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Baseline Characteristics of Patients Included in a Post-Approval Safety Study of Pfizer-BioNTech Monovalent COVID-19 Vaccine in the United States: Results From an Interim Analysis

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BACKGROUND

- A post-approval safety study [EUPAS43468] is ongoing in the United States to assess the safety of the original Pfizer-BioNTech monovalent COVID-19 vaccine (BNT162b2) using data from immunization registries and 5 health insurers participating in the FDA's Sentinel System.
- An interim analysis was conducted to inform the study design of the final analysis, which will use a matched cohort design with unexposed comparators to evaluate myocarditis/pericarditis as the primary outcome.
- Descriptive results on individuals exposed to BNT162b2 and concurrent unexposed individuals from the interim analysis focusing on the myocarditis/pericarditis outcome-specific cohort are presented here.

OBJECTIVE

- To assess the distribution of baseline demographic, clinical, and healthcare use characteristics among individuals receiving BNT162b2 and concurrent, unexposed individuals in the overall population, immunocompromised (ICs) individuals, and individuals with a recorded history of COVID-19.

METHODS

Setting and Study Design

- **Data sources:** 5 research partners who participated in the Sentinel System (4 national insurers [CVS Health/Aetna, Carelon Research, Humana, and Optum] and 1 regional insurer [HealthPartners]).
- **Study period:** Receipt of BNT162b2 was assessed from 11 December 2020 to 18 April 2023 (dates of authorization of BNT162b2).
- **Study population:** Individuals aged ≥ 6 months who received a first, second, and/or third (within 60 days of second dose) primary series dose of BNT162b2 from 11 December 2020 through 18 April 2023 (exposed group) and concurrent unvaccinated individuals (unexposed group).
- **Treatment groups:** Separate exposed and unexposed groups were constructed for each dose of BNT162b2. Dose number was assigned based on the observed ordinal number of the dose, as recorded in the data sources. Individuals in the BNT162b2-exposed group were matched in a variable ratio of up to 1:2 to concurrent unexposed comparators on age, sex, US state, calendar time, and propensity score.
- **Index date:** The index date for the exposed was the date of receipt of BNT162b2 (evaluated separately for dose 1, dose 2, and dose 3) and, for the unexposed, was a randomly selected date within the same 30-day calendar-time interval as the matched exposed individual (see Figure 1).

INDIVIDUALS WERE INCLUDED IF THEY:

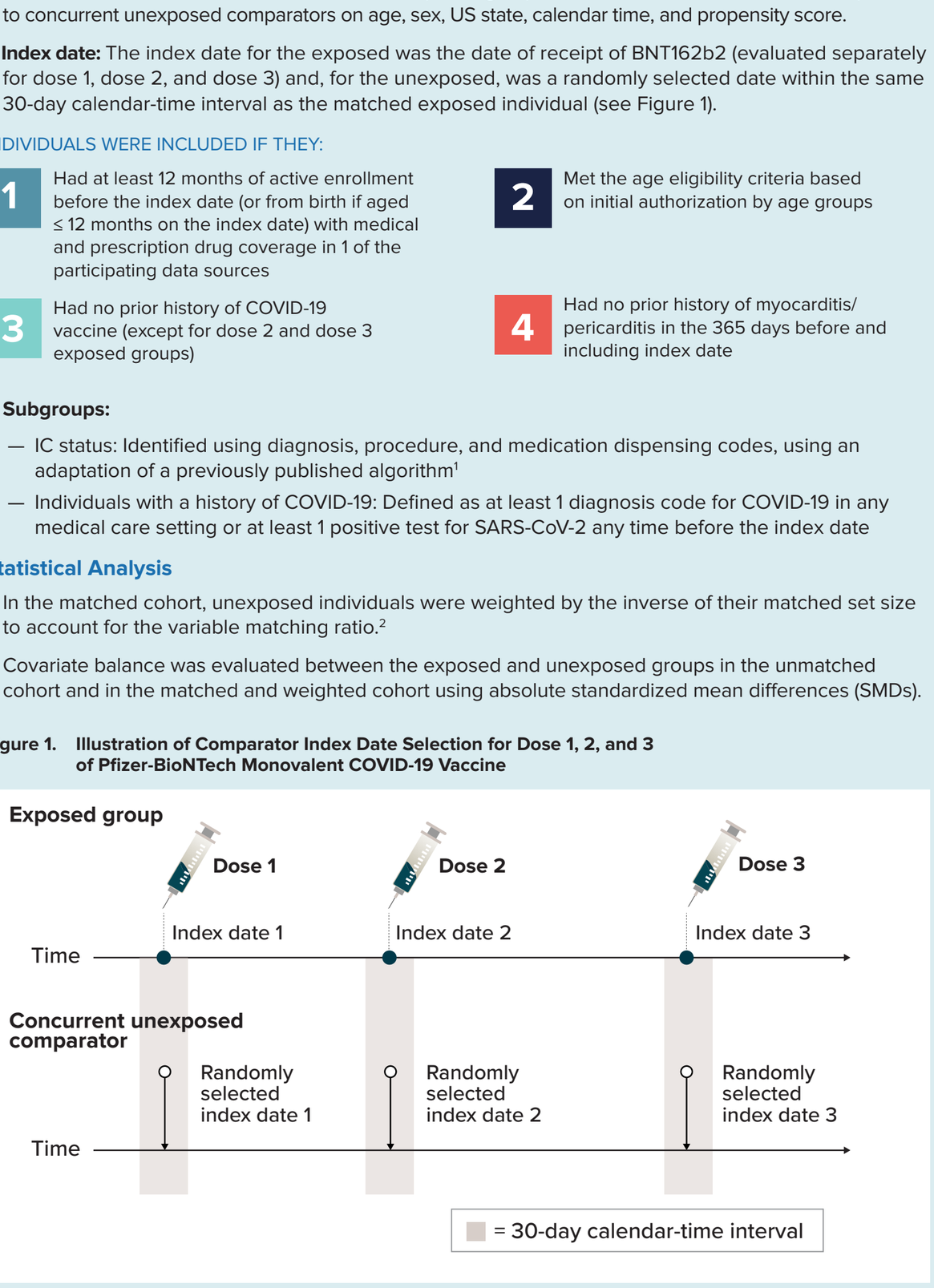
1. Had at least 12 months of active enrollment before the index date (or from birth if aged ≤ 12 months on the index date) with medical and prescription drug coverage in 1 of the participating data sources
2. Met the age eligibility criteria based on initial authorization by age groups
3. Had no prior history of COVID-19 vaccine (except for dose 2 and dose 3 exposed groups)
4. Had no prior history of myocarditis/pericarditis in the 365 days before and including index date

- **Subgroups:**
  - IC status: Identified using diagnosis, procedure, and medication dispensing codes, using an adaptation of a previously published algorithm[1]
  - Individuals with a history of COVID-19: Defined as at least 1 diagnosis code for COVID-19 in any medical care setting or at least 1 positive test for SARS-CoV-2 any time before the index date

Statistical Analysis

- In the matched cohort, unexposed individuals were weighted by the inverse of their matched set size to account for the variable matching ratio.[2]
- Covariate balance was evaluated between the exposed and unexposed groups in the unmatched cohort and in the matched and weighted cohort using absolute standardized mean differences (SMDs).

Figure 1. Illustration of Comparator Index Date Selection for Dose 1, 2, and 3 of Pfizer-BioNTech Monovalent COVID-19 Vaccine



RESULTS

Study Participants

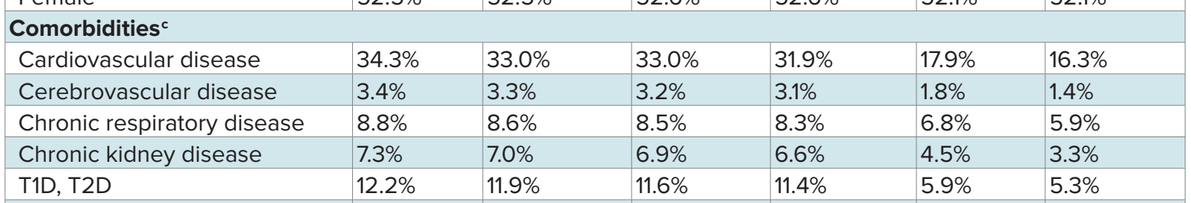


Table 1. Baseline Characteristics of Dose 1, 2, and 3 Matched and Weighted Primary Series Cohort

Characteristic	Dose 1 cohort		Dose 2 cohort		Dose 3 cohort	
	Exposed %[a,b] N = 7,196,321	Unexposed %[a] N = 7,196,321	Exposed %[a,b] N = 5,819,324	Unexposed %[a] N = 5,819,324	Exposed %[a,b] N = 32,910	Unexposed %[a] N = 32,910
Index date age (y), mean (SD)	44.7 (20.1)	44.7 (20.1)	43.7 (20.4)	43.7 (20.4)	21.7 (25.4)	21.7 (25.4)
Age group						
6-59 months	1.2%	1.2%	1.2%	1.2%	53.0%	53.0%
5-11 years	7.2%	7.2%	7.8%	7.8%	4.8%	4.8%
12-17 years	9.1%	9.1%	9.9%	9.9%	4.1%	4.1%
18-24 years	7.4%	7.4%	7.4%	7.4%	3.5%	3.5%
25-29 years	4.9%	4.9%	4.8%	4.8%	1.9%	1.9%
30-39 years	12.4%	12.4%	12.4%	12.4%	5.1%	5.1%
40-49 years	12.6%	12.6%	12.7%	12.7%	6.6%	6.6%
50-64 years	21.5%	21.5%	21.5%	21.5%	12.1%	12.1%
65-79 years	18.4%	18.4%	17.1%	17.1%	6.5%	6.5%
≥ 80 years	5.4%	5.4%	5.1%	5.1%	2.4%	2.4%
Sex						
Female	52.5%	52.5%	52.6%	52.6%	52.1%	52.1%
Comorbidities[c]						
Cardiovascular disease	34.3%	33.0%	33.0%	31.9%	17.9%	16.3%
Cerebrovascular disease	3.4%	3.3%	3.2%	3.1%	1.8%	1.4%
Chronic respiratory disease	8.8%	8.6%	8.5%	8.3%	6.8%	5.9%
Chronic kidney disease	7.3%	7.0%	6.9%	6.6%	4.5%	3.3%
T1D, T2D	12.2%	11.9%	11.6%	11.4%	5.9%	5.3%
Influenza/other resp. infections	7.8%	7.3%	7.6%	7.2%	27.3%	25.1%
History of COVID-19	9.0%	8.7%	9.4%	9.0%	15.1%	11.8%
Hypertension	29.6%	28.7%	28.5%	27.6%	14.6%	13.2%
IC on index date	15.4%	14.4%	15.0%	14.1%	15.4%	12.7%
Pregnancy status, on index date	1.5%	1.7%	1.5%	1.8%	1.3%	1.4%
Medical product use[d]						
Analgesics	22.0%	21.5%	21.4%	21.2%	12.2%	11.0%
Antibiotics	32.7%	31.2%	32.0%	30.7%	42.1%	39.7%
Antiviral medications	4.5%	4.6%	4.3%	3.7%	4.0%	2.8%
Corticosteroids	18.1%	17.0%	17.7%	16.7%	16.7%	14.8%
NSAIDs	14.4%	14.0%	14.0%	13.8%	7.8%	7.8%
Psychotropics	26.3%	24.4%	25.9%	24.2%	15.2%	13.4%
Statins	22.3%	20.3%	21.3%	19.5%	10.2%	9.7%
Other vaccines[d]						
Influenza[e]	48.6%	36.0%	48.4%	35.2%	64.6%	63.6%
Pneumococcal disease	4.2%	3.6%	4.0%	3.4%	17.7%	17.8%
DTaP[f]	7.5%	7.0%	7.5%	7.2%	30.8%	31.4%
Health service use, Intensity Metrics[d]						
HC facility visit	0.8%	0.8%	0.7%	0.8%	0.6%	0.3%
Cancer screenings	27.2%	24.6%	26.6%	24.1%	18.5%	18.3%
COVID-19 tests	17.7%	16.2%	18.1%	16.6%	21.1%	22.0%
Any HC encounter, mean (SD)	13.7 (17.9)	11.8 (17.6)	14.4 (17.8)	11.8 (17.6)	17.7 (21.0)	13.8 (20.3)
ED visits, mean (SD)	0.3 (1.1)	0.3 (1.1)	0.2 (1.0)	0.3 (1.0)	0.3 (1.1)	0.2 (0.7)
Hospitalizations, mean (SD)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.8)	0.1 (0.4)

DTaP = diphtheria, tetanus, and pertussis; ED = emergency department; HC = healthcare; NSAID = non-steroidal anti-inflammatory drug; SD = standard deviation; T1D = type 1 diabetes; T2D = type 2 diabetes; Td = tetanus and diphtheria; Tdap = tetanus, diphtheria, and pertussis.

[a] This column contains % unless the row header specifies mean and SD instead.

[b] BNT162b2 exposed.

[c] All comorbidities were assessed for 365 days before the index date, with the exception of COVID-19 history and IC status.

[d] Healthcare use, comedications, and other vaccines were assessed in the 365 days up to and including the index date, with the exception of any healthcare encounter. Number of any HC encounter, number of ED visits, and number of hospitalizations were evaluated as continuous variables.

[e] In the dose 1 and dose 2 matched cohorts, influenza vaccination was more frequently recorded in the exposed group (SMD < 0.3), indicating some residual imbalance.

[f] Includes DTaP, Td, and Tdap.

Patient Characteristics

- Before and after matching in the overall dose 1 and dose 2 cohorts, all baseline characteristics were well balanced (SMD, < 0.2), except influenza vaccination, which was more frequently recorded in the exposed group (dose 1 SMD, 0.215; dose 2 SMD, 0.226) (Table 1).
- Before matching in the dose 3 cohort, the exposed group was younger and had a lower prevalence of cardiovascular disease, hypertension, and obesity, but it had a higher prevalence of respiratory infections, receipt of other vaccines, any healthcare encounters, and COVID-19 testing than the unexposed group (Table 1). After matching, all baseline characteristics were well balanced in the overall dose 3 cohort (SMD, < 0.2).

Subgroups

- In the IC and COVID-19 history subgroups, all baseline characteristics were well balanced (SMD, < 0.2) after matching for dose 1 and dose 2 cohorts.
- In the dose 3 cohort, there were residual imbalances for rheumatologic/inflammatory conditions with corticosteroid use, which was higher in the unexposed group in the IC subgroup (SMD, 0.223), as well as for any healthcare encounter, which was higher in the exposed group in the IC subgroup (SMD, 0.333) and the COVID-19 history subgroup (SMD, 0.272).

CONCLUSIONS

- This interim analysis successfully captured a large enough number of BNT162b2-exposed individuals and matched unexposed individuals (in overall population and clinically relevant subgroups) to conduct the final comparative safety analyses.
- Compared with the dose 1 and dose 2 cohorts, the dose 3 cohort was younger, in line with the age-based authorization for a third dose in the primary series for the pediatric population.
- The balance in baseline characteristics between the exposed and unexposed groups after matching supports the use of an unexposed comparator group for the final comparative safety analyses.

Disclosures

This project was funded by Pfizer; some co-authors are employees and stockholders of Pfizer, the company that produced the vaccine being evaluated. Some co-authors are or were employed at nonprofit organizations (RTI Health Solutions, Harvard Pilgrim Health Care Institute, and HealthPartners) that conduct work for government and private organizations, including pharmaceutical companies. Some co-authors are employees of Optum and may own stock in UnitedHealth Group. Some co-authors are employees at CVS Health and may own stock in this company. One co-author was employed at CVS Health at the time of this study and is currently at Glade Oak. Some co-authors are employees at Carelon Research and may own stock in Elevance Health. Some co-authors are employees of Humana and may own stock in this company. Some co-authors are employed at StatLog.

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