoker. Table of smoking-related health factors adapted from table available at: https://medicine.yale.edu/intmed/vacs/
Alcohol Use Disorder	Any single ICD code in past year	F10.10, F10.120, F10.121, F10.129, F10.14, F10.150, F10.151, F10.159, F10.180, F10.181, F10.182, F10.188, F10.19, F10.20, F10.220, F10.221, F10.229, F10.230, F10.231, F10.232, F10.239, F10.24, F10.250, F10.251, F10.259, F10.26, F10.27, F10.280, F10.281, F10.282, F10.288, F10.29, F10.920, F10.921, F10.929, F10.94, F10.950, F10.951, F10.959, F10.96, F10.97, F10.980, F10.981, F10.982, F10.988, F10.99, G31.2, G62.1, I42.6, K29.20, K29.21, K70.0, K70.10, K70.11, K70.2, K70.30, K70.31, K70.40, K70.41, K70.9, O35.4XX0, O35.4XX1, O35.4XX2, O35.4XX3, O35.4XX4, O35.4XX5, O35.4XX9, O99.310, O99.311, O99.312, O99.313, O99.314, O99.315, Z71.4, Z71.41
Drug Use Disorder	Any single ICD code in past year	F11.10, F11.120, F11.121, F11.122, F11.129, F11.13, F11.14, F11.150, F11.151, F11.159, F11.181, F11.182, F11.188, F11.19, F11.20, F11.21, F11.220, F11.221, F11.222, F11.229, F11.23, F11.24, F11.250, F11.251, F11.259, F11.281, F11.282, F11.288, F11.29, F11.90, F11.920, F11.921, F11.922, F11.929, F11.93, F11.94, F11.950, F11.951, F11.959, F11.981, F11.982, F11.988, F11.99, F12.10, F12.120, F12.121, F12.122, F12.129, F12.150, F12.151, F12.159, F12.180, F12.188, F12.19, F12.20, F12.21, F12.220, F12.221, F12.222, F12.229, F12.23, F12.250, F12.251, F12.259, F12.280, F12.288, F12.29, F12.90, F12.920, F12.921, F12.922, F12.929, F12.93, F12.950, F12.951, F12.959, F12.980, F12.988, F12.99, F13.10, F13.120, F13.121, F13.129, F13.14, F13.150, F13.151, F13.159, F13.180, F13.181, F13.182, F13.188, F13.19, F13.20, F13.21, F13.220, F13.221, F13.229, F13.230, F13.231, F13.232, F13.239, F13.24, F13.250, F13.251, F13.259, F13.26, F13.27, F13.280, F13.281, F13.282, F13.288, F13.29, F13.90, F13.920, F13.921, F13.929, F13.930, F13.931, F13.932, F13.939, F13.94, F13.950, F13.951, F13.959, F13.96, F13.97,

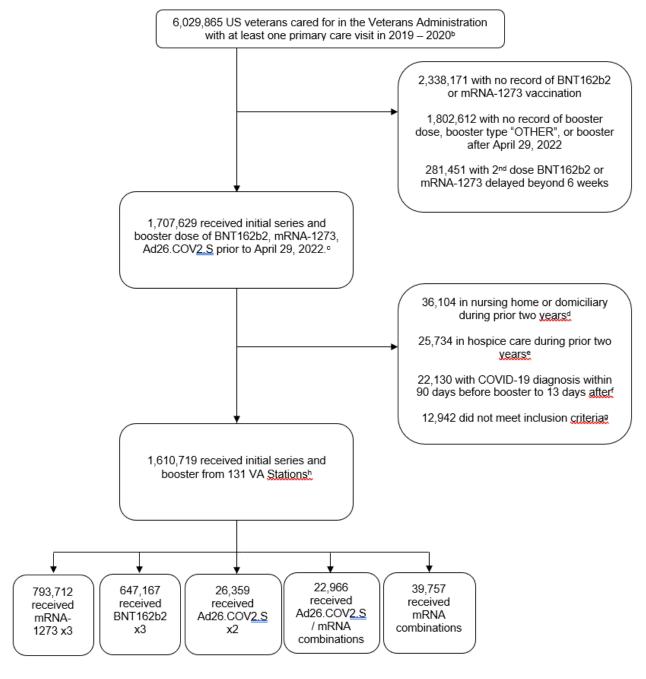
Clinic Stop codes, at least one code in past two years: 507, 522, 528, 529, 530  Body Mass Index  Used more recent measurement before index date available in the Corporate Data Warehouse  VA Priority score  VA Priority Groups  https://www.va.gov/health-care/eligibility/priority-groups/	Marginally Housed	ICD codes or clinic stop codes related to marginal housing	F13.980, F13.981, F13.982, F13.988, F13.99, F14.10, F14.120, F14.121, F14.122, F14.129, F14.13, F14.14, F14.150, F14.121, F14.122, F14.180, F14.181, F14.182, F14.188, F14.19, F14.20, F14.21, F14.220, F14.221, F14.222, F14.229, F14.23, F14.24, F14.250, F14.251, F14.259, F14.280, F14.281, F14.282, F14.288, F14.29, F14.90, F14.920, F14.921, F14.922, F14.929, F14.93, F14.94, F14.950, F14.951, F14.959, F14.980, F14.981, F14.982, F14.988, F14.99, F15.10, F15.120, F15.121, F15.122, F15.129, F15.13, F15.14, F15.150, F15.151, F15.182, F15.188, F15.19, F15.20, F15.21, F15.220, F15.221, F15.229, F15.283, F15.24, F15.250, F15.251, F15.229, F15.281, F15.282, F15.288, F15.29, F15.981, F15.982, F15.980, F15.951, F15.959, F15.980, F15.981, F15.982, F15.988, F15.99, F16.10, F16.120, F16.121, F16.122, F16.129, F16.14, F16.150, F16.151, F16.159, F16.180, F16.183, F16.188, F16.19, F16.20, F16.21, F16.220, F16.221, F16.229, F16.24, F16.250, F16.251, F16.259, F16.280, F16.283, F16.288, F16.99, F18.10, F18.120, F18.121, F18.129, F18.14, F18.150, F18.151, F18.150, F18.17, F18.180, F18.184, F18.150, F18.151, F18.159, F18.17, F18.180, F18.188, F18.19, F18.20, F18.21, F18.220, F18.221, F18.229, F18.24, F18.250, F18.251, F18.259, F18.27, F18.280, F18.288, F18.29, F18.90, F18.21, F18.220, F18.221, F18.299, F18.94, F18.950, F18.951, F18.959, F18.97, F18.980, F19.129, F19.130, F19.131, F19.132, F19.139, F19.14, F19.150, F19.151, F19.159, F19.16, F19.17, F19.180, F19.181, F19.182, F19.188, F19.19, F19.20, F19.21, F19.232, F19.239, F19.28, F19.28, F19.29, F19.20, F19.21, F19.29, F19.28, F19.29, F19.28, F19.29, F19.29, F19.28, F19.29, F19.290, F19.291, F19.292, F19.290, F19.291, F19.292, F19.280, F19.281, F19.282, F19.288, F19.29, F19.28, F19.299, F19.280, F19.98, F19.990, F19.991, F19.991, F19.991, F19.991, F19.991, F19.992, F19.990, F19.991, F19.991, F19.990, F19.99
before index date available in the Corporate Data Warehouse			Z59.9 Problem related to housing and economic circumstances, unspecified OR Clinic Stop codes, at least one code in past two years: 507,
VA Priority score VA Priority Groups https://www.va.gov/health-care/eligibility/priority-groups/	Body Mass Index	before index date available in the	
	VA Priority score	VA Priority Groups	https://www.va.gov/health-care/eligibility/priority-groups/

### Immunocompromised status defined based on receipt of three classes of drugs

- (1) Receipt IV chemotherapy in the 90 days before vaccination completion
- (2) Receipt of immunosuppressive drugs(3) Receipt of antiretroviral drugs

Chemotherapy	Bendamustine, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin, Cyclophosphamide,				
	Dacarbazine, Estramustine, Ifosfamide, Lomustine, Mechlorethamine, Melphalan, Oxaliplatin,				
	Pipobroman, Procarbazine, Streptozocin, Temozolomide, Thiotepa, Uracil Mustard, Azathioprine,				
	Capecitabine, Cladribine, Clofarabine, Cytarabine, Floxuridine, Fludarabine, Fluorouracil,				
	Gemcitabine, Hydroxyurea, Mercaptopurine, Methotrexate, Pentostatin, Pralatrexate, Thioguanine,				
	Vidarabine, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Pixantrone, Valrubicin, Vincristine,				
	Vinblastine, Vinorelbine, Etoposide, Teniposide, Irinotecan, Mitoxantrone, Topotecan, Paclitaxel,				
	Docetaxel				
Immunosuppressive drugs	Abatacept, Adalimumab, Anakinra, Belimumab, Canakinumab, Certolizumab, Denosumab,				
	Eculizumab, Etanercept, Golimumab, Infliximab, Natalizumab, Rituximab, Secukinumab,				
	Siltuximab, Tocilizumab, Sarilumab, Ustekinumab, Vedolizumab, Tofacitinib, Baricitinib,				
	Upadacitinib, Apremilast, Mercaptopurine, Azathioprine, Cyclophosphamide, Cyclosporine,				
	Hydroxychloroquine, Chloroquine, Leflunomide, Methotrexate, Mycophenolate mofetil,				
	Mycophenolic acid, Sulfasalazine, Tacrolimus, Chloroquine, Hydroxychloroquine, Prednisone,				
	Dexamethasone, Hydrocortisone, Methylprednisolone, Cortisone, Prednisolone, Triamcinolone,				
	Betamethasone				
Antiretroviral drugs	Abacavir (ABC), Didanosine (ddI), Emtricitabine (FTC), Lamivudine (3TC), Stavudine (d4T),				
	Tenofovir (TDF), Zalcitabine (ddC), Zidovudine (ZDV, AZT), Delavirdine (DLV), Efavirenz (EFV),				
	Etravirine (ETR), Nevirapine (NVP), Rilpivirine (RPV), Amprenavir (APV), Atazanavir (ATV),				
	Atazanavir-cobicistat (ATV/COBI), Darunavir (DRV), Darunavir-cobicistat (DRV/COBI),				
	Fosamprenavir (FPV), Indinavir (IDV), Lopinavir/ritonavir (LPV/r), Nelfinavir (NFV), Ritonavir				
	(RTV), Saquinavir (SQV), Tipranavir (TPV), Enfuvirtide (T-20), Dolutegravir (DTG), Elvitegravir				
	(EVG), Raltegravir (RAL), Maraviroc (MVC)				

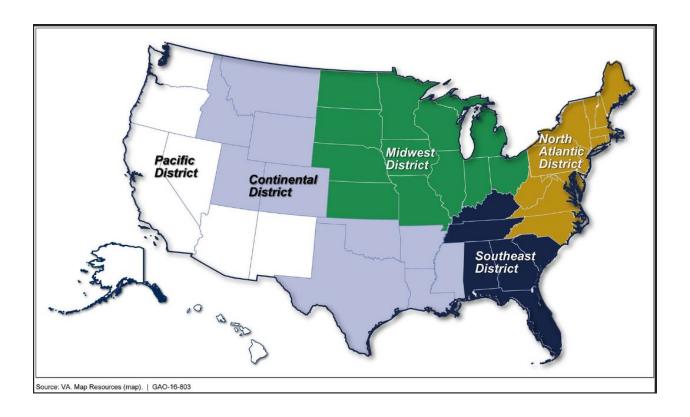
eFigure 1. Cohort Selection in a Study of U.S. Veterans Who Received Booster Vaccination for COVID-19<sup>a</sup>



- a. Note that eligibility was based on first three doses and that a small proportion (~1%) of the overall cohort received a fourth dose before the end of follow-up because of their immunocompromised status.
- b. Primary care visits defined as an outpatient visit with primary or secondary stop code:
  - 301 general internal medicine
  - 318 geriatrics
  - 319 geriatrics
  - 322 women's health
  - 323 primary care medicine
  - 338 telephone primary care
  - 348 primary care shared appt

- 350 geripact
- c. Booster dose for BNT162b2, mRNA-1273 initial series is 5+ months after initial series. Booster dose for Ad26.COV2.S initial series is 2+ months after initial series.
- d. Nursing home stays are:
  - Any single instance of ICD-10 diagnosis code Y92.12x (nursing home as the place of occurrence of the external cause) in any context (in/out patient, fee, etc)
  - Any single instance of outpatient visit with primary or secondary stop code
    - o 119 CNH follow up
    - o 121 community res care
    - o 190 adult day care
    - 191 community ADHC follow up
    - o 370 Geriatrics extended care long term)
    - o 651 state nursing home days
    - o 658 state home adult day healthcare
  - Any VA inpatient stay with medical service "NHCU" or specialty "NH"
- e. Hospice/palliative care is:
  - Any single instance of ICD-10 diagnosis code Z51.5 (encounter for palliative care) in any context (in/out patient, fee, etc)
  - Any single instance of outpatient visit with primary or secondary stop code
    - 351 (hospice care)
    - 353 (palliative care)
  - Any single instance of a patient consult where the service contains "hospice" or "palliative"
  - Any single instance of VA patient hospital stay with specialty containing "hospice" or "palliative"
  - Any single instance of a fee basis hospital stay where the purpose of stay includes "hospice" or "palliative" care.
- f. History of COVID is:
  - Any positive COVID lab appearing in the shared data resource
  - Any single instance of ICD-10 diagnosis code U07.1 (COVID-19) in any context (in/out patient, VA/fee)
- g. 12,942 patients were excluded due to either a missing Care Assessment Need (CAN) score or an unknown VA priority
- h. These 131 VA Stations are representative of all VA facilities according to the Corporate Data Warehouse

eFigure 2. Map of VA Regions



eTable 1. Incidence of Hospitalization With COVID-19 Pneumonia/Death Following Vaccination and Boosters With Follow-up Time Ending on Date of 4<sup>th</sup> Dose, by Overall Cohort and Immunocompromised Subgroup

	Events	Cumulative incidence per 10,000 patients over 24 weeks (95% CI)
Full cohort, all censored at 4 <sup>th</sup> dose (N=1,610,719)		
Overall	1,432	8.9 (8.4, 9.4)
mRNA-1273 x3 (N=793,712)	616	7.8 (7.2, 8.4)
BNT162b2 x3 (N=674,167)	719	10.7 (9.9, 11.5)
Ad26.COV2.S x2 (N=26,358)	23	8.7 (5.5, 13.1)
mRNA combination <sup>a</sup> (N=68,025)	52	7.6 (5.7, 10)
Ad26.COV2.S x2 and mRNA combination <sup>b</sup> (N=48,457)	22	4.5 (2.8, 6.9)
Full cohort, immunocompromised censored at 4th dose (N=1,610,719)		
Overall	1,433	8.9 (8.4, 9.4)
mRNA-1273 x3 (N=793,712)	617	10.7 (9.9, 11.5)
BNT162b2 x3 (N=674,167)	719	8.7 (5.5, 13.1)
Ad26.COV2.S x2 (N=26,358)	23	7.6 (5.7, 10)
mRNA combination <sup>a</sup> (N=68,025)	52	4.5 (2.8, 6.9)
Ad26.COV2.S x2 and mRNA combination <sup>b</sup> (N=48,457)	22	4.5 (2.8, 6.9)
Immunocompromised subgroup, censored at 4 <sup>th</sup> dose (N=158,684)		
Overall	598	38.3 (35.3, 41.5)
mRNA-1273 x3 (N=79,517)	284	35.7 (31.7, 40.1)
BNT162b2 x3 (N=67,780)	314	46.3 (41.4, 51.7)

<sup>a</sup>mRNA combination was a group that included all possible combinations in which mRNA-1273 and BNT162b2 were received.
<sup>b</sup>Received Ad26.COV2.S first then either mRNA-1273 or BNT162b2, or vice versa.

eTable 2. Characteristics of the Boosted Cohort by Combination of Vaccination Series<sup>a</sup>

	mRNA-1273 x3	BNT162b2 x3	Ad26.COV2. S x2	mRNA Combinations <sup>b</sup>	Ad26.COV2.S and mRNA Combinations
N	793,712	674,167	26,358	68,025	48,457
Gender (%)		3,			,
Male	735,858 (92.7)	614,717 (91.2)	23,651 (89.7)	61,013 (89.7)	43,237 (89.2)
Female	57,854 (7.3)	59,450 (8.8)	2,707 (10.3)	7,012 (10.3)	5,220 (10.8)
Age (%)					
Median age (q1, q3)	72 [63, 77]	71 [61, 75]	65 [56, 73]	67 [56, 74]	62 [53, 71]
18-65	218,183 (27.5)	221,793 (32.9)	13,037 (49.5)	29,603 (43.5)	27,823 (57.4)
65-74	300,167 (37.8)	253,742 (37.6)	9,054 (34.4)	21,646 (31.8)	14,120 (29.1)
75-84	205,736 (25.9)	152,523 (22.6)	3,428 (13.0)	12,470 (18.3)	5,245 (10.8)
85 or older	69,626 (8.8)	46,109 (6.8)	839 (3.2)	4,306 (6.3)	1,269 (2.6)
Raced (%)	, ,	, ,		,	, ,
American Indian or	( )		()	()	
Alaska Native	5,082 (0.6)	4,364 (0.6)	226 (0.9)	392 (0.8)	592 (0.9)
Asian Black or	10,051 (1.3)	10,555 (1.6)	304 (1.2)	1,148 (2.4)	1,195 (1.8)
African American	133,845 (16.9)	161,568 (24.0)	5,408 (20.5)	12,698 (18.7)	9,696 (20.0)
Native Hawaiian or other Pacific	0.000 (0.0)	0400 (0.0)	050 (4.0)	507 (4.4)	700 (4.4)
Islander	6,908 (0.9)	6198 (0.9)	253 (1.0)	537 (1.1)	726 (1.1)
White More than one	586,123 (73.8)	444,463 (65.9)	18,308 (69.5)	48,011 (70.6)	33,255 (68.6)
race	6,160 (0.8)	5,551 (0.8)	267 (1.0)	463 (1.0)	643 (0.9)
Hispanic or Latino ethnicity (regardless of race) <sup>d</sup> , n (%)	59,514 (7.5)	46,458 (6.9)	1,701 (6.5)	5,040 (7.4)	3,558 (7.3)
Not Hispanic or Latino (regardless of	704 400 (00 5)	007 700 (00 4)	04.057.(00.5)	20.005 (00.0)	44.000 (00.7)
race)d, n (%) Currently	734,198 (92.5) 478,001 (60.2)	627,709 (93.1) 386,535 (57.3)	24,657 (93.5) 13,750 (52.2)	62,985 (92.6) 37,729 (55.5)	44,899 (92.7) 23,105 (47.7)
married, n (%)	470,001 (00.2)	000,000 (07.0)	10,700 (02.2)	31,129 (33.3)	20,100 (47.7)
Urban/rural <sup>e</sup> (%)					
Highly rural or unknown	36,164 (4.6)	13,200 (2)	1,331 (5.1)	2,245 (3.3)	2,339 (4.9)
Rural	25,2957 (32)	139,050 (20.7)	9,522 (36.3)	18,206 (26.9)	15,853 (33)
Urban	502,105 (63.5)	519,241 (77.3)	15,375 (58.6)	47,209 (69.8)	29,827 (62.1)
VA region (%) <sup>f</sup>					

Continental	119,468 (15.1)	93,481 (13.9)	5,065 (19.2)	9,209 (13.5)	7,148 (14.8)
Midwest	181,432 (22.9)	147,134 (21.8)	4,865 (18.5)	15,641 (23.0)	11,088 (22.9)
North Atlantic	174,001 (21.9)	156,118 (23.2)	4,748 (18.0)	14,863 (21.8)	9,337 (19.3)
Pacific	126,792 (16.0)	122,862 (18.2)	4,739 (18.0)	13,233 (19.5)	9,842 (20.3)
Southeast	162,605 (20.5)	124,517 (18.5)	5,751 (21.8)	11,263 (16.6)	8,440 (17.4)
BMI (%)				. ,	. , ,
Median (q1,	29 [26.01,	29 [26.06,	29.8 [26.25,	29.7 [26.15,	
q3)	33.34]	33.39]	34.06]	34.01]	29.5 [26.12, 33.60]
<18.5	5,151 (0.7)	4,450 (0.7)	237 (1)	462 (0.8)	381 (0.9)
18.5-24.9	120,198 (17.5)	102,562 (17.3)	3,840 (16.6)	10,230 (17.1)	7,306 (17.1)
25-29.9	251,340 (36.6)	216,216 (36.4)	7,773 (33.5)	21,272 (35.5)	14,466 (33.9)
>30	310,919 (45.2)	270,762 (45.6)	11,325 (48.9)	27,956 (46.7)	20,520 (48.1)
Comorbidities associated with severe COVID- 19 illness (%)					
Hypertension	504,921 (63.6)	407,188 (60.4)	15,086 (57.2)	37,795 (55.6)	25,703 (53.0)
Diabetes	271,408 (34.2)	217,655 (32.3)	8,116 (30.8)	20,036 (29.5)	13,218 (27.3)
CKD <sup>g</sup>	188,127 (23.7)	143,583 (21.3)	4,959 (18.8)	13,534 (19.9)	7,786 (16.1)
Ischemic Heart Disease	144,279 (18.2)	109,860 (16.3)	3,626 (13.8)	9,776 (14.4)	5,732 (11.8)
COPD Bronchiectasis	100,751 (12.7)	72,260 (10.7)	2,969 (11.3)	6,895 (10.1)	5,079 (10.5)
CHF	47,612 (6.0)	38,216 (5.7)	1,285 (4.9)	3,633 (5.3)	2,268 (4.7)
Immunocompro	47,012 (0.0)	30,210 (3.1)	1,203 (4.9)	3,033 (3.3)	2,200 (4.7)
mised <sup>h</sup>	46,058 (5.8)	38,932 (5.8)	1,291 (4.9)	3,208 (4.7)	2,476 (5.1)
Cancer solid organ <sup>i</sup>	27,772 (3.5)	24,815 (3.7)	699 (2.7)	1,928 (2.8)	1,250 (2.6)
Severe CKD <sup>j</sup>	25,912 (3.3)	17,646 (2.6)	678 (2.6)	1,861 (2.7)	1,341 (2.8)
Stroke TIA	21,510 (2.7)	18,755 (2.8)	627 (2.4)	1,766 (2.6)	1,159 (2.4)
Dementia	15,642 (2.0)	12,173 (1.8)	339 (1.3)	1,493 (2.2)	671 (1.4)
Cirrhosis	11,559 (1.5)	11,901 (1.8)	411 (1.6)	1,044 (1.5)	791 (1.6)
Cancer lymphoma leukemia <sup>i</sup>	10,070 (1.3)	8,022 (1.2)	184 (0.7)	533 (0.8)	300 (0.6)
		•			197 (0.4)
Dialysis	4,787 (0.6)	4,438 (0.7)	75 (0.3)	512 (0.8)	, ,
Cancer otheri Spinal cord	4,639 (0.6)	4,738 (0.7)	122 (0.5)	283 (0.4)	211 (0.4)
injury	4,109 (0.5)	4,031 (0.6)	98 (0.4)	397 (0.6)	202 (0.4)
Home-based	10.000 (: =)	7.440.77.77		4.040.//.=\	070 (4.6)
primary care Date of first	12,009 (1.5)	7,440 (1.1)	427 (1.6)	1,046 (1.5)	878 (1.8)
dose of vaccination series, by 3-month period					
12/202 – 02/2021	535,848 (67.5)	422,641 (62.7)	2 (<0.1)	37,580 (55.2)	887 (1.8)

		1	1		1
03/2021 – 05/2021	249,380 (31.4)	240,788 (35.7)	21,484 (81.5)	28,946 (42.6)	37,849 (78.1)
06/2021 –					
08/2021	7,807 (1.0)	9,729 (1.4)	4,202 (15.9)	1,371 (2.0)	8,712 (18.0)
09/2021 – 11/2021	677 (0.1)	1,009 (0.1)	588 (2.2)	128 (0.2)	872 (1.8)
12/2021 – 02/2022	0 (<0.1)	0 (<0.1)	82 (0.3)	0 (<0.1)	137 (0.3)
Reinfection	5 ( 511)	5 ( 511)	0= (0.0)	0 ( 011)	101 (010)
with COVID- 19 <sup>k</sup>	36,489 (4.6)	34,801 (5.2)	1,898 (7.2)	4,070 (6.0)	3,804 (7.9)
Social and behavioral risk factors (%)					
Current smoker	160,482 (20.2)	135,378 (20.1)	7,851 (29.8)	15,446 (22.7)	14,815 (30.6)
Alcohol use disorder <sup>l</sup>	52,909 (6.7)	49,103 (7.3)	2,464 (9.3)	5,813 (8.5)	5,336 (11.0)
Substance use <sup>m</sup>	31,986 (4.0)	31,258 (4.6)	1,622 (6.2)	3,587 (5.3)	3,736 (7.7)
Housing problems <sup>n</sup>	30,777 (3.9)	30,234 (4.5)	1,748 (6.6)	3,724 (5.5)	3,911 (8.1)
\/\ prio~it +0 (0/\					
VA priority <sup>o</sup> (%)					31,309 (64.6)
1-4	496,221 (62.5)	432,293 (64.1)	17,005 (64.5)	44,282 (65.1)	, ,
5-6	159,649 (20.1)	129,078 (19.1)	5,647 (21.4)	12,988 (19.1)	10,476 (21.6)
7-8	137,842 (17.4)	112,796 (16.7)	3,706 (14.1)	10,755 (15.8)	6,672 (13.8)
CAN score <sup>p</sup> (%)					
0-49.9	274,822 (34.6)	263,101 (39.0)	13,043 (49.5)	31,421 (46.2)	26,199 (54.1)
50-74.9	256,233 (32.3)	210,656 (31.2)	7,827 (29.7)	18,750 (27.6)	12,904 (26.6)
75-100	262,657 (33.1)	200,410 (29.7)	5,488 (20.8)	17,854 (26.2)	9,354 (19.3)
Median follow- up time, days (IQR)	168 (166.0, 168.0)	168 (168.0, 168.0)	168 (158.0, 168.0)	168 (146.0, 168.0)	161 (130.0, 168.0)
Median time elapsed between initial dose and				,	101 (100.0, 100.0)
booster, days (IQR)	280 (258.0, 302.0)	258 (237.0, 282.0)	238 (205.0, 262.0)	284 (258.0, 312.0)	250 (218.0, 283.0)
High-risk populations	744,518 (93.8)	619,359 (91.9)	23,611 (89.6)	59,883 (88.0)	41,929 (86.5)
Age ≥ 65 and no high-risk co-morbid					
conditions	100,751 (12.7)	83,998 (12.5)	2,141 (8.1)	6,654 (9.8)	3,287 (6.8)
High-risk co- morbid conditions <sup>q</sup> (not immunocompro					
mised)	564,250 (71.1)	467,581 (69.4)	19,387 (73.6)	47,795 (70.3)	34,772 (71.8)

Immunocompro mised	79,517 (10.0)	67,780 (10.1)	2,083 (7.9)	5,434 (8.0)	3,870 (8.0)
Age <u>&lt;</u> 65 and					
no					
co-morbid					
conditions	23,876 (3.0)	28,063 (4.2)	1,321 (5.0)	4,430 (6.5)	3,377 (7.0)

<sup>&</sup>lt;sup>a</sup>Full version of Table 1 from manuscript.

Abbreviations: BMI: body mass index; CHF: chronic heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; TIA: transient ischemic attack

bmRNA combination was a group that included all possible combinations in which mRNA-1273 and BNT162b2 were received.

Received Ad26.COV2.S first then either mRNA-1273 or BNT162b2, or vice versa.

<sup>&</sup>lt;sup>d</sup>Race/ethnicity was assessed using self-identified data found in Veteran Health Records.

<sup>&</sup>lt;sup>e</sup>Urban/rural was assessed using defined based on the Rural Urban Commuting Area (RUCA) categories developed by the Department of Agriculture and Health and Human Services' Health Resource and Services Administration.

See eFigure 2 for map of VA regions.

<sup>&</sup>lt;sup>9</sup>CKD defined as having a glomerular filtration rate between 30 and 60.

hImmunocompromised definition based on medications and history of cancer (see supplement for list of meds).

Cancer definition based on diagnosis codes. 2 outpatient or 1 inpatient diagnosis code in the VA (see supplement).

Severe CKD defined as having a glomerular filtration rate <30.

k91 or more days prior to boosted shot.

Alcohol use defined as 1 outpatient or 1 inpatient code within 2 years of index.

<sup>&</sup>lt;sup>m</sup>Including cannabis, opioids, inhalants.

<sup>&</sup>quot;Housing problems defined as homelessness, inadequate housing, other problems related to housing and economic circumstances.

<sup>°</sup>VA-defined based on factors including military service history, disability rating and income level to identify Veterans to determine enrolment priority; score ranges from 1 to 8 with 1 being the highest priority. This is a surrogate for socioeconomic status.

PThe Care Assessment Need (CAN) Score is a predictive analytic tool that estimates the relative probability of hospitalization and death within 90 days or one-year from the calculation date. The Office of Clinical Systems Development and Evaluation (CSDE – 10E2A) produces the weekly CAN Score Report to help identify the highest risk patients in a primary care panel or a cohort. We used the one-year score.

qAs defined by the CDC, older adults, people with medical conditions, who are immunocompromised, pregnant and recently pregnant people.

eTable 3. Characteristics of Cohort by Outcome

	No Break- through COVID	Break- through COVID	No hospitalization with COVID-19 pneumonia or death <sup>a</sup>	Hospitalization with COVID-19 pneumonia or death <sup>a</sup>	No severe pneumonia <sup>b</sup> or death <sup>a</sup>	Severe pneumonia <sup>b</sup> or death <sup>a</sup>
N	1,590,581	20,138	1,609,284	1,435	1,610,178	541
Gender (%)						
Male	1,460,528 (91.8)	17,948 (89.1)	1,477,096 (91.8)	1,380 (96.2)	1,477,951 (91.8)	525 (97.0)
Female	130,053 (8.2)	2,190 (10.9)	132,188 (7.2)	55 (3.8)	132,227 (7.2)	16 (3.0)
Age (%)						
Mean age (q1, q3)	71 (62, 76)	68 (58, 74)	71 (61, 76)	74 (69, 80)		
18-65	502,287 (31.6)	8,152 (40.5) 7,121	510,246 (31.7)	193 (13.4)	510,375 (31.7)	64 (11.8)
65-74	591,608 (37.2) 375,645	(35.4)	598,143 (37.2)	568 (40.8)	598,513 (37.2)	216 (39.9)
75-84	(23.6) 121,041	(18.7)	378,973 (23.5)	429 (29.9)	379,226 (23.6)	176 (32.5)
85 or older	(7.6)	1,108 (5.5)	121,922 (7.6)	227 (15.8)	122,064 (7.6)	85 (15.7)
Race <sup>c</sup> (%)						
American Indian or Alaska Native	10,489 (0.7)	167 (0.9)	10,642 (0.7)	14 (1)	10,651 (0.7)	5 (1)
Asian	22,922 (1.5)	331 (1.7)	23,247 (1.5)	6 (0.4)	23,251 (1.5)	2 (0.4)
Black or African American	318,318 (20.0)	4,897 (24.3)	322,939 (20.1)	276 (19.2)	323,115 (20.1)	100 (18.5)
Native Hawaiian or other Pacific Islander	12,913 (0.9)	171 (0.9)	13,072 (0.9)	12 (0.9)	13,081 (0.9)	3 (0.6)
White	1,116,926 (70.2)	13,234 (65.7)	1,129,114 (70.2)	1,046 (72.9)	1,129,757 (70.2)	403 (74.5)
More than one race	1,116,926 (74.7)	13,234 (69.6)	1,129,114 (74.6)	1,046 (76.5)	1,129,757 (74.6)	403 (77.8)
Ethnicity <sup>c</sup> (%)						
Hispanic or Latino	114,090 (7.2)	2,181 (10.8)	116,176 (7.2)	95 (6.6)	116,228 (7.2)	43 (7.9)
Not Hispanic or Latino	1,476,491 (92.8)	17,957 (89.2)	1,493,108 (92.8)	1,340 (93.4)	1,493,950 (92.8)	498 (92.1)
Marital Status (%)						
Currently married	928,267 (58.4)	10,853 (53.9)	938,308 (58.3)	812 (56.6)	938,824 (58.3)	296 (54.7)
Urban/rural <sup>d</sup> (%)						
Highly rural or unknown	54,882 (3.4)	397 (2.0)	55,242 (3.4)	37 (2.6)	55,264 (3.4)	15 (2.8)
Rural	431,671 (27.2)	3,917 (19.5)	435,202 (27.1)	386 (27.0)	435,454 (27.1)	134 (24.8)

	No Break- through COVID	Break- through COVID	No hospitalization with COVID-19 pneumonia or death <sup>a</sup>	Hospitalization with COVID-19 pneumonia or death <sup>a</sup>	No severe pneumonia <sup>b</sup> or death <sup>a</sup>	Severe pneumonia <sup>b</sup> or death <sup>a</sup>
	1,097,985	15,772	1,112,750		1,113,366	
Urban	(69.4)	(78.5)	(69.4)	1,007 (70.4)	(69.4)	391 (72.4)
BMI (%)						
<18.5	10,561 (0.8)	120 (0.6)	10,658 (0.8)	23 (1.7)	10,672 (0.8)	9 (1.8)
	241,148	2,988	,	, ,	,	,
18.5-24.9	(17.4)	(16.1)	243,827 (17.3)	309 (23.4)	244,016 (17.3)	120 (24.2)
	504,589	6,478				
25-29.9	(36.3)	(34.8)	510,617 (36.3)	450 (34.0)	510,899 (36.3)	168 (33.9)
>-20	632,474	9,008	C40 040 (4F C)	E40 (40 0)	C44 000 (4F C)	100 (40 4)
>=30 Comorbidities	(45.5)	(48.4)	640,942 (45.6)	540 (40.8)	641,283 (45.6)	199 (40.1)
associated with severe COVID- 19 illness (%)						
	977,195	13,498	000 474 (04.5)	4 040 (04 0)	000 040 (04.5)	47.4 (07.0)
Hypertension	(61.4)	(67.0)	989,474 (61.5)	1,219 (84.9)	990,219 (61.5)	474 (87.6)
Diabetes	522,783 (32.9)	7,650	520 659 (22 O)	775 (54.0)	520 122 (22 0)	210 (57.2)
Diabetes	353,462	(38.0) 4,527	529,658 (32.9)	775 (54.0)	530,123 (32.9)	310 (57.3)
CKD <sup>e</sup>	(22.2)	(22.5)	357,422 (22.2)	567 (39.5)	357,774 (22.2)	215 (39.7)
Ischemic Heart	268,798	4,475	007, 122 (22.2)	007 (00.0)	007,777 (22.2)	210 (00.1)
Disease	(16.9)	(22.2)	272,689 (16.9)	584 (40.7)	273,034 (17.0)	239 (44.2)
COPD	184,631	3,323	,	,	,	,
Bronchiectasis	(11.6)	(16.5)	187,426 (11.6)	528 (36.8)	187,771 (11.7)	183 (33.8)
0.15	00 070 (7 7)	2,135	00 504 (5.0)	400 (00 0)	00.040 (5.0)	474 (00.0)
CHF	90,879 (5.7)	(10.6)	92,581 (5.8)	433 (30.2)	92,840 (5.8)	174 (32.2)
Immune Compromised <sup>f</sup>	89,294 (5.6)	2,671 (13.3)	91,555 (5.7)	410 (28.6)	91,794 (5.7)	171 (31.6)
Cancer solid	09,294 (3.0)	(13.3)	91,333 (3.1)	410 (20.0)	91,194 (3.1)	171 (31.0)
organ <sup>g</sup>	55,384 (3.5)	1,080 (5.4)	56,309 (3.5)	155 (10.8)	56,395 (3.5)	69 (12.8)
Severe CKD <sup>h</sup>	46,497 (2.9)	941 (4.7)	47,260 (2.9)	178 (12.4)	47,359 (2.9)	79 (14.6)
Stroke TIA	42,993 (2.7)	824 (4.1)	43,720 (2.7)	97 (6.8)	43,786 (2.7)	,
						31 (5.7)
Dementia	29,727 (1.9)	691 (2.9)	30,203 (1.9)	115 (8.0)	30,263 (1.9)	55 (10.2)
Cirrhosis	25,098 (1.6)	608 (3.0)	25,616 (1.6)	90 (6.3)	25,671 (1.6)	35 (6.5)
Cancer lymphoma leukemia <sup>g</sup>	18,521 (1.2)	588 (2.9)	18,947 (1.2)	162 (11.3)	19,035 (1.2)	74 (13.7)
Dialysis	9,591 (0.6)	418 (2.1)	9,905 (0.6)	104 (7.2)	9,967 (0.6)	42 (7.8)
Cancer otherg	9,730 (0.6)	263 (1.3)	9,948 (0.6)	45 (3.1)	9,974 (0.6)	19 (3.5)
Spinal cord injury	8,642 (0.5)	195 (1.0)	8,812 (0.5)	25 (1.7)	8,825 (0.5)	12 (2.2)
Home-based	04 000 (4 0)	40.4 (0.0)	04 704 (4.0)	70 (5.0)	04 770 (4 1)	00 (5.5)
primary care	21,336 (1.3)	464 (2.3)	21,724 (1.3)	76 (5.3)	21,770 (1.4)	30 (5.5)
Vaccine quarter (%)	004.005	10.000				
12/2020 – 02/2021	984,095 (61.9)	12,863 (63.9)	995,832 (61.9)	1,126 (78.5)	996,524 (61.9)	434 (80.2)

			No			
	No Break- through COVID	Break- through COVID	hospitalization with COVID-19 pneumonia or death <sup>a</sup>	Hospitalization with COVID-19 pneumonia or death <sup>a</sup>	No severe pneumonia <sup>b</sup> or death <sup>a</sup>	Severe pneumonia <sup>b</sup> or death <sup>a</sup>
03/2021 –	571,456	6,991				
05/2021	(35.9)	(34.7)	578,151 (35.9)	296 (20.6)	578,346 (35.9)	101 (18.7)
06/2021 – 08/2021	31,560 (2.0)	261 (1.3)	31,808 (2.0)	13 (0.9)	31,815 (2.0)	6 (1.1)
09/2021 – 11/2021	3,252 (0.2)	22 (0.1)	3,274 (0.2)	0 (0.0)	3,274 (0.2)	0 (0.0)
12/2021 – 02/2022	218 (0.0)	1 (0.0)	219 (0.0)	0 (0.0)	219 (0.0)	0 (0.0)
Reinfection with COVID-19i	80,672 (5.1)	390 (1.9)	81,005 (5.0)	57 (4.0)	81,045 (5.0)	17 (3.1)
Social and behavioral risk factors (%)						
Current smoker	330,293 (20.8)	3,679 (18.3)	333,736 (20.7)	236 (16.4)	333,881 (20.7)	91 (16.8)
Alcohol abuse <sup>j</sup>	113,793 (7.2)	1,832 (9.1)	115,506 (7.2)	119 (8.3)	115,578 (7.2)	47 (8.7)
Substance use <sup>k</sup>	70,850 (4.5)	1,339 (6.6)	72,108 (4.5)	81 (5.6)	72,166 (4.5)	23 (4.3)
Homelessness <sup>I</sup>	68,949 (4.3)	1,445 (7.2)	70,309 (4.4)	85 (5.9)	70,373 (4.4)	21 (3.9)
VA priority score <sup>k</sup> (%)				33 (3.3)		= : (0:0)
1-4	1,007,008 (63.3)	14,102 (70.0)	1,020,238 (63.4)	872 (60.8)	1,020,771 (63.4)	339 (62.7)
5-6	314,299 (19.8)	3,539 (17.6)	317,461 (19.7)	377 (26.3)	317,702 (19.7)	136 (25.1)
7-8	269,274 (16.9)	2,497 (12.4)	271,585 (16.9)	186 (13.0)	271,705 (16.9)	66 (12.2)
CAN score <sup>m</sup> (%)						
0-49.9	600,274 (37.7)	8,312 (41.3)	608,481 (37.8)	105 (7.3)	608,562 (37.8)	24 (4.4)
50-74.9	501,205 (31.5)	5,165 (25.6)	506,117 (31.4)	253 (17.6)	506,276 (31.4)	94 (17.4)
75-100	489,102 (30.7)	6,661 (33.1)	494,686 (30.7)	1,077 (75.1)	495,340 (30.8)	423 (78.2)
Breakthrough outcome follow-up	168 [166.0,	75 [43.0,	NIA	NIA	NIA	NΙΔ
(median [IQR]) Hospitalization for COVID-19 pneumonia follow-up	168.0]	107.0]	NA 168 [166.0,	NA	NA	NA NA
(median [IQR]) Hospitalization	NA	NA	168.0]	82 [44.0, 115.5]	NA	NA
for severe COVID-19 pneumonia	NA	NA	NA	NA	168 [166.0, 168.0]	92 [56.0, 121.0]

	No Break- through COVID	Break- through COVID	No hospitalization with COVID-19 pneumonia or death <sup>a</sup>	Hospitalization with COVID-19 pneumonia or death <sup>a</sup>	No severe pneumonia <sup>b</sup> or death <sup>a</sup>	Severe pneumonia <sup>b</sup> or death <sup>a</sup>
follow-up (median [IQR])						
Days elapsed between initial						
dose and booster	270 [245.0,	265 [240.0,	270 [245.0,	260 [231.0,	270 [245.0,	258 [230.0,
(median [IQR])	295.0]	290.0]	295.0]	289.0]	295.0]	289.0]
Age <u>&lt;</u> 65 and						
no						
co-morbid conditions	60,166 (3.8)	901 (4.5)	61,062 (3.8)	5 (0.3)	61,065 (3.8)	2 (0.4)
High-risk co-						
morbid	1,275,409	17,060	1,291,083		1,291,943	
conditions <sup>n</sup>	(80.2)	(84.7)	(80.2)	1,386 (96.6)	(80.2)	526 (97.2)
Immunocompr	154,707	3,977				
omised	(9.7)	(19.7)	158,055 (9.8)	629 (43.8)	158,419 (9.8)	265 (49.0)

<sup>&</sup>lt;sup>a</sup>Death from all causes within 30 days of breakthrough COVID-19 infection.

Abbreviations: BMI: body mass index; CHF: chronic heart failure; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; TIA: transient ischemic attack

<sup>&</sup>lt;sup>b</sup>Severe pneumonia defined as having mechanical ventilation or an intubation procedure during hospitalization.

<sup>°</sup>Race/ethnicity was assessed using self-identified data found in Veteran Health Records.

<sup>&</sup>lt;sup>d</sup>Urban/rural was assessed using defined based on the Rural Urban Commuting Area (RUCA) categories developed by the Department of Agriculture and Health and Human Services' Health Resource and Services Administration.

<sup>°</sup>CKD defined as having a glomerular filtration rate between 30 and 60.

Immunocompromised definition based on medications and history of cancer (see supplement for list of meds).

<sup>&</sup>lt;sup>9</sup>Cancer definition based on diagnosis codes. 2 outpatient or 1 inpatient diagnosis code in the VA (see supplement).

<sup>&</sup>lt;sup>h</sup>Severe CKD defined as having a glomerular filtration rate <30.

<sup>&</sup>lt;sup>i</sup>91 or more days prior to boosted shot.

<sup>&</sup>lt;sup>j</sup>Alcohol use defined as1 outpatient or 1 inpatient code within 2 years of index.

<sup>&</sup>lt;sup>k</sup>Including cannabis, opioids, inhalants.

Housing problems defined as homelessness, inadequate housing, other problems related to housing and economic circumstances.

<sup>&</sup>quot;VA-defined based on factors including military service history, disability rating and income level to identify Veterans to determine enrolment priority; score ranges from 1 to 8 with 1 being the highest priority. This is a surrogate for socioeconomic status.

The Care Assessment Need (CAN) Score is a predictive analytic tool that estimates the relative probability of hospitalization and death within 90 days or one-year from the calculation date. The Office of Clinical Systems Development and Evaluation (CSDE – 10E2A) produces the weekly CAN Score Report to help identify the highest risk patients in a primary care panel or a cohort. We used the one-year score. "As defined by the CDC, older adults, people with medical conditions, who are immunocompromised, pregnant and recently pregnant people.

eTable 4. Incidence of Outcomes Following Vaccination and Booster With mRNA-1273 x3, BNT162b2 x3, and Ad26.COV2.S x2 by Delta Variant vs Omicron Variant **Eras** 

Breakthrough C	:OVID-19						
Dieaktinough C	Delta Omicron						
	Patients	Incidents over 24 weeks (95% CI) Events per 10,000 persons	Patients	Incidents over 24 weeks (95% CI) Events per 10,000 persons	Cumulative Incidents Ratios (95% CI) (Delta vs. Omicron)		
Overall	996,254	7.3 (6.8, 7.9)	398,328	96.8 (93.8, 99.9)	7.0 (5.8, 8.4)		
mRNA-1273 x3	468,143	6.2 (5.5, 6.9)	200,274	90.7 (86.6, 94.9)	6.8 (5.4, 8.7)		
BNT162b2 x3	474,681	8.6 (7.8, 9.5)	134,701	107 (101.6, 112.6)	8.1 (6.4, 10.2)		
Ad26.COV2.S x2	11,565	8.6 (4.1, 15.9)	8,826	133.7 (110.8, 159.9)	5.6 (3, 10.4)		
llaanitali-atian	i4b CO\/II	2 40 manumania au d	a a 4 la 3				
Hospitalization	With COVIL	D-19 pneumonia or d Delta	eatn <sup>e</sup>	Omicron			
		Incidents over 24		Incidents over 24	Cumulative		
	Patients	weeks (95% CI) Events per 10,000 persons	Patients	weeks (95% CI) Events per 10,000 persons	Incidents Ratios (95% CI) (Delta vs. Omicron)		
Overall	996,254	1.6 (1.3, 1.8)	398,328	4.7 (4.1, 5.5)	2.5 (1.8, 3.5)		
mRNA-1273 x3	468,143	1.3 (1, 1.7)	200,274	4.4 (3.5, 5.4)	2.6 (1.6, 4.0)		
BNT162b2 x3	474,681	2.0 (1.6, 2.4)	134,701	4.9 (3.8, 6.2)	2.5 (1.5, 4.0)		
Ad26.COV2.S x2	11,565	NC	8,826	7.9 (3.2, 16.3)	All outcomes in omicron period		
		00)//0		41.0			
Hospitalization	with sever	e COVID-19 pneumo	nia" or dea				
		Delta Incidents over 24		Omicron Incidents over 24	Cumulative		
	Patients	weeks (95% CI) Events per 10,000 persons	Patients	weeks (95% CI) Events per 10,000 persons	Incidents Ratios (95% CI) (Delta vs. Omicron)		
Overall	996,254	0.5 (0.4, 0.7)	398,328	1.7 (1.3, 2.2)	2.2 (1.3, 3.9)		
mRNA-1273 x3	468,143	0.4 (0.2, 0.6)	200,274	1.7 (1.2, 2.4)	2.7 (1.2, 6.6)		
BNT162b2 x3	474,681	0.7 (0.4, 0.9)	134,701	1.6, (1, 2.4)	2.0 (0.9, 4.4)		
Ad26.COV2.S x2	11,565	NC	8,826	NC	All outcomes in omicron period		

<sup>a</sup>Death from all causes within 30 days of breakthrough COVID-19 infection.
<sup>b</sup>Severe pneumonia defined as having mechanical ventilation or an intubation procedure during hospitalization.