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Real-World Comparative COVID-19 Vaccine Effectiveness of a Third Dose of mRNA-1273 Versus BNT162b2 Among Immunocompromised Adults in the United States

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BACKGROUND

- The risk of SARS-CoV-2 infection and COVID-19–related hospitalization and death has been substantially mitigated by the availability of mRNA vaccines, as noted by real-world data[1,2]
- However, immunocompromised individuals remain at increased risk of COVID-19–associated morbidity and mortality[3,4]
  - The overall vaccine effectiveness of a 2-dose regimen of any mRNA COVID-19 vaccine was 62.9% against COVID-19 hospitalization among immunocompromised individuals compared with 91.3% in individuals without an immunocompromising condition[5]
  - Given the vulnerability of immunocompromised individuals, a third dose of a COVID-19 vaccine is recommended as part of the primary series to increase protection[4]
- We previously showed that immunocompromised individuals who received 2 doses of mRNA-1273 (Spikevax; Moderna, Inc., Cambridge, MA) were better protected against breakthrough medically attended COVID-19 than those who received 2 doses of BNT162b2 (Comirnaty; Pfizer Inc., New York, NY)[6]
  - An evaluation of the comparative effectiveness of a third dose of mRNA-1273 and BNT162b2 in immunocompromised individuals is necessary to inform ongoing vaccination strategies in this population

OBJECTIVE

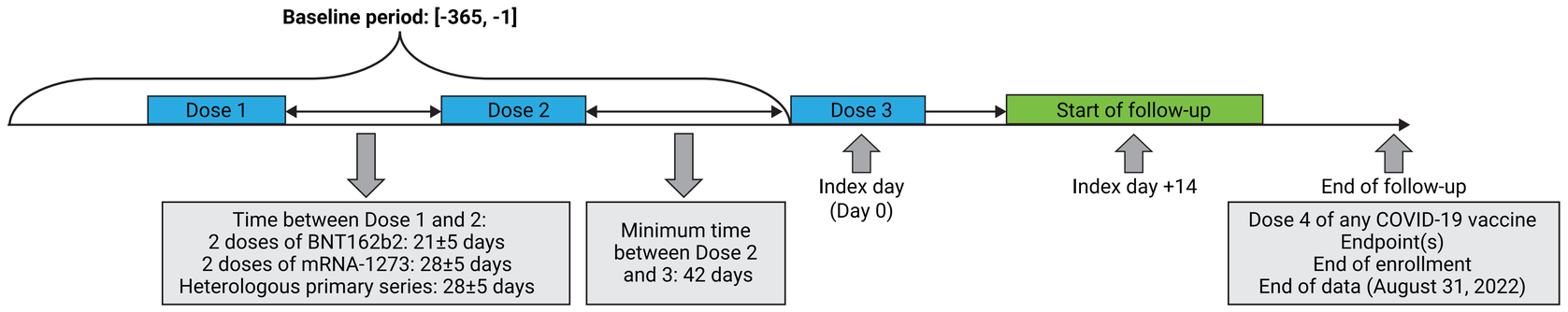
- To evaluate the comparative effectiveness of a third dose of mRNA-1273 compared with a third dose of BNT162b2 against medically attended breakthrough COVID-19 and COVID-19 hospitalization among insured US adults with immunocompromising conditions who previously received a 2-dose primary series

METHODS

Study Design

- This observational comparative vaccine effectiveness study utilized de-identified, individual-level US medical and pharmacy HealthVerity (HV) claims data (Private Source 17 and 20) from December 11, 2020, through August 31, 2022
- This analysis included individuals with moderate or severe immunocompromise, including those with underlying immunocompromising conditions and those prescribed immune-modifying therapies (≥18 years) who previously received homologous or heterologous regimens of 2 doses of either mRNA-1273 or BNT162b2 and received a third dose ≥42 days after dose 2 (**Figure 1**); identification criteria for immunocompromised participants is shown in **Supplementary Table 1** (accessible through the QR code)

Figure 1. Study Design



Outcomes and Analyses

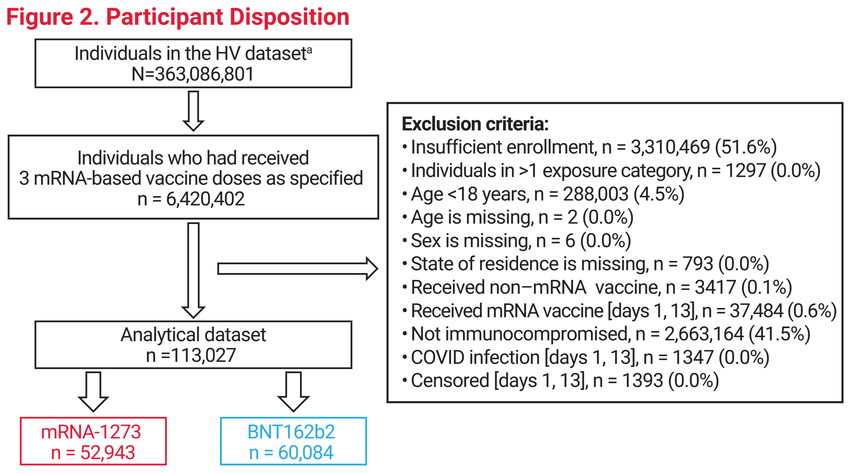
- The primary outcome was medically attended breakthrough SARS-CoV-2 infection in any setting (eg, inpatient, outpatient, emergency department, or urgent care); the secondary outcome was breakthrough COVID-19 hospitalization
- Inverse probability treatment weighting was applied; groups were considered balanced if the absolute standardized differences for baseline covariates before and after weighting were ≤0.10[7,8]
- Incidence rates for outcomes were calculated for the mRNA-1273 and BNT126b2 groups and reported as per thousand person-years
- Propensity score–weighted Kaplan-Meier curves were created, and risk differences and relative risks at different time points were estimated

RESULTS

Participants

- A total of 113,027 immunocompromised adults were included in the analytical dataset (**Figure 2**)
- No residual imbalance after weighting was observed (**Supplementary Table 2**)

Figure 2. Participant Disposition



[a]HV dataset provided by Aetion Evidence Platform (AEP). Dataset on AEP contains multiple years and data sources of HV. Individuals may appear in multiple sources at multiple times.

Rates of Medically Attended COVID-19 and COVID-19 Hospitalization Among Immunocompromised Individuals

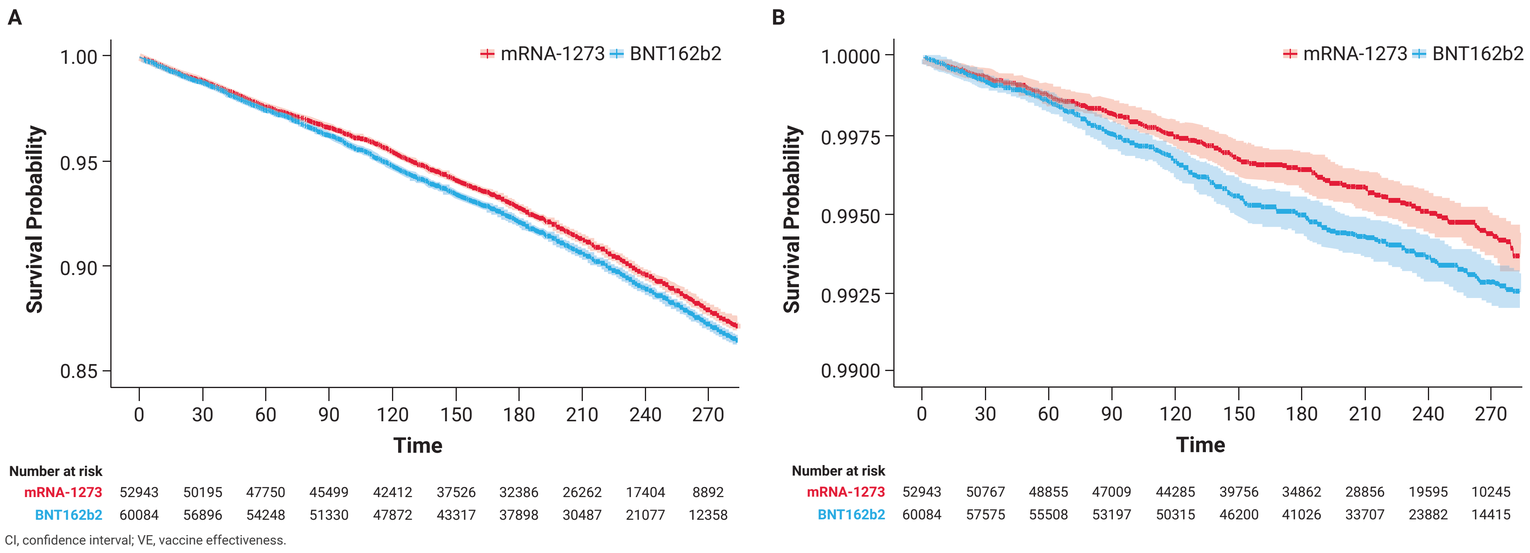
- Immunocompromised individuals who received mRNA-1273 as their third dose had lower crude rates of medically attended COVID-19 and hospitalization compared with those who received BNT162b2 (**Supplementary Table 3**)
- After weighting, results were similar to the crude analysis over the duration of the study, with significantly lower risk of medically attended COVID-19 at 90 and 180 days, and significantly lower risk of COVID-19 hospitalization at 90, 180 and 270 days **Figure 3; Table 1**)
- In subgroup analyses, those with specific immunocompromising conditions, individuals without recent COVID-19 diagnosis (within 180 days before index date), and individuals aged ≥65 years had consistently lower rates of medically attended COVID-19 and hospitalization among the mRNA-1273 group compared with the BNT162b2 group (**Supplementary Table 4**)

Table 1. Comparison of Study Endpoints in Immunocompromised Adults Receiving a Third Dose of mRNA-1273 Versus BNT162b2

		Risk difference between third dose: mRNA-1273 vs BNT162b2[a] (95% bootstrap CI)		Relative risk between third dose: mRNA-1273 vs BNT162b2 (95% bootstrap CI)	
Endpoint	Time point (days)	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]
COVID-19 hospitalization	90	-0.689 (-1.249, -0.132)	-0.812 (-1.370 to -0.265)	0.723 (0.550-0.936)	0.676 (0.506, 0.887)
	180	-1.478 (-2.315 to -0.625)	-1.488 (-2.343 to -0.663)	0.709 (0.586-0.860)	0.707 (0.573-0.858)
	270	-1.542 (-2.711 to -0.329)	-1.707 (-2.909 to -0.501)	0.784 (0.647-0.949)	0.766 (0.626-0.927)
Medically attended COVID-19	90	-3.709 (-6.045 to -1.527)	-3.142 (-5.373 to -0.879)	0.902 (0.845-0.959)	0.916 (0.860-0.976)
	180	-7.124 (-10.482 to -3.890)	-5.015 (-8.327 to -1.697)	0.910 (0.870-0.949)	0.936 (0.895-0.978)
	270	-6.095 (-11.310 to -1.063)	-3.047 (-8.256 to 2.054)	0.952 (0.912-0.991)	0.976 (0.935-1.017)

CI, confidence interval.
[a]Risk difference in 1000 persons: mRNA-1273 – BNT162b2.
[b]Propensity score weighted.

Figure 3. Comparative VE Over 270 Days (95% CI) in A) Medically Attended COVID-19 and B) COVID-19 Hospitalization



CI, confidence interval; VE, vaccine effectiveness.

CONCLUSIONS

- For at least 180 days following vaccination, a third dose of mRNA-1273 is more effective than a third dose of BNT162b2 in reducing breakthrough medically attended COVID-19 and subsequent hospitalization among immunocompromised individuals
- Limitations of this study include the use of secondary data sources, which can result in residual confounding, measurement error, and selection bias
- This study and other real-world studies contribute to further understanding of vaccine effectiveness by studying populations that were largely excluded from clinical trials and are among the most vulnerable for severe outcomes from COVID-19
- As COVID-19 disease burden remains high in the immunocompromised population, these individuals should follow updated vaccination guidance for the fall 2023-2024 season

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Disclosures

EB, TS, LL, MG, and NVV are employees of Moderna, Inc., and hold stock/stock options in the company.

ADDITIONAL INFORMATION

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