Real-World Comparative Effectiveness of the First COVID-19 mRNA Booster, mRNA-1273 Versus BNT162b2, Among US Medicare Fee-for-Service Non-Immunocompromised Beneficiaries Aged 65 Years and Older

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BACKGROUND

- COVID-19 is a leading cause of preventable hospitalizations among US adults aged ≥65 years, accounting for most of the direct medical costs associated with the disease[1,2]
- In 2023, adults aged ≥65 years accounted for 62.9% of COVID-19 hospitalizations and 87.9% of COVID-19 in-hospital deaths in the United States[1]
- COVID-19 vaccines, including mRNA-1273 (Spikevax; Moderna, Inc., Cambridge, MA, USA), have substantially mitigated the impact of the COVID-19 pandemic[3]
  - Real-world effectiveness studies have demonstrated that mRNA-1273 is more effective than BNT162b2 (Comirnaty; Pfizer Inc., New York, NY, USA; BioNTech GmbH, Mainz, Germany) in preventing COVID-19 hospitalizations and death among individuals aged ≥65 years mostly in Medicare Advantage[4,5]
  - However, their effectiveness against hospitalization and associated expenditures has not been compared in a large sample of Medicare fee-for-service (FFS) beneficiaries

OBJECTIVE

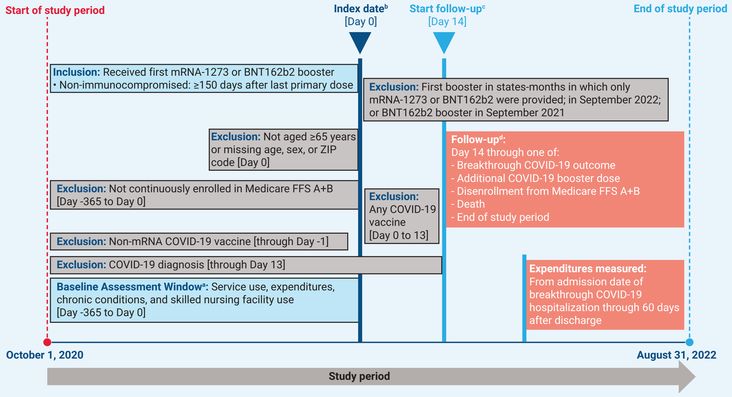
- To compare the real-world effectiveness of the first booster dose of mRNA-1273 50 µg (original Moderna COVID-19 vaccine against the ancestral strain) and BNT162b2 30 µg in preventing COVID-19 hospitalizations and associated expenditures among non-immunocompromised Medicare FFS beneficiaries aged ≥65 years who received ≥1 primary series dose

METHODS

Study Design and Population

- This was a retrospective cohort study using Medicare FFS claims data from October 2020 through August 2022 (**Figure 1**)
- The study included Medicare FFS beneficiaries aged ≥65 years without known immunocompromising conditions who received their first booster dose of either mRNA-1273 50 µg (original Moderna COVID-19 vaccine against the ancestral strain) or BNT162b2 30 µg between October 1, 2021, and August 16, 2022, at least 5 months after their last mRNA primary series vaccine dose

Figure 1. Study Design



FFS, fee-for-service.
[a]Measures described were defined over the yearlong period. Beneficiary demographics, eligibility, and location were defined as of the index date.
[b]The index date was defined as the date of receipt of the first mRNA vaccine booster dose.
[c]The follow-up period started 14 days after receipt of the first mRNA vaccine booster dose.
[d]In a sensitivity analysis of Medicare expenditures, the follow-up time for hospitalizations was extended until December 31, 2022.

Outcomes and Analyses

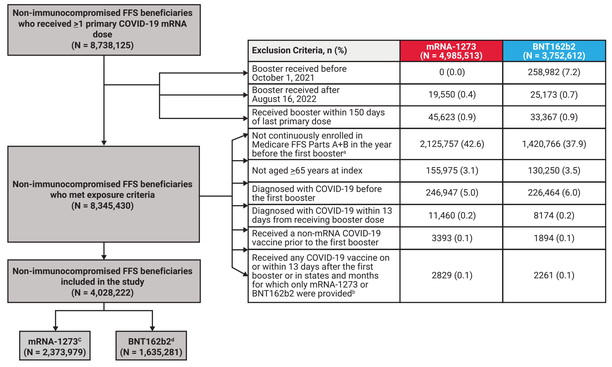
- This study estimated the effectiveness of the first booster dose of mRNA-1273 compared with BNT162b2 against
  - COVID-19 hospitalizations (primary or secondary diagnosis based on U071 [COVID-19] or J1282 [pneumonia due to COVID-19] codes)
  - Total Medicare FFS Parts A and B expenditures during and after COVID-19 hospitalization
- Stabilized inverse probability of treatment weighting (IPTW) was used to adjust for baseline confounding variables such as time and place of booster receipt
- In the survival analysis of COVID-19 hospitalizations, a Cox proportional hazards model was used to calculate hazard ratios (HRs) and 95% confidence intervals
- Group differences in Medicare FFS Parts A and B expenditures during and following the 60 days after discharge from the first COVID-19 hospitalization were estimated using IPTW generalized linear models
  - The analytic cohort for the expenditure analyses excluded beneficiaries who were alive but not enrolled in Medicare continuously for the duration of the expenditure measurement period
  - Several sensitivity analyses were conducted to assess differences in Medicare expenditures using alternate expenditure measures

RESULTS

Participant Disposition

- A total of 8,738,125 Medicare FFS beneficiaries without known immunocompromising conditions who received at least 1 dose of the primary series of the mRNA COVID-19 vaccine were identified (**Figure 2**)
  - Of these beneficiaries, 2,373,979 mRNA-1273 and 1,635,281 BNT162b2 first booster recipients met inclusion/exclusion criteria and were included in the study
- After weighting, all absolute standardized differences (ASDs) were <0.10, indicating balanced baseline characteristics between the 2 vaccine groups
- Recipients of the first mRNA-1273 or BNT162b2 booster were followed for an average of 198 and 207 days, respectively

Figure 2. Flow Chart of Participant Disposition



Exclusion Criteria, n (%)	mRNA-1273 (N = 4,985,513)	BNT162b2 (N = 3,752,612)
Booster received before October 1, 2021	0 (0.0)	258,982 (7.2)
Booster received after August 16, 2022	19,550 (0.4)	25,173 (0.7)
Received booster within 150 days of last primary dose	45,623 (0.9)	33,367 (0.9)
Not continuously enrolled in Medicare FFS Parts A+B in the year before the first booster[a]	2,125,757 (42.6)	1,420,766 (37.9)
Not aged ≥65 years at index	155,975 (3.1)	130,250 (3.5)
Diagnosed with COVID-19 before the first booster	246,947 (5.0)	226,464 (6.0)
Diagnosed with COVID-19 within 13 days from receiving booster dose	11,460 (0.2)	8174 (0.2)
Received a non-mRNA COVID-19 vaccine prior to the first booster	3393 (0.1)	1894 (0.1)
Received any COVID-19 vaccine on or within 13 days after the first booster or in states and months for which only mRNA-1273 or BNT162b2 were provided[b]	2829 (0.1)	2261 (0.1)

FFS, fee-for-service.
[a]Among this group, only 322 mRNA-1273 and 222 BNT162b2 booster recipients were not observable in enrollment data.
[b]Among this group, we dropped <20 participants with index dates in state-month with only mRNA-1273 or BNT162b2 booster recipients.
[c]The mean follow-up time for mRNA-1273 booster recipients was 198 days.
[d]The mean follow-up time for BNT162b2 booster recipients was 207 days.

Comparative Effectiveness of mRNA-1273 and BNT162b2 Against COVID-19 Hospitalizations

- Among non-immunocompromised Medicare FFS beneficiaries, the first mRNA-1273 booster was more effective against COVID-19 hospitalization than the first BNT162b2 booster (adjusted HR, 0.789; 95% CI, 0.766-0.813; **Table 1**, **Figure 3**)

Comparison of mRNA-1273 and BNT162b2 Medicare FFS Expenditures for COVID-19 Hospitalizations

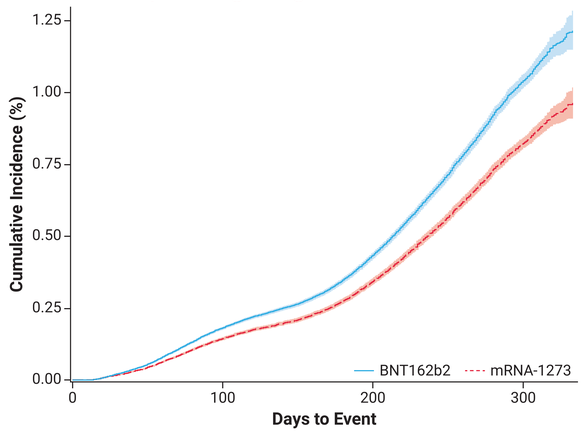
- Non-immunocompromised Medicare FFS beneficiaries who received the mRNA-1273 monovalent booster had 1.8% lower total Medicare FFS expenditures during COVID-19 hospitalizations and up to 60 days post-discharge ($723 USD; *P*=0.08) compared with those who received the BNT162b2 booster, demonstrating cost savings compared with BNT162b2 (**Figure 4**); differences in total expenditures for hospitalizations with COVID-19 as principal diagnosis (up to 60 days post-discharge) were $-2224 USD (-6.3%; *P*<0.001)
- Differences in total expenditures during hospitalization and up to 30 days post-discharge were $-678 USD (-2.4%; *P*=0.02) and up to 90 days post-discharge were $10 USD (0.0%; *P*=0.99)

Table 1. Comparative Effectiveness of mRNA-1273 vs BNT162b2 Monovalent Boosters in Preventing COVID-19 Hospitalizations Among Non-Immunocompromised Medicare FFS Beneficiaries

Outcome Type	Incidence[a] (95% CI)		Unadjusted Median Days to Event		mRNA-1273 vs BNT162b2[b]	
	mRNA-1273	BNT162b2	mRNA-1273	BNT162b2	HR (95% CI)	*P* value
COVID-19 hospitalizations (principal or secondary diagnosis)	75.8 (74.3-77.3)	97.8 (95.8-99.9)	169	166	0.789 (0.766-0.813)	<0.001
COVID-19 hospitalizations (principal diagnosis)	35.5 (34.4-36.5)	45.8 (44.5-47.2)	176	175	0.726 (0.695-0.759)	<0.001

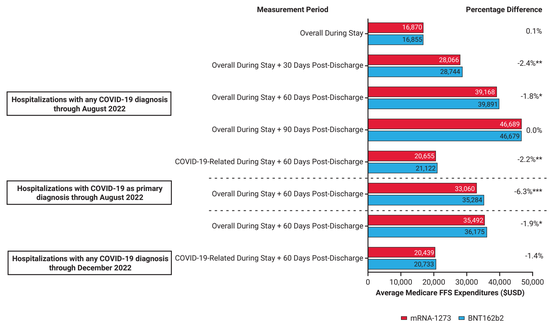
CI, confidence interval; HR, hazard ratio.
[a]Per 10,000 person-years.
[b]Covariate-adjusted and weighted survival model results.

Figure 3. Cumulative COVID-19 Hospitalizations by Vaccine Group Through August 2022



Displayed are the estimated cumulative incidence rates with 95% confidence intervals.

Figure 4. Differences in Regression-Adjusted Medicare FFS Expenditures During and After COVID-19 Hospitalizations by Vaccine Group



Displayed are regression-adjusted mean expenditures by vaccine group, with differences in percentage terms; significant differences are indicated by asterisks. For example, regression-adjusted total mean expenditures for COVID-19 inpatient stay ('Overall during stay') of mRNA-1273 group was $16,870.
Different sensitivity analysis assessing different scenarios were conducted.
FFS, fee-for-service.
*Significant at 10% level, 2-tailed test.
**Significant at 5% level, 2-tailed test.
***Significant at 1% level, 2-tailed test.

CONCLUSIONS

- In alignment with existing literature, our analysis showed that the first mRNA-1273 booster was more effective than the first BNT162b2 booster in preventing COVID-19 hospitalizations in non-immunocompromised Medicare FFS beneficiaries aged ≥65 years[4,5]
- Furthermore, compared with the BNT162b2 booster, the first mRNA-1273 booster was associated with lower medium-term (up to 60 days post-discharge) Medicare expenditures for hospitalized non-immunocompromised individuals
- Given that Medicare FFS covers nearly half of adults aged ≥65 years in the United States, this is the largest comparative effectiveness analysis of mRNA-1273 and BNT162b2 boosters in the elderly population and the first one to examine differences between vaccine groups in Medicare expenditures for the elderly hospitalized with COVID-19
- While the use of secondary data sources can be impacted by confounding, measurement error, and selection bias, we employed rigorous methods to address those limitations

ADDITIONAL INFORMATION

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Acknowledgments

Medical writing and editorial assistance for this poster were provided by Alejandra De Angulo, PhD, of MEDiSTRAVA in accordance with Good Publication Practice (GPP 2022) guidelines, funded by Moderna, Inc., and under the direction of the authors. This study was funded by Moderna, Inc.

Disclosures

JZ and MB are employees of Mathematica, Inc., which was contracted by Moderna, Inc., to conduct this study. MG, TL, MAM, DE, SSL, AMR, HK, NVDV, and EB are employees of Moderna, Inc., and hold stock/stock options in the company.

Presented at the Annual Meeting for the International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 5-8, 2024; Atlanta, GA, USA