Effectiveness of Monovalent COVID-19 Booster/ Additional Vaccine Doses in the United States

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DISCLOSURES

This project was funded by the US Food and Drug Administration and performed in collaboration with BEST Initiative contributors as part of its public health mandate.

BACKGROUND

- Monovalent booster or additional doses of coronavirus disease 2019 (COVID-19) vaccines were first authorized in the United States (US) in 2021.
- Booster/additional dose authorizations and recommendations for different risk groups have varied over time and by brand.

OBJECTIVE

To evaluate the real-world effectiveness of receipt of a monovalent booster/additional dose of COVID-19 vaccine by brand (BNT162b2 [Pfizer-BioNTech], mRNA-1273 [Moderna], and JNJ-7836735 [Janssen]) compared with receiving a complete primary vaccine series without a booster dose in the US overall and by immunocompromised status, eras of viral variant predominance, and homologous/heterologous status (i.e., whether booster brand matches primary series brand (protocol posted on BEST Initiative website[1]).

METHODS

Population and Exposure Assessment

- Among individuals who received a complete primary series of a COVID-19 vaccine and were eligible to receive a booster/additional dose, individuals receiving a booster/additional dose ("boosted" individuals) and matched individuals who had not received a booster/additional dose ("comparator" individuals) were identified (Figure 1).
- Boosted individuals aged 12 to 64 years (depending on timing of brand-specific age authorizations) were identified and placed into cohorts based on the brand of the booster/additional dose.
- Comparator individuals were matched 1-to-1 to boosted individuals on calendar date, demographics, clinical characteristics, brand of primary series vaccine, and time since primary series completion (Figure 1).
- Time 0 was set at the date of receipt of the booster/additional dose for boosted individuals and the date of matching for the comparator group.

Data Source

- Optum pre-adjudicated insurance claims data linked with Immunization Information Systems (IIS) from 9 US jurisdictions.
- The study period began on 12 August 2021 (first booster/additional dose authorizations in the US) and ended on 28 February 2022 (the end of data availability in each IIS). Data were included from 11 December 2020 (first authorization of COVID-19 vaccines in the US) to identify COVID-19 vaccination history.

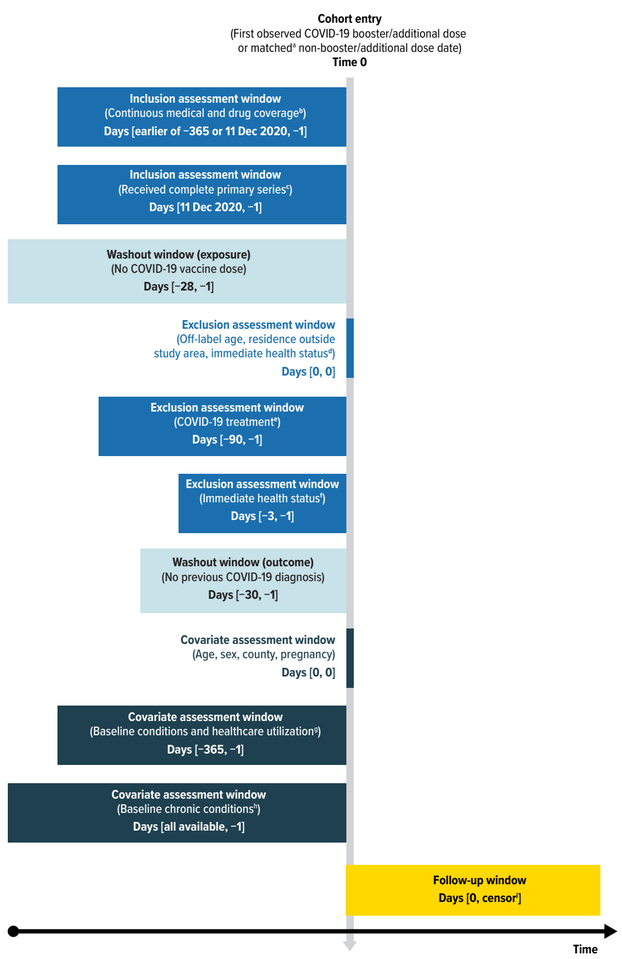
Variables

- Booster/additional COVID-19 vaccines were identified in insurance claims and linked IIS vaccination records.
- COVID-19 diagnoses were identified from claims in any medical care setting (medically diagnosed COVID-19) and separately in the hospital/emergency department (ED) setting (hospital/ED-diagnosed COVID-19).
- Covariates included demographic characteristics, indicators of booster/additional dose eligibility, comorbidities, frailty indicators, risk factors for COVID-19, and characteristics of the primary series (Figure 1).

Statistical Analyses

- In the matched cohorts, propensity score models that include prespecified demographic and clinical characteristics were used to estimate stabilized inverse probability of treatment weights.
- Weighted hazards ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models. Vaccine effectiveness (VE) was estimated as 1 minus the HR.
- Quantitative bias analysis was used to evaluate the impact of missing vaccine records. Ranges of missing vaccination records were derived from comparing the state-level vaccination rates observed in the study data with state-level estimates from the CDC, state health departments, and capture-recapture estimates.
- Analyses were performed overall and within subgroups based on vaccine brand, immunocompromised status, SARS-CoV-2 variant era (Delta [time 0 on or after 1 June 2021 with follow-up censored on 24 December 2021] and Omicron [time 0 on or after 25 December 2021 with follow-up censored at the end of data availability]), and heterologous or homologous booster.

Figure 1. Schematic for Assessing Eligibility, Covariates, and COVID-19 Outcomes Among Individuals Receiving a Booster/Additional Dose and Matched Comparators



LTC = long-term care.

[a] Matching characteristics: calendar date, age, sex, US county, immunocompromised status, influenza vaccination in previous year, condition increasing risk of severe COVID-19, brand of primary series, and time since primary series completion.

[b] Gaps in medical and pharmacy coverage < 32 days permitted.

[c] Primary series is 1 dose of JNJ-7836735 or 2 doses of BNT162b2 or mRNA-1273, with the second dose occurring on or after 17 or 24 days, respectively, and within 42 days (inclusive) of the first dose.

[d] Hospitalization or LTC residence on time 0.

[e] COVID-19 monoclonal antibodies or convalescent plasma.

[f] Fever, nausea/vomiting, rash, hospitalization, ED visit.

[g] Hospitalizations, ED visits, skilled nursing facility stay, influenza vaccination, pneumococcal vaccination, encounter for cancer screening, eye examination, colonoscopy, bone mineral density test, well-check/well-child preventive healthcare visit, arthritis, lipid abnormality, ambulance use/life support services, weakness, pregnancy completion.

[h] Autoimmune disorders, cancer, chronic kidney disease or renal disease, chronic liver disease, chronic lung diseases, dementia or other neurological conditions, diabetes mellitus, Down syndrome, heart conditions, hypertension, immunocompromised state, mental health conditions, obesity or severe obesity, sickle cell disease or thalassemia, stroke or cerebrovascular disease, tuberculosis, COVID-19 laboratory test performed, COVID-19 diagnoses occurring outside a hospital or ED setting, hospital/ED-diagnosed COVID-19, brand of the primary series, time since primary series completion.

[i] End of study period, end of continuous health plan enrollment, or receipt of any additional COVID-19 vaccination.

RESULTS

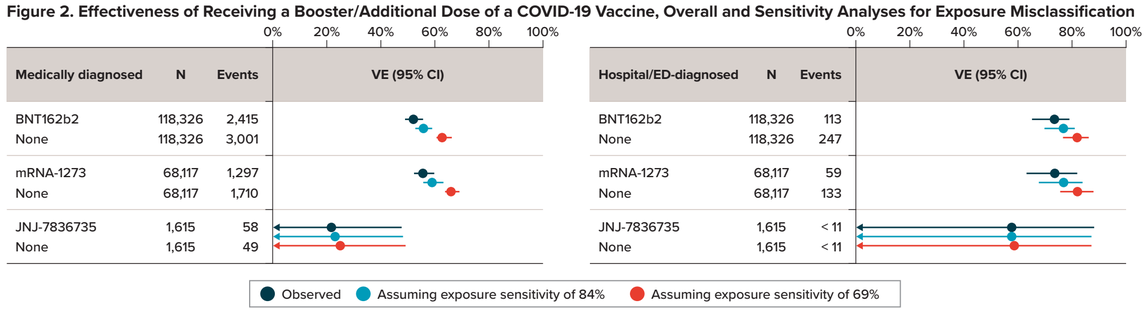
- Within each vaccine brand–specific matched cohort, all characteristics were well-balanced between exposure groups (selected characteristics shown in Table 1).
- For all vaccine brands, the boosted group had lower rates of COVID-19 compared with the unboosted group. VEs for hospital/ED-diagnosed COVID-19 were higher than for any medically diagnosed COVID-19 (Figure 2).
- Bias analyses of missing vaccine records suggest the observed VE measures may be underestimates of true VE (Figure 2).
- VE was generally lower during the Omicron era (Figure 3), and there was little difference observed by immunocompromised status (Figure 3) or homologous/heterologous booster status (Figure 4).

Table 1. Selected Characteristics of COVID-19 Booster/Additional Dose Recipients and Matched Unboosted Comparators

Characteristic	BNT162b2		mRNA-1273		JNJ-7836735	
	Boosted N = 118,326	Comparator N = 118,326	Boosted N = 68,117	Comparator N = 68,117	Boosted N = 1,615	Comparator N = 1,615
Mean age (SD)	41.45 (14.75)	41.44 (14.72)	44.71 (12.46)	44.68 (12.44)	47.85 (11.83)	47.71 (11.79)
Female sex, %	51.63%	51.63%	50.81%	50.81%	43.28%	43.28%
Mean days since primary series (SD)	228.10 (31.69)	227.75 (31.88)	232.31 (31.36)	231.99 (31.60)	232.31 (33.90)	232.14 (33.94)
Immunocompromised state, %	3.15%	3.15%	2.84%	2.84%	2.29%	2.29%
Diabetes, %	7.88%	7.72%	8.39%	9.21%	11.27%	9.10%
Hypertension, %	21.19%	21.37%	23.51%	24.68%	30.77%	29.72%
Chronic lung disease, %	12.08%	11.64%	12.02%	11.85%	12.01%	12.14%
Cancer, %	6.38%	6.22%	7.20%	6.67%	7.80%	7.24%

SD = standard deviation.

Figure 2. Effectiveness of Receiving a Booster/Additional Dose of a COVID-19 Vaccine, Overall and Sensitivity Analyses for Exposure Misclassification



Note: Counts of individuals < 11 cannot be displayed due to privacy restrictions.

Figure 3. Effectiveness of Receiving a Booster/Additional Dose of a COVID-19 Vaccine, Overall and by Subgroup

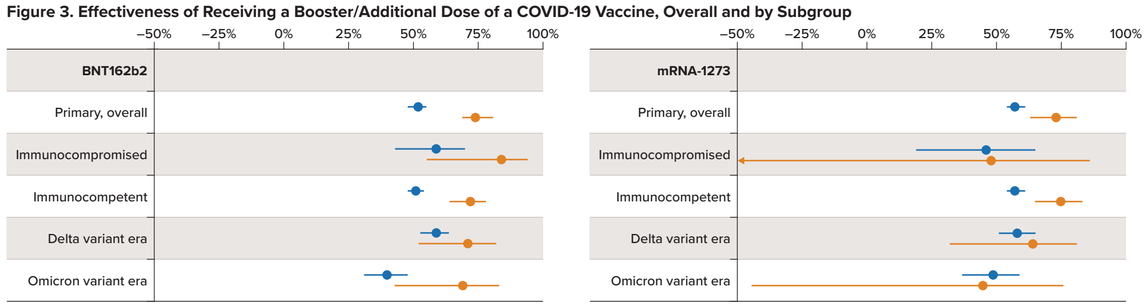
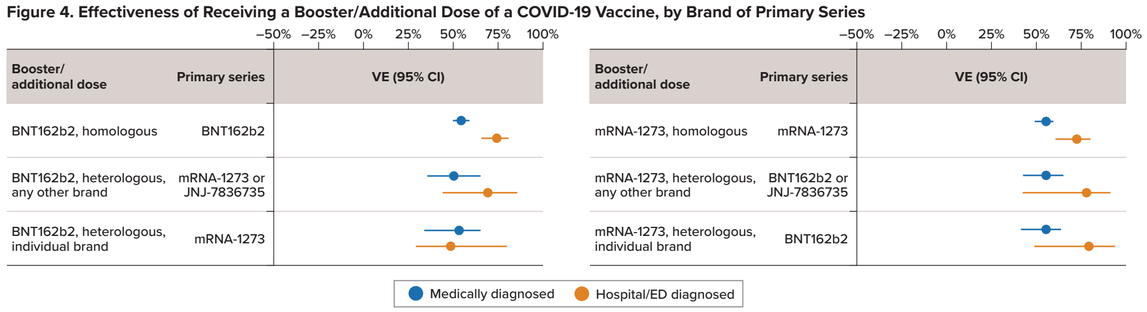


Figure 4. Effectiveness of Receiving a Booster/Additional Dose of a COVID-19 Vaccine, by Brand of Primary Series



Note: JNJ-7836735 analyses not performed due to small sample sizes.

DISCUSSION AND CONCLUSIONS

- Among those who completed a primary series, booster/additional doses were effective compared with being unboosted for all vaccine brands during all COVID-19 eras, regardless of immunocompromised status, and for both homologous and heterologous vaccine dosing, although VE varied by these subgroups.
- Due to differences in age group eligibility and timing of authorizations, brand-specific results should not be directly compared with one another.
- Updated estimates of VE are needed in individuals receiving bivalent boosters, expanded eligible age groups, newly authorized or approved vaccines, and in new eras of predominant viral variants.

REFERENCES

1. CBER Surveillance Program. FDA. 2022. https://bestinitiative.org/wp-content/uploads/2022/03/C19-VX-Effectiveness-Protocol_2022_508.pdf.

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