Comparative Efficacy over time of the mRNA-1273 (Moderna) vaccine and the BNT162b2 (Pfizer-BioNTech) vaccine

Kenneth Cohen (ken.cohen@nwphysicians.com)
Optum https://orcid.org/0000-0002-6141-9142
Nazmul Islam, PhD, MBA
Optum
Megan S. Jarvis, MS
Optum
Natalie E. Sheils, PhD
Optum

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Abstract

Importance

Real-world analysis of the incidence of SARS-CoV-2 infection post vaccination is important in determining the comparative efficacy of the available vaccines.

Objective

To study the incidence of SARS-CoV-2 infection in individuals fully vaccinated with either the BNT162b2 or the mRNA-1273 at 30-, 60-, and 90-days post vaccination

Design

Retrospective cohort study

Setting

Deidentified administrative claims for Medicare Advantage and commercially insured individuals in a research database.

Participants

Over 3.5 million fully-vaccinated individuals including 6,434 individuals with SARS-CoV-2 infection with a follow up period between 14 and 151 days after their second dose.

Exposure

Vaccination by either mRNA-1273 or BNT162b2.

Main Outcome and Measures

The rate of Covid-19 infection occurring at 30, 60, and 90 days at least 14 days after the second dose of either the mRNA-1273 vaccine or the BNT162b2 vaccine. Sub analyses included the incidence of hospitalization, ICU admission, and death/hospice transfer. Separate analysis was conducted for individuals ≥ age 65 and those without a prior diagnosis of Covid-19 and both yielded results similar to the general population.

Results

The mRNA-1273 vaccine provided slightly superior protection against SARS-CoV-2 infection compared to the BNT162b2 vaccine. In the full population, there were no significant differences in the risk of hospitalization, ICU admission, or death/hospice transfer.

Conclusion

Immunization with mRNA-1273, compared to BNT162b2, provided slightly more protection against SARS-CoV-2 infection that reached statistical significance at 90 days with a number needed to vaccinate of ≥292.There were no differences in vaccine efficacy for protection against hospitalization, ICU admission, or death/hospice transfer.

Key Points

Question: How do the BNT162b2 (Pfizer-BioNTech) and the mRNA-1273 (Moderna) vaccines compare in terms of effectiveness in the prevention of both infection and severe disease from SARS-CoV-2?

Findings: The mRNA-1273 vaccine provided slightly superior protection against SARS-CoV-2 infection compared to the BNT162b2 vaccine. There were no significant differences in the risk of hospitalization, ICU admission, or death/hospice transfer.

Meaning: Our results suggest that for every 1 million individuals vaccinated with the BNT162b vaccine compared to the mRNA-1273 vaccine, there would be 3,425 additional care-seeking-cases of Covid-19 at 90 days.

Introduction

Both the emergence of the Delta variant of concern (VOC) and reports of infections post vaccination emphasize the need to study the relative real-world effectiveness of the available vaccines against Covid-19. The mRNA-1273 (Moderna) vaccine and the BNT162b2 (Pfizer-BioNTech) vaccine have both proven highly effective in preventing severe disease, hospitalization, and death from Covid-19. However, emerging data suggests that the humoral antibody response to the vaccines differ, with two doses of the mRNA-1273 vaccine providing significantly higher humoral antibody response compared to two doses of the BNT162b2 vaccine in both uninfected and previously infected individuals across all age categories.[1] This is clinically relevant as several studies have demonstrated that higher humoral antibody responses correlate with enhanced protection against Covid-19.[2]

Data also suggest that infection rates follow the same trend as the humoral antibody response. Recent observational data incorporating cases of Delta VOC have suggested a higher rate of infection in individuals immunized with two doses of the BNT162b2 vaccine compared to two doses of the mRNA-1273 vaccine.[3]

We therefore conducted a retrospective cohort study which examined the incidence and severity of Covid-19 infections as a function of the time from vaccination in over 3.5 million individuals across the United States who were fully vaccinated via either the mRNA-1273 or the BNT162b2 vaccine, including over 6400 infections. Understanding the clinical performance of each vaccine is critically important both to determine the comparative effectiveness of the vaccines as well as to determine when booster doses of each of the vaccines might be recommended.

Methods

This paper follows STROBE reporting guidelines for cohort studies.

DATA SOURCES

We used administrative claims for Medicare Advantage and commercially insured individuals in a research database, including vaccination status through May 31, 2021. This study was reviewed and deemed exempt by the institutional review board of UnitedHealth Group.

POPULATION

Starting with all Medicare Advantage or commercial enrollees 18 years or older vaccinated after emergency use authorization (EUA) for either mRNA-1273 or BNT162b2 who were fully vaccinated (received their second dose with 14 days additional observation) on or before May 31, 2021. We excluded patients whose second dose was administered more than 4 days before EUA approved time (21 days for BNT162b2 and 28 days for mRNA-1273) or more than 42 days after their first dose. We then required valid zip code information and excluded any patients who experienced a Covid-related event (ICD-10 code U07.1 in inpatient or outpatient setting or positive PCR laboratory test for SARS-CoV-2) within 13 days of their second dose and none after “full vaccination” which is considered 14 days after the second dose in order to eliminate those whose infections occurred before they were fully vaccinated (Figure 1). For subsequent analyses we subdivided this group into those who had at least 30, 60, and 90 days of follow up observation period. In the supplementary information, we also look in particular at the subset of 6,434 fully vaccinated individuals who become infected with Covid-19 (identified either by a positive PCR test or ICD-10 code U07.1 including ER, outpatient, and inpatient hospital visits).

OUTCOME MEASURE

Our main outcome was SARS-CoV-2 infection identified either by a positive PCR test or Covid-19 ICD-10 code U07.1 in claims including ER, outpatient, and inpatient hospital visits. We define this as a “care-seeking” population. We also considered ICU admission, hospital admission, and the composite of either inpatient mortality or discharge to hospice within 30-, 60-, and 90-days of initial admission for Covid-19. We considered this composite measure a more complete representation of the outcome of interest than mortality alone as it reflects an outcome closer to any-site mortality, and given known racial differences in hospice use.[4]

STATISTICAL ANALYSIS

Binary outcomes such as SARS-CoV-2 infection, hospital admission, composite outcomes such as ICU, death, or hospice transfer with and without hospitalization occurred within 30-, 60-, and 90-days post-vaccination were considered. A series of multivariable logistic regressions[4] were performed to estimate the odds of experiencing events for those vaccinated with mRNA-1273 compared to BNT162b2 adjusting for risk factors (demographic, nursing facility admission source, socio-economic status (SES) index, comorbidities, time of vaccination, residence by state, prior Covid diagnosis). To mitigate any potential selection bias, sample propensity scores, signaling conditional probability of receiving mRNA-1273 and BNT162b2, were estimated via multivariable generalized linear model with logit link function and inverse probability of treatment weights (IPTWs) were calculated using stabilization.[5,6] Both weighted univariate and multivariable logistic regressions[7–12] were performed to validate the results of unweighted samples. As a sensitivity, propensity score subclassification models were fitted with respect to quintiles of the estimated propensity scores.[13,14]

Kaplan-Meier analysis was performed for time-to-infection and time-to-composite-outcomes assuming right censoring utilizing June 1, 2021 as censoring date; log-rank based p-values were provided. Multivariable Cox proportional hazard (PH) models[15] were fitted with and without IPTWs. We performed two sensitivity analyses by (a) stratifying data for vaccinated individuals aged 65 and above and (b) excluding patients with a history of any prior Covid-19 diagnoses before complete vaccination. PH model-based predictions of experiencing events for a mRNA-1273 and a BNT162b2 vaccinated individual are provided.

Weighted standardized mean differences and statistical significance tests based on weighted regressions[16] were used to check balances within measured covariates. Standard errors of the parameters were estimated by robust sandwich covariance estimators for all models. Mean predicted marginal probabilities

(risk) were calculated via "recycled" predictions[17–19,] assuming everyone in the sample received each vaccine, and number needed to vaccinate (NNV) were obtained with respect to absolute risk differences based on each model.[19,20]

As sensitivity, we reported "E-values"[21] to assess the magnitude of unmeasured confounding. Summary measures[22] to determine the strength of selection bias were provided for binary outcomes. Multivariable generalized linear models with respect to seven negative control outcomes were fitted and empirical null distribution of systematic error was used to quantify the mean of bias.[23,24] All statistical tests were two-sided, with a significance level of 5%. All analyses were conducted using R, version 3.6.3.[25] Technical details are included in the Supplementary Material.

Results

In a population of over 3.5million fully vaccinated individuals, 6,434 experienced documented Covid-19 infections. Of those, 2,281 (35%) received mRNA-1273 and 4,153 (65%) received BNT162b2 (Table 1).

Median age and prevalence of many comorbid conditions were similar across groups considered (Table 1). Models for the seven negative outcomes, included to assure there were no unaccounted-for differences between groups receiving BNT162b and mRNA-1273, exhibited negligible mean bias arising from systemic errors (Table S2).

Kaplan-Meier curves report the estimated time to infection and time to severe negative outcomes defined as any hospitalization, ICU admission, death, or discharge to hospice, whichever occurs first are reported Figure 2. In the raw data, a statistically significant difference (p-value <.001) with a diverging trend over time is observed between BNT162b and mRNA-1273 (Figure 2C). This difference persists in the PH model-based predictions for a general patient (Figure 2A). There are no statistically significant differences between the predicted probabilities of the two vaccines (Figures 2B, 2D) for the composite outcome of hospitalization, ICU admission, death, or transfer to hospice.

Adjusted odds ratios for likelihood of infection 30-, 60-, and 90-days post vaccination (14 days after second dose) show that the mRNA-1273 vaccine is associated with lower odds of infection. For the unadjusted model with IPTW as sampling weights, the NNV to observe this difference ranges from 1351 over 30 days to 292 over 90 days (Figure 4) signaling superior mRNA-1273 vaccine effects over time in reducing the likelihood of infection. This difference is consistent across all the models considered. However, for severe adverse outcomes (ICU admission, composite ICU admission/ death/ referral to hospice, or composite hospitalization/ ICU admission/ death/ referral to hospice), while events are rare, no statistically significant differences between the two vaccines were observed (Figures S3-S5). Time-to-event analysis assuming right censoring, was performed and provided similar results for different model specifications. Risk differences between mRNA-1273 and BNT162b2 for both infection and composite outcomes increase over time (Figure 3); this observation is in alignment with the binary outcome results (Figure 4).

We further considered time to event analyses among all those experiencing infections in our sample for ICU admission, composite ICU admission/ death/ referral to hospice, and composite hospitalization/ ICU admission/ death/ referral to hospice. No statistically significant differences between vaccines were observed for adverse composite outcomes (Figures S10-S12).

Results are similar for the stratified analyses of (1) including only patients with no prior diagnosis of Covid-19 or (2) including only patients who are aged 65 or older (Figures S8-S9). Since the population considered is different in each model, between-model comparisons are not valid, however both models show directionally the same results.

It is known that certain comorbidities worsen prognosis in an unvaccinated population. Our models indicate that in a vaccinated population congestive heart failure (aHR 2.26, 95% CI (1.25,4.09)), hypertension (aHR 2.50, 95% CI (1.38,4.52)), immunologic diagnosis (aHR 1.69, 95% CI (1.09,2.63)), and lymphoma (aHR 5.63, 95% CI (2.71,11.67)) increase the likelihood of experiencing the composite adverse event of hospitalization, ICU admission, or death/ transfer to hospice. This difference persisted even after adjusting for which vaccine a person received, socio-demographic variables, transfer from nursing facility, timing of vaccination, place of residence, and historical comorbidities (Figure S6).

Discussion

Multiple recent studies have shown that the incidence of SARS-CoV-2 infection in vaccinated individuals has increased over the last several months. This increase may be related to the higher transmissibility of the Delta VOC and/or the potential contribution of waning immunity post vaccination. These data underscore the need to understand the comparative efficacy of the available vaccines.

Two important questions must be answered to address the comparative efficacy of the BNT162b and mRNA-1273 vaccines. The first is whether each vaccine is equivalent in its ability to prevent severe disease from Covid-19. The data available from our large population of patients suggests that at 90 days out from vaccination, there is no significant difference between BNT162b and mRNA-1273 in terms of the risk of the composite outcome of hospitalization, ICU admission, or death/ transfer to hospice. We analyzed data both from a binary and time-to-event outcome point-of-view each quantifying the association between patient outcomes and vaccine types with different model specifications. Conclusions remain similar irrespective of modeling framework, highlighting the robustness of our methods. The second question is whether there is a higher incidence of SARS-CoV-2 infections with the BNT162b vaccine compared to the mRNA-1273 vaccine, and here there is a statistically significant difference in favor of the mRNA-1273 vaccine. This difference appears very early post vaccination and increases over time. The NNV with the mRNA-1273 vaccine compared to the BNT162b vaccine to prevent one case of SARS-CoV-2 is 1351 at thirty days post vaccination but is 292 at ninety days post vaccination. Although this incremental risk is small at the individual level, it is meaningful at the population level. Our results suggest that for every 1 million individuals vaccinated with the BNT162b vaccine compared to the mRNA-1273 vaccine, this would represent 3,425 additional care-seeking-cases of Covid-19 at 90 days. Continuing to follow this trend going forward will be important.

These data can help inform the decision for and timing of booster doses for the mRNA-1273 and BNT162b vaccines. There are potential risks to booster doses, particularly if immune related side effects are more frequent than prevented serious infections. The decision has recently been made by the FDA to recommend booster doses to those who received the BNT162b vaccine and are age 65 or over, immunocompromised, or otherwise at increased risk. The data from this current cohort of individuals can help inform the decision around when others who received the BNT162b vaccine might benefit from a booster dose, as well as when booster doses may be recommended for those who received the mRNA-1273 vaccine.

This study has limitations. First, the analysis is restricted to Commercially insured and Medicare Advantage beneficiaries from a single U.S. insurer, a group that is unevenly distributed across the U.S. geographically and demographically. Nevertheless, this study reflects a large and comprehensive sample of U.S. vaccinations. Second, we are unable to measure SARS-CoV-2 infection that isn't apparent in medical claims or via laboratory testing which likely results in an overestimate of the vaccines' protective effects. This includes the fact that our "time-to-infection" represents date of infection from our data (positive PCR test, or ICD-10 code of U07.1 in claims), rather than the date on which SARS-CoV-2 was contracted. Notably, asymptomatic or mild disease for which an individual did not seek care are not captured. However, serious adverse events which pose the most strain on the healthcare system and for individuals, are reliably observable in our data and are less affected by diagnosis-dependent biases over time.

This study also has strengths. It represents a geographically and socio-demographically diverse group of 3,543,438 patients allowing confidence in the estimation of individual level patient factors associated with documented breakthrough SARS-CoV-2 infection and resulting serious adverse events.

Conclusion

The incidence of SARS-CoV-2 infection in this large cohort of individuals post full vaccination with mRNA-1273 or BNT162b, suggests that the efficacy of the mRNA-1273 vaccine exceeds that of the BNT162b vaccine by a small margin. However, both vaccines compared equally with respect to the incidence of severe disease defined by hospitalization, ICU admission, discharge to hospice, or death.

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Declarations

Conflicts of Interest: None

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Tables

Table 1: Descriptive statistics for baseline characteristics (demographics, socio-economic, comorbidities, negative controls, study outcomes, and other prognostic factors) among fully vaccinated individuals by BNT162b2 and mRNA-1273. Analytical datasets are truncated on May 1, 2021, April 1, 2021, and March 2, 2021, ensuring each patient had at-least 30, 60, and 90 days of post-vaccination follow-up period to experience events, respectively. For time-to-event outcomes among vaccinated individuals, data are censored to June 1, 2021.

	30 day post-vaccination binary outcome		60 day post-vaccination binary outcome		90 day post-vaccination binary outcome		Post-va time-
	BNT162b2	mRNA-1273	BNT162b2	mRNA-1273	BNT162b2	mRNA-1273	BNT162b
N	1198109	890688	480339	455458	209261	161971	212548
Age, mean (SD)	53.13 (16.38)	55.87 (16.97)	56.69 (17.99)	58.18 (17.85)	52.88 (17.97)	53.12 (17.51)	48.53 (16.
Acquired immune deficiency syndrome (%)	3784 (0.3)	2421 (0.3)	1290 (0.3)	1022 (0.2)	512 (0.2)	337 (0.2)	5516 (0.
Alcohol use disorder (%)	10892 (0.9)	7844 (0.9)	4207 (0.9)	3688 (0.8)	1694 (0.8)	1027 (0.6)	19555 (0.
Iron deficiency anemia (%)	70867 (5.9)	61641 (6.9)	35541 (7.4)	35847 (7.9)	13984 (6.7)	10648 (6.6)	101555 (4
Rheumatoid arthritis (%)	38483 (3.2)	32050 (3.6)	17398 (3.6)	17672 (3.9)	6318 (3.0)	5191 (3.2)	54147 (2.
Blood loss anemia (%)	8524 (0.7)	6749 (0.8)	3898 (0.8)	3731 (0.8)	1543 (0.7)	1177 (0.7)	13831 (0.
Congestive heart failure (%)	27391 (2.3)	26310 (3.0)	16146 (3.4)	16525 (3.6)	6104 (2.9)	4050 (2.5)	33341 (1.
Chronic obstructive pulmonary disease (%)	97866 (8.2)	82271 (9.2)	45306 (9.4)	45482 (10.0)	17631 (8.4)	13529 (8.4)	142432 (6
Coagulopathy (%)	14355 (1.2)	12186 (1.4)	7267 (1.5)	7057 (1.5)	2619 (1.3)	1950 (1.2)	20001 (0.
Depression (%)	107858 (9.0)	80224 (9.0)	45931 (9.6)	42305 (9.3)	20285 (9.7)	14262 (8.8)	184136 (8
Diabetes without chronic complication (%)	125640 (10.5)	110253 (12.4)	57210 (11.9)	60514 (13.3)	20188 (9.6)	16406 (10.1)	169445 (8
Diabetes with chronic complication (%)	90729 (7.6)	81209 (9.1)	43021 (9.0)	44799 (9.8)	14670 (7.0)	11897 (7.3)	120654 (5
Substance use disorder (%)	9023 (0.8)	7373 (0.8)	4160 (0.9)	3863 (0.8)	1820 (0.9)	1177 (0.7)	15378 (0.
Hypertension (%)	365690 (30.5)	312552 (35.1)	169751 (35.3)	174605 (38.3)	61183 (29.2)	48788 (30.1)	504061 (23
Hypothyroidism (%)	117655 (9.8)	97116 (10.9)	54802 (11.4)	54710 (12.0)	21428 (10.2)	16953 (10.5)	169396 (8
Liver disease (%)	37811 (3.2)	29173 (3.3)	15334 (3.2)	14870 (3.3)	5566 (2.7)	4507 (2.8)	56949 (2.
Lymphoma (%)	5635 (0.5)	4356 (0.5)	2865 (0.6)	2623 (0.6)	868 (0.4)	667 (0.4)	7214 (0.3
Fluid & electrolyte disorder (%)	43123 (3.6)	36840 (4.1)	22062 (4.6)	21371 (4.7)	8705 (4.2)	5937 (3.7)	60020 (2.
Metastatic cancer (%)	8764 (0.7)	6480 (0.7)	4129 (0.9)	3769 (0.8)	1274 (0.6)	990 (0.6)	11090 (0.
Neurological disorder (%)	45473 (3.8)	37574 (4.2)	24214 (5.0)	22109 (4.9)	10190 (4.9)	6262 (3.9)	63204 (3.
Obesity (%)	155597 (13.0)	123121 (13.8)	60961 (12.7)	62662 (13.8)	23761 (11.4)	20180 (12.5)	241325 (11
Paralysis (%)	5843 (0.5)	4847 (0.5)	3307 (0.7)	2798 (0.6)	1579 (0.8)	791 (0.5)	7737 (0.4
Peripheral vascular disease (%)	48938 (4.1)	46199 (5.2)	30215 (6.3)	29470 (6.5)	11124 (5.3)	7289 (4.5)	58875 (2.
Psychosis (%)	30692 (2.6)	22132 (2.5)	13233 (2.8)	11684 (2.6)	5834 (2.8)	3896 (2.4)	52444 (2.
Pulmonary circulation disorder (%)	6320 (0.5)	5182 (0.6)	3093 (0.6)	2941 (0.6)	1118 (0.5)	768 (0.5)	8545 (0.4
Chronic kidney disease (%)	46018 (3.8)	45419 (5.1)	27954 (5.8)	29067 (6.4)	9438 (4.5)	6960 (4.3)	55241 (2.
Solid tumor without metastasis (%)	56712 (4.7)	45507 (5.1)	27691 (5.8)	26807 (5.9)	9060 (4.3)	7114 (4.4)	72930 (3.
Peptic ulcer disease (%)	4583 (0.4)	3775 (0.4)	2206 (0.5)	2152 (0.5)	820 (0.4)	591 (0.4)	6552 (0.3
Valvular disorder (%)	44779 (3.7)	41237 (4.6)	24262 (5.1)	25427 (5.6)	8524 (4.1)	7015 (4.3)	57190 (2.
Weight loss (%)	16195 (1.4)	12903 (1.4)	8688 (1.8)	7642 (1.7)	3744 (1.8)	2162 (1.3)	23793 (1.
Stroke cerebrovascular (%)	47300 (3.9)	43965 (4.9)	27160 (5.7)	27405 (6.0)	9892 (4.7)	7311 (4.5)	59003 (2.
Down syndrome (%)	297 (0.0)	223 (0.0)	109 (0.0)	126 (0.0)	44 (0.0)	24 (0.0)	393 (0.0
Thalassemia (%)	1384 (0.1)	993 (0.1)	552 (0.1)	508 (0.1)	226 (0.1)	163 (0.1)	2197 (0.1
Smoking (%)	50699 (4.2)	41513 (4.7)	21275 (4.4)	21580 (4.7)	8178 (3.9)	6467 (4.0)	80225 (3.
Transplant (%)	888 (0.1)	647 (0.1)	374 (0.1)	344 (0.1)	105 (0.1)	101 (0.1)	1230 (0.1
Elixhauser mortality score, mean (SD)	1.27 (4.09)	1.46 (4.37)	1.68 (4.81)	1.71 (4.75)	1.45 (4.56)	1.29 (4.10)	0.97 (3.5
Elixhauser readmission score, mean (SD)	4.73 (9.98)	5.41 (10.71)	5.91 (11.58)	6.09 (11.47)	5.17 (11.22)	4.76 (10.13)	3.78
Transferred from nursing facility/SNF (%)	712 (0.1)	269 (0.0)	645 (0.1)	204 (0.0)	521 (0.2)	122 (0.1)	770 (0.0)
Immunologic Rx (%)	261289 (21.8)	216866 (24.3)	116250 (24.2)	118930 (26.1)	46756 (22.3)	37957 (23.4)	407353 (19.2)
Immunologic dx (%)	312683 (26.1)	241976 (27.2)	135892 (28.3)	132922 (29.2)	50225 (24.0)	40972 (25.3)	466599 (22.0)
Sex							
Female (%)	675085 (56.3)	509990 (57.3)	297351 (61.9)	275717 (60.5)	138447 (66.2)	102879 (63.5)	1132193 (53.3)
Male (%)	523024 (43.7)	380698 (42.7)	182988 (38.1)	179741 (39.5)	70814 (33.8)	59092 (36.5)	993296 (46.7)
Residence by region (%)							
Midwest	416757 (34.8)	280953 (31.5)	166624 (34.7)	146552 (32.2)	66149 (31.6)	39545 (24.4)	728875 (34.3)
Northeast	216958 (18.1)	174121 (19.5)	93076 (19.4)	92828 (20.4)	45667 (21.8)	41103 (25.4)	397533 (18.7)
South	363289 (30.3)	292090 (32.8)	123928 (25.8)	142138 (31.2)	53685 (25.7)	58664 (36.2)	621156 (29.2)
West	201105	143524	96711 (20.1)	73940 (16.2)	43760 (20.9)	22659 (14.0)	377925 (17.8)

	(16.8)	(16.1)					
First dose administered before Feb 1, 2021 (%)	278895 (23.3)	298112 (33.5)	278895 (58.1)	298112 (65.5)	209261 (100.0)	161971 (100.0)	278895 (13.1)
First dose administered before Jan 10, 2021 (%)	94597 (7.9)	85201 (9.6)	94597 (19.7)	85201 (18.7)	94597 (45.2)	85201 (52.6)	94597 (4.5)
SES index, mean (SD)	53.78 (3.00)	53.38 (3.22)	53.53 (2.98)	53.23 (3.27)	53.36 (2.95)	53.37 (3.37)	54.10 (3.01)
Prior any Covid dx (ER/IP/ICU) (%)	83046 (6.9)	56296 (6.3)	34476 (7.2)	27716 (6.1)	17204 (8.2)	10634 (6.6)	147880 (7.0)
Prior positive PCR (%)	18607 (1.6)	12763 (1.4)	6915 (1.4)	5886 (1.3)	3244 (1.6)	2227 (1.4)	35839 (1.7)
Negative outcomes							
Bilateral prim osteoarthritis knee (%)	14039 (1.2)	12068 (1.4)	6880 (1.4)	7067 (1.6)	2307 (1.1)	1848 (1.1)	18500 (0.9)
Frequency of micturition (%)	24034 (2.0)	19443 (2.2)	11316 (2.4)	11157 (2.4)	4331 (2.1)	3374 (2.1)	35888 (1.7)
Presbyopia (%)	27042 (2.3)	22655 (2.5)	13138 (2.7)	13336 (2.9)	4963 (2.4)	3626 (2.2)	36952 (1.7)
Sensorineural hear loss bilateral (%)	17673 (1.5)	15300 (1.7)	9653 (2.0)	9684 (2.1)	3404 (1.6)	2708 (1.7)	22785 (1.1)
Tinea unguium (%)	28007 (2.3)	24591 (2.8)	16681 (3.5)	15490 (3.4)	7117 (3.4)	4351 (2.7)	36512 (1.7)
UTI site not specified (%)	44819 (3.7)	38280 (4.3)	23033 (4.8)	22469 (4.9)	9937 (4.7)	7529 (4.6)	65461 (3.1)
Agerel nuclear cataract bilateral (%)	46256 (3.9)	41840 (4.7)	24055 (5.0)	25317 (5.6)	7715 (3.7)	6680 (4.1)	57387 (2.7)
Study-related outcomes							
Infection (%)	2592 (0.2)	1401 (0.2)	2230 (0.5)	1242 (0.3)	1659 (0.8)	698 (0.4)	4153 (0.2)
Hospitalization/ ICU/ deceased/ transferred to hospice (%)	32 (0.0)	24 (0.0)	42 (0.0)	28 (0.0)	24 (0.0)	11 (0.0)	70 (0.0)
ICU/ deceased/ transferred to hospice (%)	12 (0.0)	8 (0.0)	14 (0.0)	8 (0.0)	10 (0.0)	3 (0.0)	27 (0.0)
Hospitalization (%)	26 (0.0)	21 (0.0)	35 (0.0)	25 (0.0)	23 (0.0)	11 (0.0)	56 (0.0)
ICU (%)	9 (0.0)	8 (0.0)	11 (0.0)	8 (0.0)	8 (0.0)	3 (0.0)	24 (0.0)
Deceased/ transferred to hospice (%)	3 (0.0)	2 (0.0)	3 (0.0)	1 (0.0)	2 (0.0)	0 (0.0)	4 (0.0)

Figures

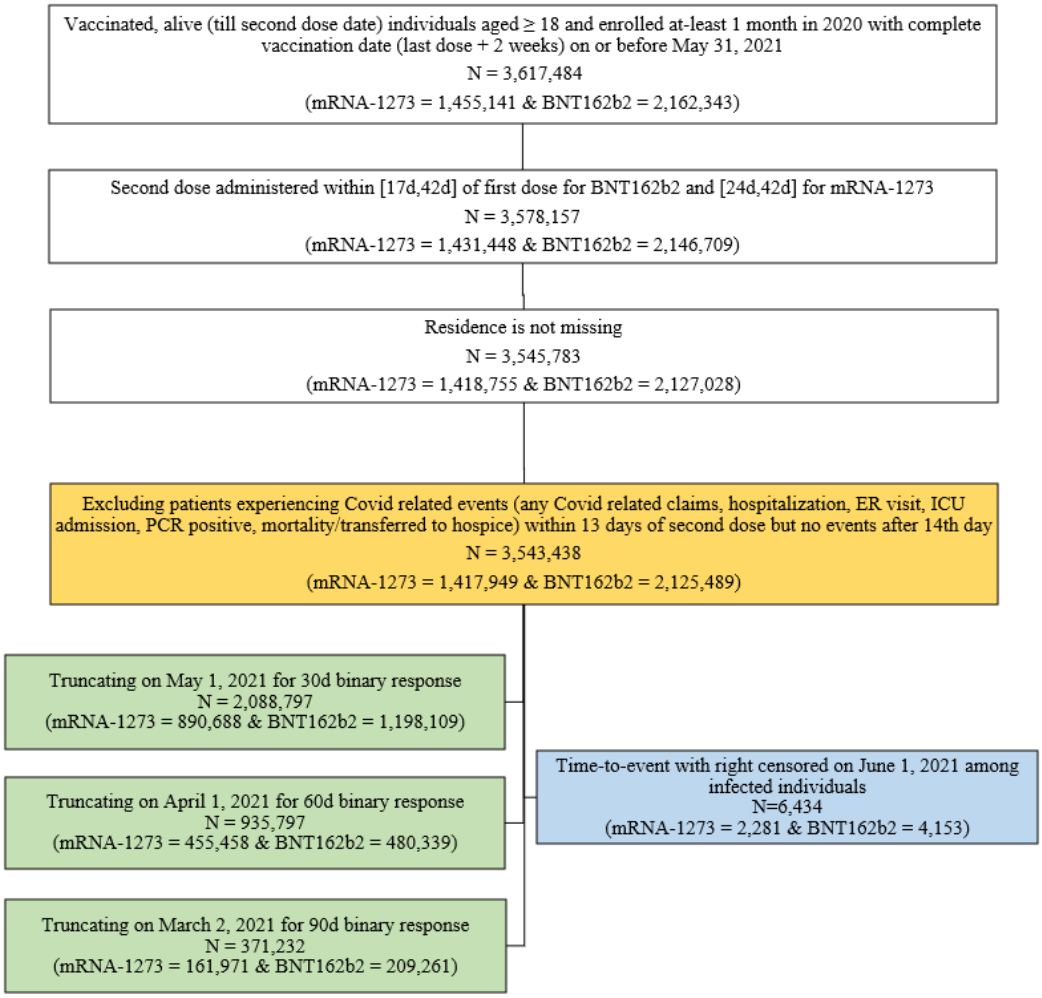

Figure 1

Description of analytical datasets

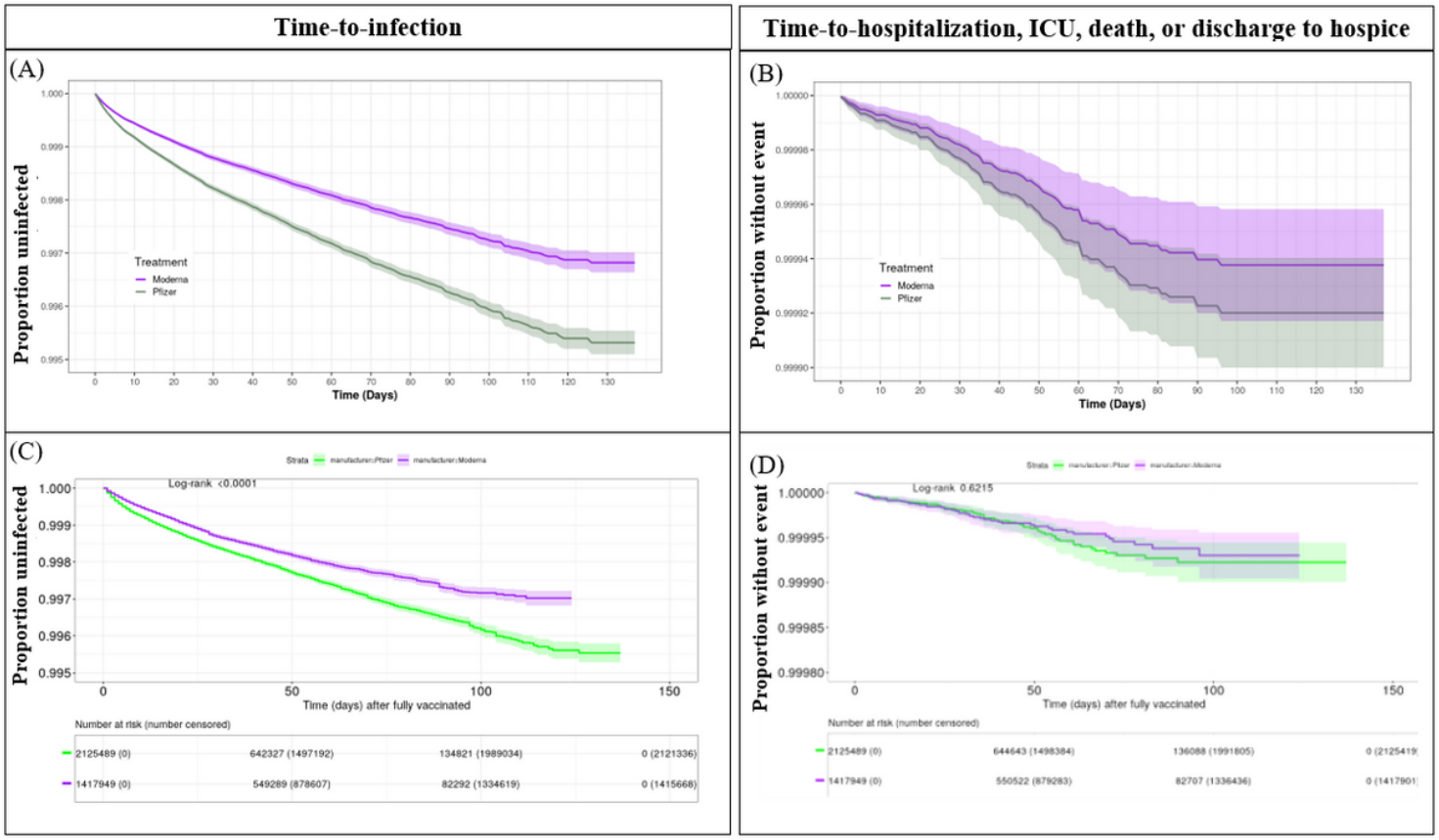

Figure 2

Panels (A) and (B) show predicted survival probabilities based on the univariate model with inverse probability of treatment weight (IPTW) for (A) SARS-CoV-2 infection and (B) hospitalization/ICU/death/hospice whichever occurring first. Raw data are shown in (C) and (D) via Kaplan-Meier curves for time-to-events without truncation among all vaccinated individuals for the event of (C) infection, (D) hospitalization/ ICU/death/hospice whichever occurs first.

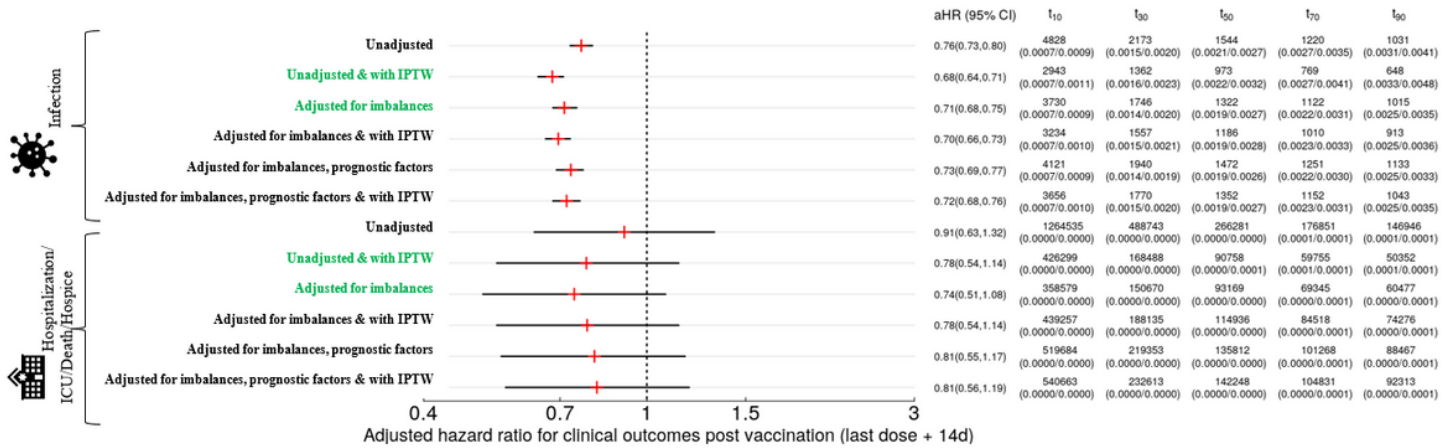

Figure 3

Adjusted hazard ratios (aHRs) along with 95% confidence intervals, number needed to vaccinate (NNV), and marginal probabilities (in parenthesis) of experiencing events at 10d, 30d, 50d, 70d, and 90d post vaccination (last dose + 14d) for mRNA-1273 (Moderna) and BNT162b2 (Pfizer), respectively. Time-to-event for (top-panel) infection and (bottom-panel) adverse outcome of hospitalization/ICU admission /death /transfer to hospice whichever occurs first among all vaccinated individuals. Note that six models are considered for each outcome. 1) Unadjusted: A univariate model adjusting only for vaccine type; 2) Unadjusted & with IPTW: Weighted univariate model adjusting only for vaccine type; 3) Adjusted for imbalances: Multivariable model adjusting for age, timing of vaccine, residence, prior history of Covid-19 diagnosis, and socio-economic status; 3) Adjusted for imbalances & with IPTW: Weighted multivariable model adjusting for age, timing of vaccine, residence, prior history of Covid-19 diagnosis, and socio-economic status; 4) Adjusted for imbalances, prognostic factors: Multivariable model adjusting for all the above variables plus nursing facility residence and comorbidities that are selected in the variable screening step; 5)

Adjusted for imbalances, prognostic factors & with IPTW: Weighted multivariable model adjusting for all the above variables plus nursing facility residence and comorbidities that are selected in the variable screening step

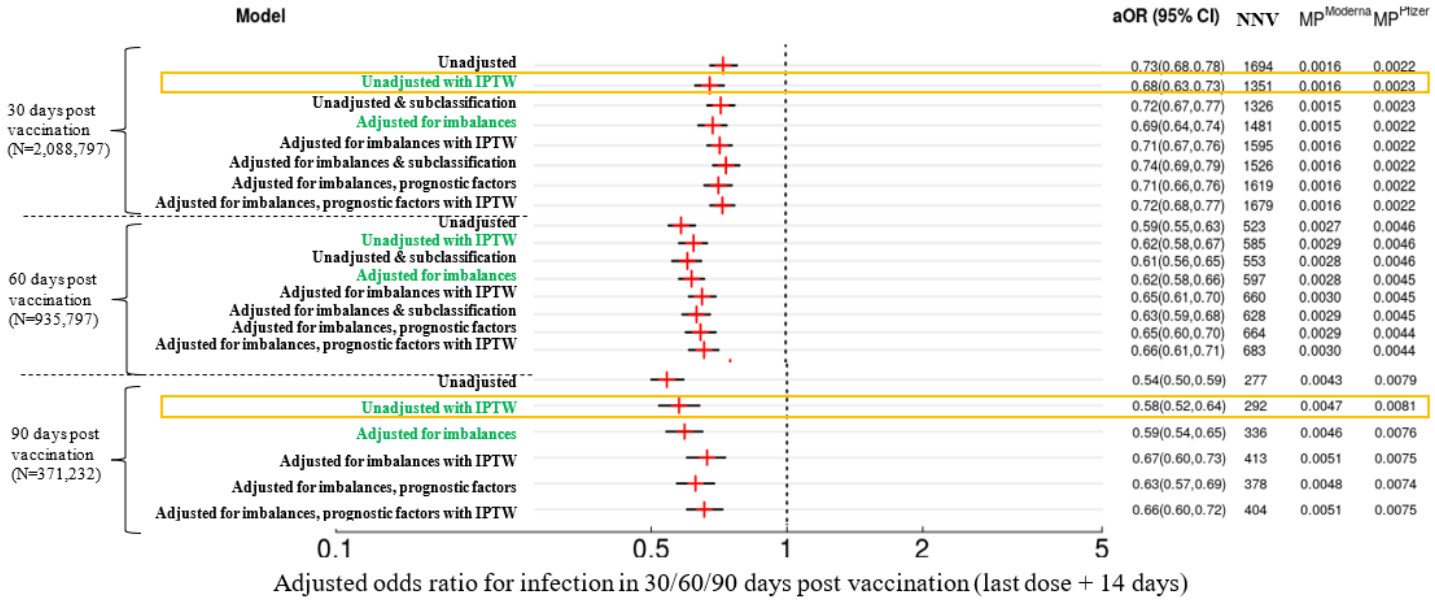

Figure 4

Adjusted odds ratio along with 95% confidence intervals, number needed to vaccinate (NNV), and marginal probabilities (MP) of infection within 30/60/90 days post vaccination (last dose + 14 days) for BNT162b2 and mRNA-1273. Note that up to eight models are considered for each outcome. 1) Unadjusted: A univariate model adjusting only for vaccine type; 2) Unadjusted & with IPTW: Weighted univariate model adjusting only for vaccine type; 3) Unadjusted & subclassification: Univariate model, stratified by quintiles of propensity scores, adjusting only for vaccine type; 4) Adjusted for imbalances: Multivariable model adjusting for age, timing of vaccine, residence, prior history of Covid-19 diagnosis, and socio-economic status; 5) Adjusted for imbalances with IPTW: Weighted multivariable model adjusting for age, timing of vaccine, residence, prior history of Covid-19 diagnosis, and socio-economic status; 6) Adjusted for imbalances & subclassification: Multivariable model, stratified by quintiles of propensity scores, adjusting for age, timing of vaccine, residence, prior history of Covid-19 diagnosis, and socio-economic status; 7) Adjusted for imbalances, prognostic factors: Multivariable model adjusting for all the above variables plus nursing facility residence and comorbidities that are selected in the variable screening step; 8) Adjusted for imbalances, prognostic factors with IPTW: Weighted multivariable model adjusting for all the above variables plus nursing facility residence and comorbidities that are selected in the variable screening step

Supplementary Files

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- ComparativeEfficacySupp100121Final.docx