Supplementary Appendix

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This appendix has been provided by the authors to give readers additional information about the work.

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Supplementary Appendix to:

Comparative effectiveness of BNT162b2 vs. mRNA-1273 vaccines in U.S. veterans

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Contents

Supplementary Methods 1: VA Databases

In this study, we identified users of the U.S. Veteran Health Administration (VHA) using U.S. Department of Veterans Affairs (VA) electronic healthcare databases.

The U.S. VHA provides health care to discharged veterans of the U.S. armed forces. It is the largest integrated healthcare system in the U.S., providing care at 1,293 health care facilities, including 171 VA Medical Centers and 1,112 outpatient sites of care located across the U.S. Enrolled Veterans have access to the VA comprehensive medical benefits package, including inpatient hospital care; outpatient services; preventive, primary, and specialty care; prescriptions; mental healthcare; home healthcare; geriatric and extended care; medical equipment; and prosthetics.

Data used in this study come from the electronic health records from the VA Corporate Data Warehouse (CDW), a national repository that combines data from 130 separate VHA clinical and administrative systems. This data repository includes detailed information on demographics, inpatient and outpatient encounters, medications, and laboratory results. The specific CDW domains accessed were as follows:

- *Patient* domain to assess demographics and death;
- *Lab Chemistry* domain to assess laboratory test results;
- *Outpatient, Inpatient, Vital Signs, Health Factors,* and *Fee* domains to assess recorded symptoms;
- *Inpatient* domain to assess hospitalizations;
- *Outpatient, Inpatient, Fee* domains to assess diagnoses;
- *Health Factors* domain to assess smoking status;
- *Vital Signs* domain to assess height and weight;
- *Inpatient, Outpatient, Fee*, and *Health Factors* domains to assess homelessness;
- *Inpatient* and *Fee* domains to assess long-term care;
- *Outpatient Pharmacy* domain to assess medications;
- *Immunization, Outpatient,* and *Inpatient* domains to assess vaccinations.

CDW data are refreshed nightly, allowing for real-time analyses. Data are available from October 1, 1999, allowing for long-term follow-up of patients.

Since April 2020, the VA COVID-19 Shared Data Resource has also been collecting information related to Covid-19 from both inside and outside of the VA. This resource includes data on all patients who have received a SARS-CoV-2 test (positive or negative) within the VA or who tested positive outside the VA with information pertaining to the positive test recorded in VA clinical notes. We used the COVID-19 Shared Data

Resource to assess SARS-CoV-2 test information for patients. These data are refreshed weekly.

We identified SARS-CoV-2 infections using the VA Covid-19 National Surveillance Tool, which integrates data on laboratory tests conducted at VA clinics with natural language processing of clinical notes to capture documented infections inside and outside the VA healthcare system.[1] The algorithm to identify persons with SARS-CoV-2 infection is continually updated to ensure new annotations are captured from clinical notes, with chart reviews performed periodically to validate the algorithm.[1]

Supplementary Methods 2: Matching Algorithm

Persons newly vaccinated with the BNT162b2 vaccine were matched in a 1:1 ratio to persons vaccinated with the mRNA-1273 vaccine, using the following variables in the following ways:

- Calendar date of first vaccine dose – coarsened exact matching (5-day bins)
- Age – coarsened exact matching (5-year bins)
- Sex – exact matching
- Race – exact matching
- Urbanicity of residence (urban/not urban) – exact matching
- Veterans Integrated Services Network (VISN) – exact matching

Matching variables were selected in two stages. First, a set of variables was chosen based on domain expertise on factors associated with the probability of both receiving a particular vaccine and infection or severity of Covid-19 (age [3-year bins], and calendar date, sex, race, urbanicity of residence, and VA station [all exact]). Second, this set was gradually coarsened while ensuring that exchangeability was maintained.

Exchangeability was evaluated using the risk of symptomatic Covid-19 in the first 10 days after the first vaccine dose, during which there is expected to be no difference in risk when comparing two different vaccines based on randomized trial evidence of near-zero vaccine effectiveness in this period of early follow-up.[2,3] See **Figure S2**.

Matching was performed during the period from January 4, 2021, to May 14, 2021. On each day during this period, all newly vaccinated persons who met the study's eligibility criteria were candidates for matching.

The period above captures a time of SARS-CoV-2 B.1.1.7 (alpha) variant predominance. To compare estimates of vaccine effectiveness derived from this period with those derived from a time of SARS-CoV-2 B.1.617.2 (delta) variant predominance, we repeated the above matching process among persons newly vaccinated during the period from July 1, 2021, to September 20, 2021.

Supplementary Methods 3: Author Contributions

B.A.D. and M.A.H. designed the study.

H.G. and K.E.K. designed the data extraction and assembly workflow.

H.G., K.E.K., B.R.F., and M.J.F.M. gathered the data.

B.A.D. analyzed the data.

B.A.D. and M.A.H. vouch for the data and analysis.

B.A.D. wrote the first draft of the manuscript. All authors critically reviewed the manuscript and decided to proceed with publication.

All authors are bound by VA's security and data privacy directives.

Supplemental Results 1: Secondary Analyses during a Period of SARS-CoV-2 Delta-Variant Predominance

To evaluate the influence of SARS-CoV-2 variants on the estimated comparative effectiveness of the BNT162b2 vs. mRNA-1273 vaccines, we conducted separate analyses in time periods marked by alpha (B.1.1.7) variant and delta (B.1.617.2) variant predominance. That is, our primary analysis study period (January 4, 2021, to July 1, 2021) captures a time of SARS-CoV-2 alpha (B.1.1.7) variant predominance. Our secondary analysis study period (July 1, 2021, to September 22, 2021) captures a time of delta (B.1.617.2) variant predominance.

Among 36,056 veterans who received their first dose of any Covid-19 vaccine between July 1, 2021, and September 20, 2021, 10,208 recipients of the BNT162b2 vaccine and 9,714 recipients of the mRNA-1273 vaccine were eligible for the study. Among these, 3,580 recipients of the BNT162b2 vaccine were matched to 3,580 recipients of the mRNA-1273 vaccine, using the same matching procedure previously described. Compared with the eligible population, the matched population was generally similar with respect to baseline demographic and clinical characteristics but included a higher proportion of men, white individuals, and individuals with an urban residence (**Table S3**). Baseline characteristics of the matched persons are shown in **Table S4**. All variables were well-balanced between the two vaccine groups (**Figure S1**).

Over the 12-week follow-up (median, 43 days, interquartile range, 28-56 days), 91 SARS-CoV-2 infections were documented. Among persons who received a dose of the BNT162b2 vaccine and had at least 21 days of follow-up, 87% received a second dose of the vaccine (of whom 87% received it before day 24 and 93% received it before day 28). Among persons who received a dose of the mRNA-1273 vaccine and had at least 28 days of follow-up, 89% received a second dose of the vaccine (of whom 86% received it before day 31 and 93% received it before day 35).

Compared with recipients of the mRNA-1273 vaccine, recipients of the BNT162b2 vaccine had a higher 12-week risk of documented SARS-CoV-2 infection (risk ratio, 1.58; 95% CI, 0.85 to 2.33); risk difference, 6.54 events per 1,000 persons; 95% CI, -2.58 to 11.82). See below cumulative incidence curves for any documented SARS-CoV-2 infection.

Secondary analyses: Cumulative Incidence of Documented SARS-CoV-2 Infection during a Period of Delta-Variant Predominance (July 1–September 22, 2021). Shaded areas represent pointwise 95% confidence intervals.

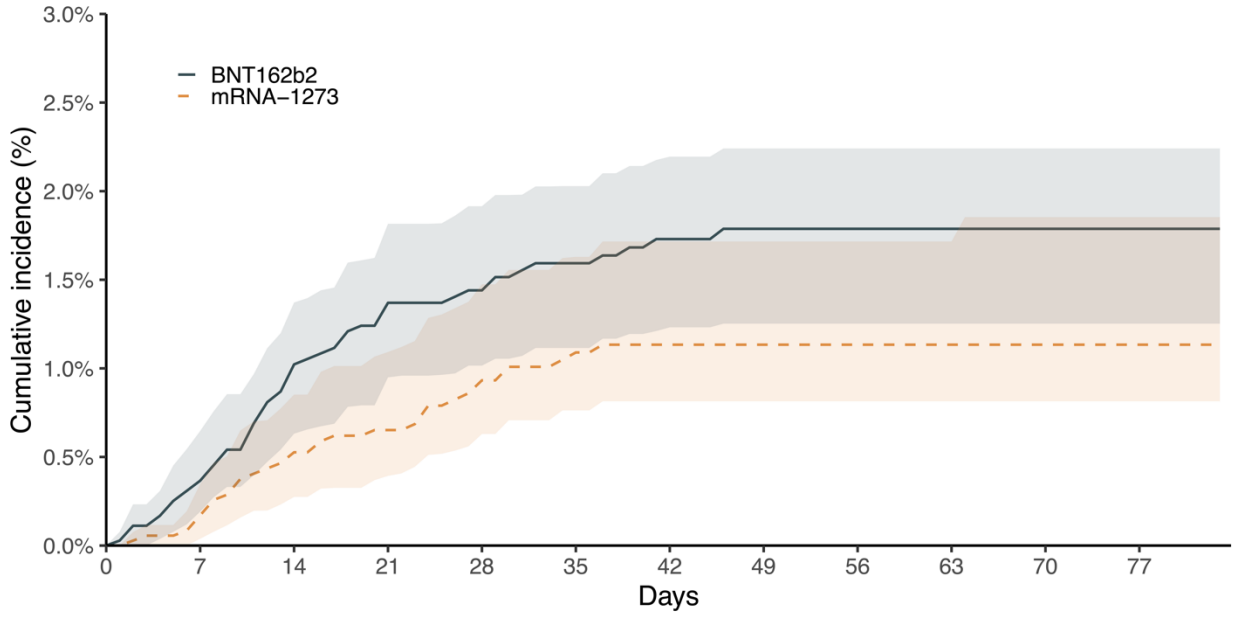
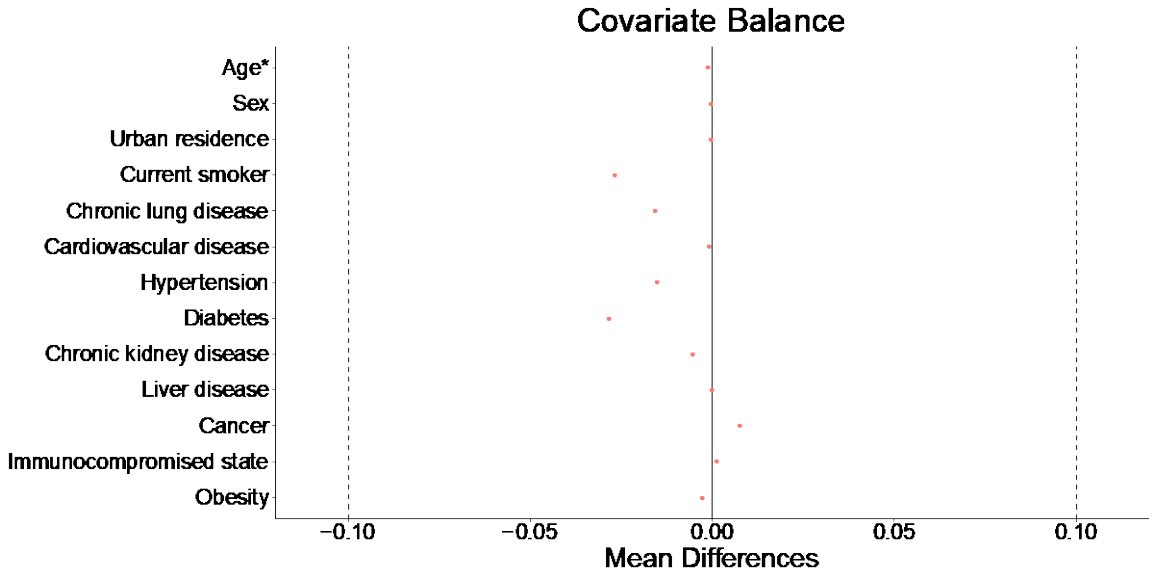
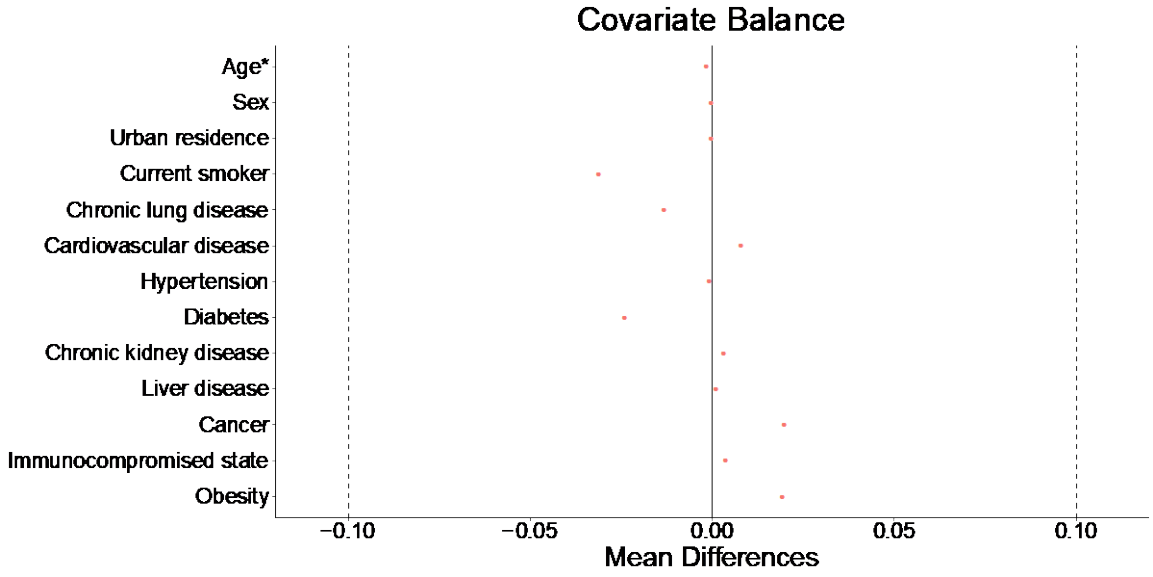


Figure S1: Covariate Balance (Love) Plot

A Matched Population from Primary Analysis during a Period of Alpha-Variant Predominance

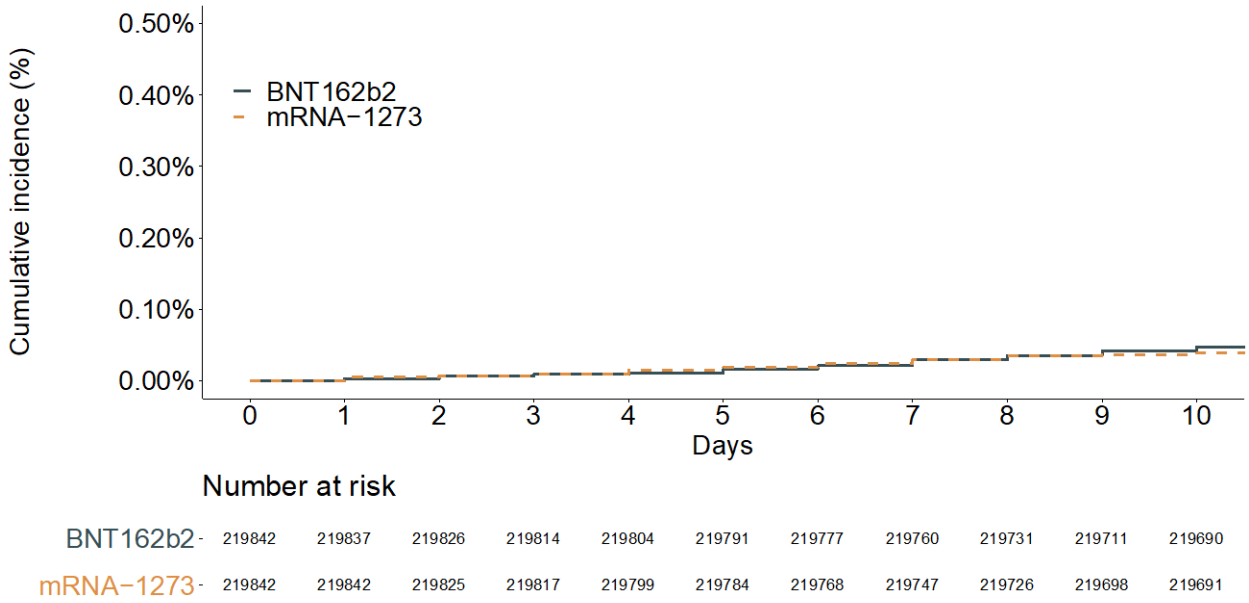


B Matched Population from Secondary Analysis during a Period of Delta-Variant Predominance



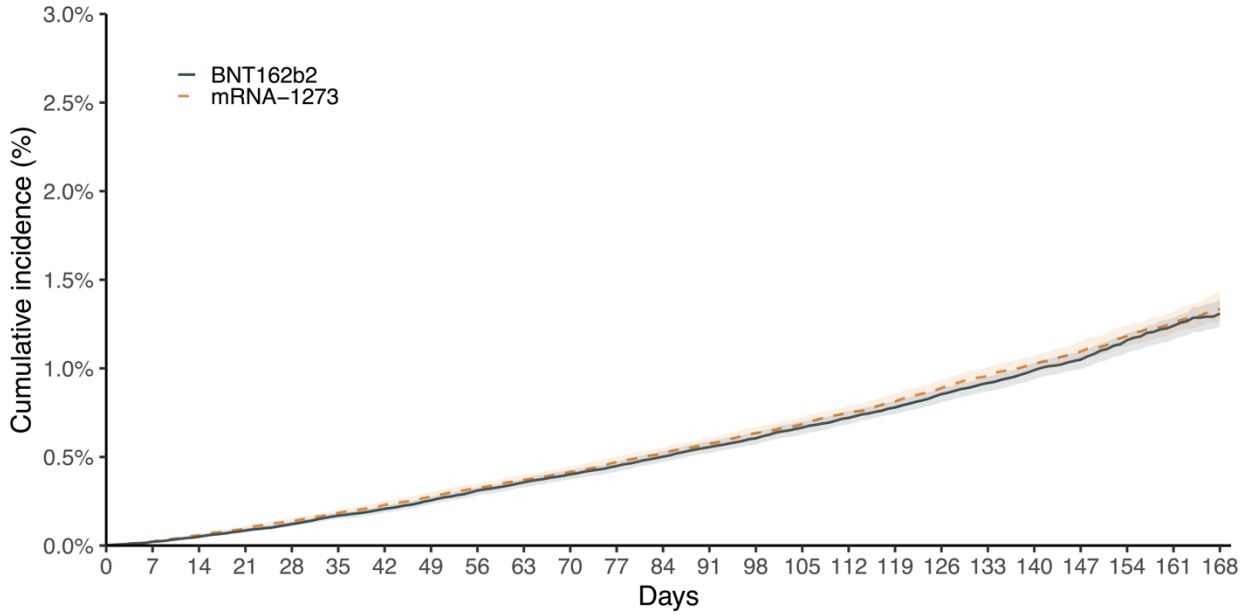
Legend: Covariate Balance (Love) Plot. Shows the difference in means for conditions identified by the Centers for Disease Control and Prevention (CDC) as risk factors for severe Covid-19. A strict balance cut-off was set at 0.1.
*The mean difference for age (a continuous variable) is standardized.

Figure S2: Negative control 1: Cumulative Incidence of Symptomatic Covid-19 in the First 10 Days After the First Vaccine Dose



Legend: *Negative control #1:* Cumulative Incidence of Symptomatic Covid-19 in the First 10 Days After the First Vaccine Dose (January 4–July 1, 2021).

Figure S3: Negative control 2: Cumulative Incidence of Non-Covid-19 Death Over the Follow-up



Legend: *Negative control #2:* Cumulative Incidence of Non-Covid-19 Death Over the Follow-up (January 4–July 1, 2021).

Table S1: Target Trial Specification and Emulation

Table S1. Specification and Emulation of a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Protocol component	Target trial specification	Target trial emulation

Eligibility criteria	• Aged ≥18 years between January 4, 2021, and May 14, 2021
	• No previously documented positive SARS-CoV-2 polymerase-chain-reaction (PCR) test
	• No interactions with the health care system in the past 3 days, which may indicate the start of symptomatic disease and preclude vaccination
	• No previous Covid-19 vaccination
	• No contraindication for Covid-19 vaccination:
	  ○ Severe allergic reaction (e.g., anaphylaxis) or immediate reaction of any severity to the vaccine or any of its components
	  ○ Immediate allergic reaction of any severity to polysorbate (due to potential cross-reactive hypersensitivity with the vaccine ingredient PEG)
	• Known residential address
	• Not in a long-term care facility
	• User of VA health care system (defined as receiving care at a station eligible to administer the vaccines under study and having at least one in-person or telehealth primary care visit in the past year)
	• Known smoking status and body mass index (BMI) in the past year
	• At least 6 weeks of potential follow-up, based on the planned end of follow-up on July 1, 2021
		Same as for the target trial, except:
		• We identified previously documented SARS-CoV-2 infections using the VA Covid-19 National Surveillance Tool,[1] which integrates data on PCR laboratory tests with natural language processing of clinical notes to capture diagnoses inside and outside the VA system.
		• Data on the listed allergic reactions are not consistently available for all Veterans, but we assumed that receiving the vaccine indicates there was a determination of no previous allergic reaction.

Treatment strategies	(1) Receive one dose of BNT162b2 vaccine at baseline and an additional dose 21 days later, or (2) Receive one dose of mRNA-1273 vaccine at baseline and an additional dose 28 days later	Same as for the target trial. We defined the date of vaccination using records in both the *Immunization* domain and procedures recorded in the *Outpatient* or *Inpatient* domains. There was strict adherence to vaccine deployment protocols in this population.*
Treatment assignment	Individuals are randomly assigned to a strategy at baseline within strata defined by calendar date (5-day bins), age (5-year bins), sex (male, female), race (white, black, other, unknown), urbanicity of residence (urban, not urban), and geographic location coded as	We assumed random assignment after matching individuals who were vaccinated with the BNT162b2 vaccine in a 1:1 ratio to eligible individuals vaccinated with the mRNA-1273 vaccine, using the same

	19 categories of Veterans Integrated Services Network (VISN). Individuals will be aware of the assigned treatment strategy.	factors used for stratified randomization as in the target trial.
Outcomes	• Documented SARS-CoV-2 infection • Symptomatic Covid-19 (defined as ≥1 of the following symptoms within 4 days of SARS-CoV-2 infection): fever, chills, cough, shortness of breath or difficulty breathing, sore throat, loss of taste or smell, headache, myalgia, diarrhea, vomiting • Hospitalization due to Covid-19 • ICU admission due to Covid-19 • Death due to Covid-19 (defined as death within 30 days of SARS-CoV-2 infection)	Same as for the target trial.
Follow-up	For each person, follow-up starts on the day of vaccination (baseline) and ends on the day of the outcome of interest, death, 168 days (24 weeks) after baseline, or the end of the study period (July 1, 2021), whichever happens first.	Same as for the target trial.
Causal contrasts	Intention-to-treat effect. Per-protocol effect, i.e., the effect if all individuals had received the vaccination they were assigned to at baseline and the corresponding second dose at the scheduled time.	Observational analogue of the per-protocol effect.
Statistical analysis	Cumulative incidence (risk) curves and estimates of 24-week risk, risk differences, and risk ratios comparing the vaccination groups. Subgroup analyses by baseline age and race.	Same as for the target trial.

Abbreviations: PCR, polymerase chain reaction.

* Among persons who received a dose of the BNT162b2 vaccine and had at least 21 days of follow-up, 99% received a second dose of the vaccine (of whom 93% received it before day 24 and 97% received it before day 28). Among persons who received a dose of the mRNA-1273 vaccine and had at least 28 days of follow-up, 98% received a second dose of the vaccine (of whom 92% received it before day 31 and 97% received it before day 35). Therefore, we defined treatment strategies based on the first dose only.

Table S2: Study Variables

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
Time-fixed (baseline)*				
Age (years)	Linear	N/A	Based on records in the *Patient* domain.	N/A
Sex	Indicator	Male/Female	Based on records in the *Patient* domain.	N/A
Race	4 categories	White Black Other Unknown	In the case of multiple reported races, the most frequently reported race was selected. Based on records in the *Patient* domain.	N/A
Ethnicity	3 categories	Not Hispanic Hispanic Unknown	In the case of multiple reported ethnicities, the most frequently reported ethnicity was selected. Based on records in the *Patient* domain.	N/A
Veterans Integrated Services Network (VISN)	19 categories	19 VISNs representing different geographic regions of the country	Defined as the location of the most recent station utilized prior to baseline. In the case of multiple station visits on the most recent visit date prior to baseline, the station with the most visits on that day was selected. In the case of a tie, the most commonly visited station in the past year was selected among those tied. In the case of another tie, a random station was selected among those tied. Based on records in the *Outpatient* domain.	N/A
Received care at a station that offered the BNT162b2 vaccine	Indicator	Yes/No	Defined using the history of stations utilized prior to baseline. Assessed daily.	N/A

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
			Based on records in the *Patient* domain.	
Received care at a station that offered the mRNA-1273 vaccine	Indicator	Yes/No	Defined using the history of stations utilized prior to baseline. Assessed daily. Based on records in the *Patient* domain.	N/A
Primary care visit in the past year	Indicator	Yes/No	Defined as an in-person or telehealth primary care visit, based on stop codes in any position. Based on records in the *Outpatient* domain.	PCP: 301, 322, 323, 348, 350 Tele-PCP: 338
Interaction with healthcare system within the past 3 days	Indicator	Yes/No	Defined as a primary care, inpatient, or emergency room visit, based on stop codes in the primary position. Assessed daily. Based on records in the *Inpatient* and *Outpatient* domains.	PCP: 301, 322, 323, 348, 350 ER: 1, 101, 130, 131
In long-term care within the past 2 years	Indicator	Yes/No	Includes admissions and inpatient transfers to or from a community living center (nursing home or domiciliary) or non-VA community nursing home. Based on records in the *Inpatient* and *Fee* domains.	Inpatient sources: AdmitSourceName, PlaceOfAdmit, MedicalService, Specialty, BedSection *Fee* domain: FeePurposeOfVisit or AustinCode in 40-44 or 89
Known residential address in the past year	Indicator	Yes/No	Based on Homeless Services Registry algorithm codes, using stop codes, specialty codes, ICD10 diagnosis codes, and adjudicated health factor codes. Based on records in the *Inpatient, Outpatient, Fee*, and *Health Factors* domains.	Stop codes: 504, 507, 508, 511, 522, 528, 529, 530, 590, 591, 592 Specialty codes: 25-29, 37-39, 85, 86, 88, 109-111 ICD10: V60.0, Z59.0
Urban residence	Indicator	Yes/No	Defined as having an address with a GIS zip code	N/A

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
			considered to be urban. Based on records in the *Patient* domain.	
Number of influenza vaccinations in the past 5 years	4 categories	0 1-2 3-4 ≥5	Based on records in the *Immunization* domain.	CVX codes: 15-17, 69, 88, 111, 123, 125-128, 135, 140, 141, 144, 149-151, 153, 155, 158, 160, 161, 166, 168, 171, 185, 186, 194, 197, 200-202, 205
Number of primary care visits in the past 5 years	4 categories	1-9 10-19 20-29 ≥30	Defined using stop codes, with PCP or Tele-PCP in the primary position, or in the secondary position if the primary position had a Tele-PCP combo stop code. Based on records in the *Outpatient* domain.	PCP: 301, 322, 323, 348, 350 Tele-PCP: 338 Tele-PCP combo: 147, 182, 324, 326, 683
Body mass index (kg/m^2)	Linear	N/A	Calculated using the most recent height and weight measurements. Based on records in the *Vital Signs* domain.	N/A
Obesity (body mass index ≥30 kg/m^2)	Indicator	Yes/No	Based on the most recent body mass index in the past year. Based on records in the *Vital Signs* domain.	N/A
Smoking status	3 categories	Never Current Former	Defined as the most common self-reported smoking status prior to baseline. Based on records in the *Health Factors* domain.	
Chronic lung disease	Indicator	Yes/No	A flag for at least one of the following conditions: asthma, bronchitis, chronic obstructive pulmonary disorder. Each component described below is based on records in the *Inpatient,*	See below

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
			Outpatient, and *Fee* domains.	
Asthma	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: J45.X
Bronchitis	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: J20.X, J21.X, J40.X, J41.X, J42.X
Chronic obstructive pulmonary disorder	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: J41.0X, J41.1X, J41.8X, J42.X, J43.0X, J43.1X, J43.2X, J43.8X, J43.9X, J44.0X, J44.1X, J44.9X
Cardiovascular disease	Indicator	Yes/No	A flag for at least one of the following conditions: acute myocardial infarction, cardiomyopathy, cerebrovascular accident, coronary heart disease, heart failure, peripheral vascular disease. Each component described below is based on records in the *Inpatient, Outpatient,* and *Fee* domains.	See below
Acute myocardial infarction	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I21.X (not including I21.AX), I22.X
Cardiomyopathy	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I42.X, I43.X
Cerebrovascular accident	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I60.X-I69.X, G45.X, G46.X, H34.0
Coronary heart disease	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I20.X, I21.X, I24.X, I25.10, I25.110, I25.2, I25.3, I25.41, I25.42, I25.5, I25.700, I25.710, I25.720, I25.730, I25.750, I25.760, I25.790, I25.810, I25.811, I25.812, I25.82, I25.83, I25.84, I25.89, I25.9

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
Heart failure	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I11.0, I13.0, I13.2, I50.20, I50.21, I50.22, I50.23, I50.30, I50.31, I50.32, I50.33, I50.40, I50.41, I50.42, I50.43, I50.814, I50.9, I50.1, I50.810, I50.811, I50.812, I50.813, I50.82, I50.83, I50.84, I50.89
Peripheral vascular disease	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years.	ICD10: I70.X, I71.X, I73.9, Z95.8, Z95.9, I73.1, I73.8, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9
Hypertension	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years. Based on records in the *Inpatient, Outpatient,* and *Fee* domains.	ICD10: I10.X-I13.X, I15.X, I16.X
Diabetes	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years. Based on records in the *Inpatient, Outpatient,* and *Fee* domains.	ICD10: E08.X, E10.X, E11.X, E13.X
Chronic kidney disease	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years. Based on records in the *Inpatient, Outpatient,* and *Fee* domains.	ICD10: I12.0, I13.1, N03.2X-N03.7X, N18.X, N19.X, N05.2X-N05.7X, N25.0, Z49.0X - Z49.2X, Z94.0, Z99.2
Liver disease	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 2 years. Based on records in the *Inpatient, Outpatient,* and *Fee* domains.	ICD10: K72.1X, K72.9X, K76.6X, K76.7X, I85.0X, I85.9X, I86.4X, I98.2X, K70.4X, K71.1X, K76.5X
Cancer	Indicator	Yes/No	Defined as ≥2 diagnoses in the past 5 years, except non-melanoma skin cancer, benign neoplasms, cancers in situ, and neoplasms of uncertain behavior. Based	ICD10: C00.X-C41.X, C43.X, C45.X, C47.X-C86.X, C88.X, C90.X-C96.X, C7A.X, C7B.0

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
			on records in the *Inpatient, Outpatient,* and *Fee* domains.	
Immunocompromised state	Indicator	Yes/No	Includes ever-diagnosis of human immunodeficiency virus infection, organ or tissue transplant, bone marrow biopsy, or use of any of the following medications (prescribed ≥2 times over the past year): systemic glucocorticoids, anti-inflammatory or anti-rheumatic agents in combination with glucocorticoids, immunosuppressants. Based on ICD codes, procedure codes, and medication records in the *Inpatient, Outpatient,* and *Fee* domains.	Organ transplant ICD9 Dx: 996.8, 996.9, E878.0, V42.0-4, V42.6-9, V43.2; HIV ICD9 Dx: 042.X, 043.X, 044.X, 079.53, 795.71, V08.X; Organ Transplant ICD9 Proc: 00.18, 00.91-93, 07.94, 33.5X, 33.6, 37.5, 41.0X, 41.94, 46.97, 50.5X, 52.80, 52.82-86, 55.53, 55.6X, 63.53, 65.92; Organ Transplant CPT: 0585T-86T, 32851-54, 33935, 33945, 33950, 44135-7, 47135-6, 48160, 48550, 48554, 48556, 50360, 50365-6, 50370, 50380, 51580, 51585, 51597, 54680, 58240, 60510, 60512, 81595, G0341, S2052-4, S2060-1, S2065, S2102-3, S2152, T3829, T5005, T5010, T5015, T5025, T5035, T5079; Immunocompromised state ICD9 Proc: 41.0X, 0.18; Immunocompromised state CPT: 38205-15, 38230-2, 38240-1; ICD10 Dx codes were mapped from ICD9 Dx codes using 2-way GEMS mapping table

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
				and ICD10 proc codes were mapped using 1-way GEMS mapping table; Select meds from the following VA drug classes: HS051, MS190, IM600
Time-varying				
BNT162b2 vaccination	Indicator	Yes/No	Defined using records in both the *Immunization* domain and procedures recorded in the *Outpatient* or *Inpatient* domains.	CPT: 0001A, 0002A, 91300 CVX: 208
mRNA-1273 vaccination	Indicator	Yes/No	Defined using records in both the *Immunization* domain and procedures recorded in the *Outpatient* or *Inpatient* domains.	CPT: 0011A, 0012A, 91301 CVX: 207
Documented infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)	Indicator	Yes/No	Defined as a nasopharyngeal swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2. Identified using the VA Covid-19 National Surveillance Tool, which integrates data on laboratory tests conducted at VA clinics with natural language processing of clinical notes to capture diagnoses inside and outside the VA healthcare system. The algorithm to identify persons with SARS-CoV-2 infection is continually updated to ensure new annotations of Covid-19 are captured from	N/A

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
			clinical notes, with chart reviews performed periodically to validate the algorithm.[1] Based on records in the COVID-19 Shared Data Resource. The event date is the specimen collection date.	
Symptomatic Covid-19	Indicator	Yes/No	Defined as ≥1 of the following symptoms documented within the VA health care system within 4 days after documented SARS-CoV-2 infection: fever, chills, cough, shortness of breath or difficulty breathing, sore throat, loss of taste or smell, headache, myalgia, diarrhea, vomiting. The event date is the specimen collection date. Based on records in the *Outpatient, Inpatient, Vital Signs, Health Factors,* and *Fee* domains.	Outpatient codes: ICD10: A68.9, B33.0, M79.1, M79.10, M79.11, M79.12, M79.18, R05., R06.00, R06.01, R06.02, R06.03, R06.09, R07.0, R09.3, R43.0, R43.2, R43.8, R43.9, R50.2, R50.81, R50.82, R50.83, R50.84, R50.9, R56.00, R56.01, R68.83
Hospitalization due to Covid-19	Indicator	Yes/No	Defined as a hospitalization within 21 days after documented SARS-CoV-2 infection. Based on records in the *Inpatient* domain. The event date is the hospital admission date.	N/A
ICU admission due to Covid-19	Indicator	Yes/No	Defined as an ICU admission during a Covid-19 hospitalization. Based on records in the *Inpatient* domain and specialty transfer codes. The event date is the ICU admission date.	SpecialityIEN: 12, 13, 63

Table S2. Variables Used in the Analysis when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Alpha-Variant Predominance Using Observational Data from Veterans Health Administration Electronic Health Records (January 4–July 1, 2021).

Variable	Functional form	Values	Detail	Codes
Death due to Covid-19	Indicator	Yes/No	Defined as a death within 30 days after documented SARS-CoV-2 infection. Date of death is based on records in the *Patient domain.* The event date is the death date.	N/A
Death due to other causes	Indicator	Yes/No	Based on records in the *Patient* domain.	N/A

* Baseline variables were assessed on January 4, 2021, unless otherwise noted.

Table S3: Baseline Characteristics of Eligible vs. Matched Vaccinated Persons during Periods of SARS-CoV-2 Alpha- and Delta-Variant Predominance

Table S3. Baseline Demographic and Clinical Characteristics of Eligible vs. Matched Persons when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during Periods of Alpha- and Delta-Variant Predominance, Veterans Health Administration.*

	"Alpha period"		"Delta period"	
Characteristics	**Eligible (N=764,803)**	**Matched (N=439,684)**	**Eligible (N=19,922)**	**Matched (N=7,160)**
Age (years), median (IQR)	69 (59-74)	69 (60-74)	58 (44-68)	59 (48-68)
Age group, no. (%)				
18 to 39 years	38,229 (5.0)	18,194 (4.1)	3,443 (17.3)	954 (13.3)
40 to 49 years	46,709 (6.1)	24,444 (5.6)	3,127 (15.7)	1,060 (14.8)
50 to 59 years	106,475 (13.9)	62,110 (14.1)	4,361 (21.9)	1,619 (22.6)
60 to 69 years	200,821 (26.3)	120,512 (27.4)	4,799 (24.1)	1,948 (27.2)
70 to 79 years	285,204 (37.3)	168,918 (38.4)	3,518 (17.7)	1,470 (20.5)
≥80 years	87,365 (11.4)	45,506 (10.3)	674 (3.4)	109 (1.5)
Sex, no. (%)				
Male	698,024 (91.3)	407,452 (92.7)	16,483 (82.7)	6,460 (90.2)
Female	66,779 (8.7)	32,232 (7.3)	3,439 (17.3)	700 (9.8)
Race, no. (%)				
White	553,507 (72.4)	327,518 (74.5)	12,035 (60.4)	4,768 (66.6)
Black	160,794 (21.0)	89,934 (20.5)	6,491 (32.6)	2,276 (31.8)
Other	21,080 (2.8)	8,760 (2.0)	592 (3.0)	42 (0.6)
Unknown	29,422 (3.8)	13,472 (3.1)	804 (4.0)	74 (1.0)
Ethnicity, no. (%)				
Not Hispanic	682,984 (89.3)	391,757 (89.1)	17,574 (88.2)	6,323 (88.3)
Hispanic	58,307 (7.6)	35,432 (8.1)	1,766 (8.9)	696 (9.7)
Unknown	23,512 (3.1)	12,495 (2.8)	582 (2.9)	141 (2.0)
Urban residence, no. (%)	540,571 (70.7)	322,046 (73.2)	14,509 (72.8)	5,690 (79.5)
Smoking status, no. (%)				
Never	260,463 (34.1)	149,052 (33.9)	7,667 (38.5)	2,751 (38.4)
Former	238,897 (31.2)	136,488 (31.0)	3,635 (18.2)	1,272 (17.8)
Current	265,443 (34.7)	154,144 (35.1)	8,620 (43.3)	3,137 (43.8)
Chronic lung disease†, no. (%)	133,063 (17.4)	76,959 (17.5)	2,666 (13.4)	1,016 (14.2)
Cardiovascular disease‡, no. (%)	207,173 (27.1)	120,734 (27.5)	3,438 (17.3)	1,327 (18.5)
Hypertension, no. (%)	486,875 (63.7)	282,184 (64.2)	9,791 (49.1)	3,648 (50.9)
Diabetes, no. (%)	266,083 (34.8)	153,945 (35.0)	4,975 (25.0)	1,877 (26.2)
Chronic kidney disease, no. (%)	75,912 (9.9)	43,286 (9.8)	1,248 (6.3)	444 (6.2)
Liver disease, no. (%)	2,758 (0.4)	1,643 (0.4)	75 (0.4)	29 (0.4)
Cancer§, no. (%)	101,704 (13.3)	60,021 (13.7)	1,712 (8.6)	692 (9.7)

Table S3. Baseline Demographic and Clinical Characteristics of Eligible vs. Matched Persons when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during Periods of Alpha- and Delta-Variant Predominance, Veterans Health Administration.*

Immunocompromised state¶, no. (%)	60,304 (7.9)	35,409 (8.1)	1,493 (7.5)	528 (7.4)
Obesity‖, no. (%)	353,935 (46.3)	204,020 (46.4)	9,596 (48.2)	3,390 (47.3)
No. of primary care visits in the past 5 years, no. (%)				
1-9	100,514 (13.1)	56,059 (12.7)	2,908 (14.6)	1,005 (14.0)
10-19	250,454 (32.7)	142,833 (32.5)	7,046 (35.4)	2,553 (35.7)
20-29	187,499 (24.5)	109,080 (24.8)	4,821 (24.2)	1,712 (23.9)
≥30	226,336 (29.6)	131,712 (30.0)	5,147 (25.8)	1,890 (26.4)
No. of influenza vaccinations in the past 5 years, no. (%)				
0	102,307 (13.4)	58,870 (13.4)	7,161 (35.9)	2,668 (37.3)
1 or 2	138,494 (18.1)	78,850 (17.9)	5,398 (27.1)	1,829 (25.5)
3 or 4	243,942 (31.9)	140,399 (31.9)	4,655 (23.4)	1,678 (23.4)
≥5	280,060 (36.6)	161,565 (36.7)	2,708 (13.6)	985 (13.8)

Abbreviation: IQR, interquartile range.

Percentages may not sum to 100% due to rounding.

* Persons included in the “alpha period” analyses received a first dose of BNT162b2 or mRNA-1273 between January 4 and May 14, 2021. Persons included in the “delta period” analyses received a first dose of BNT162b2 or mRNA-1273 between July 1 and September 20, 2021.

† Chronic lung disease included asthma, bronchitis, and chronic obstructive pulmonary disease.

‡ Cardiovascular disease included acute myocardial infarction, cardiomyopathy, cerebrovascular disease, coronary heart disease, heart failure, and peripheral vascular disease.

§ Not included here are non-melanoma skin cancer, benign neoplasms, cancers in situ, and neoplasms of uncertain behavior.

¶ Immunocompromised state included human immunodeficiency virus infection, organ or tissue transplant, bone marrow biopsy, or use of any of the following medications (prescribed ≥2 times over the past year): systemic glucocorticoids, anti-inflammatory or anti-rheumatic agents in combination with glucocorticoids, and immunosuppressants.

‖ Obesity was defined as a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or greater.

Table S4: Baseline Characteristics of Matched Vaccinated Persons during a Period of SARS-CoV-2 Delta-Variant Predominance

Table S4. Baseline Demographic and Clinical Characteristics of Matched Persons when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Delta-Variant Predominance, Veterans Health Administration.*

Characteristics	BNT162b2 recipients (N=3,580)	mRNA-1273 recipients (N=3,580)
Age (years), median (IQR)	59 (47-68)	59 (48-68)
Age group, no. (%)		
18 to 39 years	487 (13.6)	467 (13.0)
40 to 49 years	524 (14.6)	536 (15.0)
50 to 59 years	810 (22.6)	809 (22.6)
60 to 69 years	985 (27.5)	963 (26.9)
70 to 79 years	717 (20.0)	753 (21.0)
≥80 years	57 (1.6)	52 (1.5)
Sex, no. (%)		
Male	3,230 (90.2)	3,230 (90.2)
Female	350 (9.8)	350 (9.8)
Race, no. (%)		
White	2,384 (66.6)	2,384 (66.6)
Black	1,138 (31.8)	1,138 (31.8)
Other	21 (0.6)	21 (0.6)
Unknown	37 (1.0)	37 (1.0)
Ethnicity, no. (%)		
Not Hispanic	3,174 (88.7)	3,149 (88.0)
Hispanic	344 (9.6)	352 (9.8)
Unknown	62 (1.7)	79 (2.2)
Urban residence, no. (%)	2,845 (79.5)	2,845 (79.5)
Smoking status, no. (%)		
Never	1,419 (39.6)	1,332 (37.2)
Former	648 (18.1)	624 (17.4)
Current	1,513 (42.3)	1,624 (45.4)
Chronic lung disease†, no. (%)	485 (13.5)	531 (14.8)
Cardiovascular disease‡, no. (%)	678 (18.9)	649 (18.1)
Hypertension, no. (%)	1,823 (50.9)	1,825 (51.0)
Diabetes, no. (%)	896 (25.0)	981 (27.4)
Chronic kidney disease, no. (%)	228 (6.4)	216 (6.0)
Liver disease, no. (%)	17 (0.5)	12 (0.3)
Cancer§, no. (%)	382 (10.7)	310 (8.7)

Table S4. Baseline Demographic and Clinical Characteristics of Matched Persons when Emulating a Target Trial Evaluating the Comparative Effectiveness of the BNT162b2 and mRNA-1273 Vaccines during a Period of Delta-Variant Predominance, Veterans Health Administration.*

Immunocompromised state¶, no. (%)	271 (7.6)	257 (7.2)
Obesity||, no. (%)	1,730 (48.3)	1,660 (46.4)
No. of primary care visits in the past 5 years, no. (%)		
1-9	516 (14.4)	489 (13.7)
10-19	1,290 (36.0)	1,263 (35.3)
20-29	830 (23.2)	882 (24.6)
≥30	944 (26.4)	946 (26.4)
No. of influenza vaccinations in the past 5 years, no. (%)		
0	1,322 (36.9)	1,346 (37.6)
1 or 2	934 (26.1)	895 (25.0)
3 or 4	847 (23.7)	831 (23.2)
≥5	477 (13.3)	508 (14.2)

Abbreviation: IQR, interquartile range.

Percentages may not sum to 100% due to rounding.

* Persons included in the “delta period” analyses received a first dose of BNT162b2 or mRNA-1273 between July 1 and September 20, 2021.

† Chronic lung disease included asthma, bronchitis, and chronic obstructive pulmonary disease.

‡ Cardiovascular disease included acute myocardial infarction, cardiomyopathy, cerebrovascular disease, coronary heart disease, heart failure, and peripheral vascular disease.

§ Not included here are non-melanoma skin cancer, benign neoplasms, cancers in situ, and neoplasms of uncertain behavior.

¶ Immunocompromised state included human immunodeficiency virus infection, organ or tissue transplant, bone marrow biopsy, or use of any of the following medications (prescribed ≥2 times over the past year): systemic glucocorticoids, anti-inflammatory or anti-rheumatic agents in combination with glucocorticoids, and immunosuppressants.

|| Obesity was defined as a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or greater.

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