Monitoring Results From a Postapproval Safety Study of Pfizer-BioNTech COVID-19 Vaccine in the United States: Vaccine Utilization and Incidence Rates of Myocarditis/Pericarditis

Alison Kawai,[1*] Candace C. Fuller,[2*] Nana Koram,[3] Anna Agan,[2] Jeffrey Brown,[2,4] Jillian Burk,[2] Bing Cai,[3] Kimberly Daniels,[5] Julia Fearrington,[2] Jessica M. Franklin,[6] Christian Hague,[2] Aziza Jamal-Allial,[5] Catherine B. Johannes,[1] Maria Kempner,[2] J. Bradley Layton,[1] Qianli Ma,[7] Xiaodan (Melody) Mai,[2] Sophie Mayer,[8] Pamala A. Pawloski,[9] Juliane Reynolds,[2] Ryan Seals,[6] Mano Selvan,[7] Samantha Smith,[2] Cheryl N. McMahill-Walraven,[10] Alicia Gilsenan,[1†] Richard Platt[2†]

*Co-lead authors †Co-senior authors

[1]RTI Health Solutions; [2]Harvard Pilgrim Health Care Institute; [3]Pfizer; [4]TriNetX; [5]Carelon Research; [6]Optum Epidemiology; [7]Humana Healthcare Research, Inc.; [8]Harvard Pilgrim Health Care Institute (formerly of RTI Health Solutions); [9]HealthPartners; [10]CVS Health

DISCLOSURES

This study was funded by Pfizer. AK, JBL, CBJ, and AG are full-time employees of RTI-HS, a unit of RTI international, an independent, nonprofit organization that conducts work for government, public, and private organizations, including pharmaceutical companies. SM was full-time employee at RTI-HS at time of content development. NK and BC are employees of Pfizer. CF, AA, JB, JF, CH, MK, XM, JR, SS, and RP are employees of Harvard Pilgrim Health Care Institute. JB is an employee of TriNetX. KD and AJA are employees of Carelon Research. CNW is an employee of CVS Health. JMF and RS are employees of Optum, and QM and MS are employees of Humana.

BACKGROUND

- A postapproval safety study of Pfizer-BioNTech coronavirus 2019 (COVID-19) vaccine (BNT162b2) [EUPAS43468] using claims and electronic health records data from 5 research partners (RPs) is underway in the United States.
- The final analysis will use a cohort design with concurrent, unexposed comparators to assess the association between BNT162b2 and predetermined safety events of interest, including myocarditis/pericarditis (m/p).
- An initial monitoring analysis was implemented in 2022 to inform the final comparative analyses.

OBJECTIVES

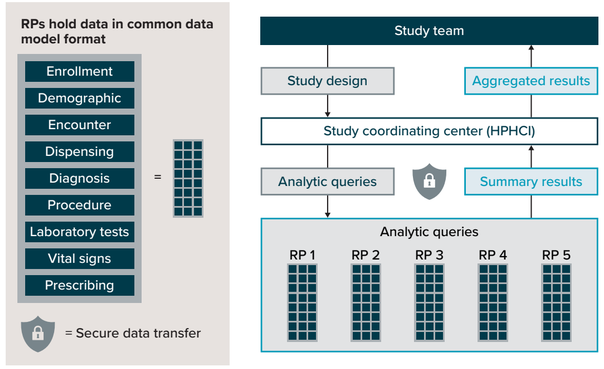
- To describe results from initial monitoring analysis on utilization of BNT162b2 and incidence rates of m/p in BNT162b2 vaccinees.

METHODS

Setting

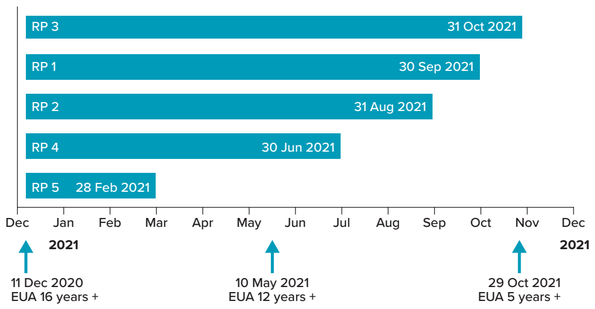
- Data sources: 5 participating RPs (4 providing claims data only and 1 providing claims and structured electronic health records data) in the Sentinel Distributed Research Network (Figure 1).

Figure 1. Distributed Data Network



HPHCI = Harvard Pilgrim Health Care Institute; RP = research partner.

Figure 2. Observation Period for Monitoring Analysis, by RP



EUA = emergency use authorization.

Note: The EUA dates in this figure refer to those for Pfizer-BioNTech monovalent COVID-19 vaccine. Query was distributed in July 2022; additional data will be available for the final analysis.

- **Study population eligibility criteria**
  - **Vaccine utilization analysis:** First- and/or second-dose recipients of BNT162b2 enrolled in a health plan associated with 1 of the participating RPs, with ≥ 365 days of prior health plan enrollment (eligibility assessed separately at each dose)
  - **Analysis of incidence rates of m/p:** In addition to the above eligibility criteria, individuals had to be aged 5 years or older and have no history of m/p in the 365 days before vaccination

Descriptive Measures

- **Vaccine utilization analysis:** Counts of first doses (dose 1 cohort) and second doses (dose 2 cohort), overall and stratified by age group, history of COVID-19 before vaccination, and immunocompromised (IC) status[a]
- **Analysis of incidence rates of m/p:** Unadjusted incidence rates of m/p 1-21 days after BNT162b2, stratified by age, sex, and dose number

Exposure and Outcome Identification

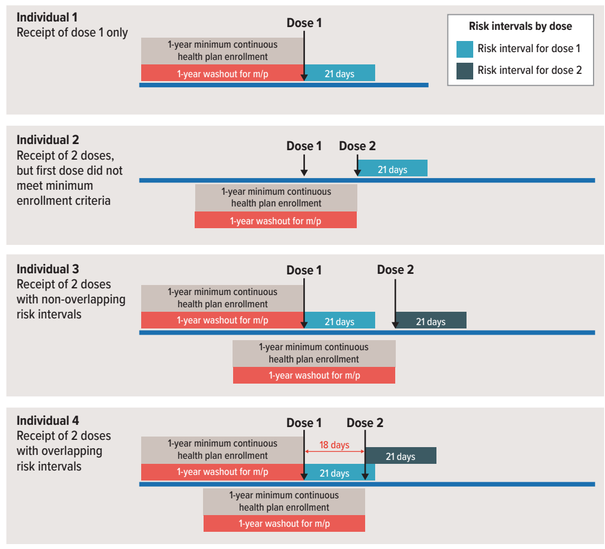
- **Exposure:** BNT162b2 was identified using Current Procedural Terminology (CPT) vaccine codes, CPT vaccine administration codes, or National Drug Codes (NDCs). Dose number was assigned based on the observed ordinal record.
- **Outcome:** M/p was identified in the 1-21 days after BNT162b2 using ICD-10-CM diagnosis codes for m/p in any medical care setting.

Other Variables to Describe BNT162b2 Vaccinees

- **IC status:** At least 1 diagnosis code in the inpatient setting or at least 2 diagnosis codes in the outpatient setting for an immunocompromising condition[a]; or at least 14 days of immunocompromising treatment[b] in the 365 days before vaccination[1]
- **History of COVID-19:** 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 vaccination
- **Age as of vaccination:** 0-4, 5-11, 12-17, 18-64, ≥ 65 years

Follow-up for M/P

Figure 3. Assessment of Incidence Rates of M/P in BNT162b2 Vaccinees by Dose Number



- Incidence was assessed independently in the risk interval (1-21 days) after dose 1 and in the risk interval (1-21 days) after dose 2. Individuals were followed from the day after vaccination until the earliest of any of the following criteria (Figure 3):
  - Occurrence of m/p, death, disenrollment from the health plan, end of data availability, 21 days after vaccination, or receipt of a COVID-19 vaccine other than BNT162b2.
- For the analysis of dose 1, if an individual received dose 2 within the risk interval after the first dose (i.e., ≤ 21 days after the first dose), the risk interval for the first dose was extended past the second dose and ended on day 21 after the first dose.

[a] Defined as HIV/AIDS, solid malignancy, bone marrow transplant, organ transplant, rheumatologic/other inflammatory condition, primary immunodeficiency, other immune conditions, chronic kidney disease/end-stage renal disease, or hematologic malignancy.

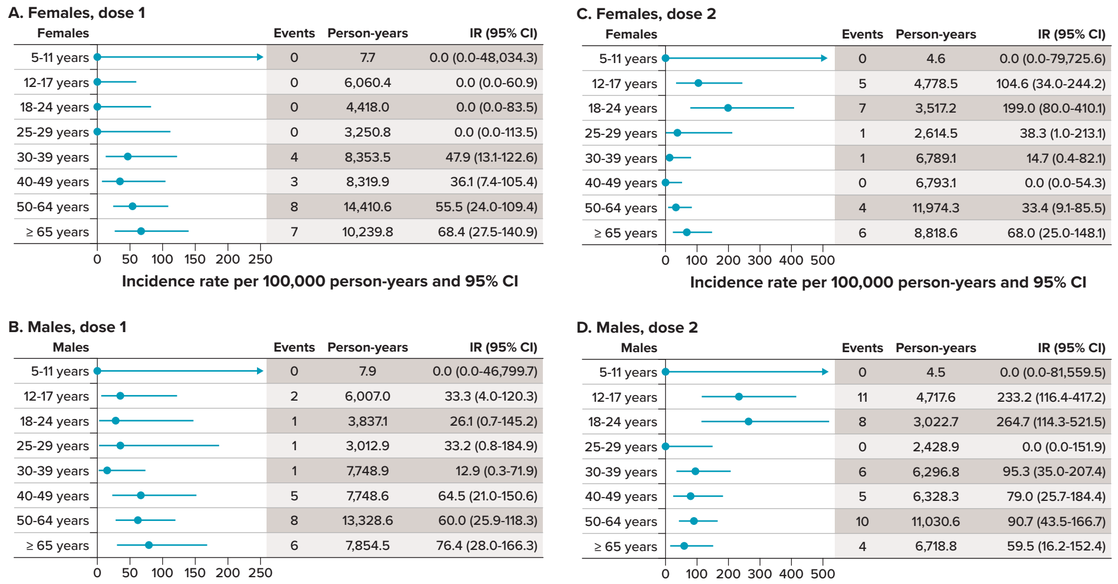
[b] Defined as use of an immunomodulator, chemotherapeutic, systemic corticosteroid (at least 60 mg/day of prednisone), or antimetabolite treatment.

RESULTS

Table 1. Counts and Proportions of Individuals in the Dose 1 and Dose 2 Cohorts by Select Characteristics

Characteristic	Dose 1 cohort	Dose 2 cohort
All eligible individuals	1,875,997 (100%)	1,542,764 (100%)
Immunocompromised individuals	380,274 (20.3%)	313,915 (20.3%)
History of COVID-19	165,158 (8.8%)	136,766 (8.9%)
By age group		
0-4 years	56 (< 0.01%)	33 (< 0.01%)
5-11 years	283 (< 0.1%)	172 (< 0.1%)
12-17 years	217,966 (11.6%)	175,872 (11.4%)
18-64 years	1,338,552 (71.4%)	1,093,431 (70.9%)
≥ 65 years	319,140 (17.0%)	273,256 (17.7%)

Figure 4. Unadjusted Incidence Rates of M/P, Stratified by Age, Sex, and Dose Number



CI = confidence interval; IR = incidence rate.

CONCLUSIONS

- The large number of BNT162b2 vaccinees will enable robust inferences for the final analyses.
- The relatively low number of doses in individuals aged ≥ 65 years reflects the age distribution of the data sources, while the low number of doses in individuals aged < 12 years is due to the timing of this analysis in relation to the authorization of BNT162b2 (in October 2021 for individuals aged 5-11 years). More doses among the youngest age groups are anticipated to be captured in the final comparative analyses.
- The highest unadjusted incidence rates of m/p per 100,000 person-years were among males aged 12-17 years who were receiving a second dose (233.2; 95% CI, 116.4-417.2) and among males aged 18-24 years who were receiving a second dose (264.7; 95% CI, 114.3-521.5).
  - Estimates of m/p incidence are consistent with those from other studies, such as the Biologics Effectiveness and Safety Initiative[2]; the observation that the highest incidence rates were in young males after dose 2 is likewise consistent with these studies.
- As the observed prevalence of IC status (a subgroup of interest in the final analyses) in BNT162b2 vaccinees was higher (20%) than that of published estimates in the general population (3% according to a study conducted by the Centers for Disease Control and Prevention),[3] consideration will be given to increase the specificity of the IC algorithm in the final analysis.

REFERENCES

1. Di Fusco M, Moran MM, Cane A, Curcio D, Khan F, Malhotra D, et al. Evaluation of COVID-19 vaccine breakthrough infections among immunocompromised patients fully vaccinated with BNT162b2. J Med Econ. 2021 Jan-Dec;24(1):1248-60. doi: 10.1080/13696998.2021.2002063
2. Wong HL, Hu M, Zhou CK, Lloyd PC, Amend KL, Beachler DC, et al. Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases. Lancet. 2022 Jun 11;399(10342):2191-9. doi: 10.1016/S0140-6736(22)00791-7
3. Harpaz R, Dahl RM, Dooling KL. Prevalence of Immunosuppression Among US Adults, 2013. JAMA. 2016 Dec 20;316(23):2547-8. doi: 10.1001/jama.2016.16477

CONTACT INFORMATION

Alicia Gilsenan, PhD, FISPE
RTI Health Solutions
agilsenan@rti.org

Candace Fuller, PhD
Harvard Pilgrim Health Care Institute
Candace_Fuller@harvardpilgrim.org

Alison Kawai, ScD
RTI Health Solutions
akawai@rti.org

Presented at: 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management; 23-27 August 2023; Halifax, Nova Scotia, Canada