

Incidence Rates of Safety Events of Interest in a Post-Approval Study of Original Pfizer-BioNTech Monovalent COVID-19 Vaccine in the United States: Primary Series Analysis

Alison Kawai,¹ Candace C. Fuller,^{1,2} Nana Koram,³ Anna A. Agan,² Jeffrey Brown,^{5,2} Jillian Burk,² Bing Cai,³ Brian Calingaert,¹ Andrea Chomistek,⁷ John G. Connolly,^{5,2} Kimberly Daniels,⁴ Katherine Dea,⁵ Andrea DeVries,⁶ Brandon Diessner,⁷ Djeneba Audrey Djibo,⁸ Steve Ezzy,⁷ Rebecca Hawrusik,² Catherine B. Johannes,^{8,9} J. Bradley Layton,¹ Shelly-Ann M. Love,⁴ Qianli Ma,⁶ Sophie E. Mayer,² Cheryl N. McMahill-Walraven,^{8,8} Erick Moyneur,⁵ Margaret B. Nolan,¹⁰ Sapna Rao,¹ Juliane S. Reynolds,² Mano Selvan,⁶ Joy Vetter,⁷ Xi Wang,⁸ Kimberly Wideman,¹ Yongming Zhao,⁸ Najat J. Ziyadeh,⁷ Richard Platt,^{1,2} Alicia Gilseman¹

¹ RTI Health Solutions, Durham, NC, United States; ² Harvard Pilgrim Health Care Institute, Boston, MA, United States; ³ Pfizer Inc., New York, NY, United States; ⁴ Celeron Research, Wilmington, DE, United States; ⁵ StatLog, Montreal, Canada; ⁶ Humana Healthcare Research, Louisville, KY, United States; ⁷ Optum, Boston, MA, United States; ⁸ CVS Health, Blue Bell, PA, United States; ⁹ RTI Health Solutions, Waltham, MA, United States; ¹⁰ HealthPartners, Bloomington, MN, United States

* Co-lead authors; † Co-senior authors; ‡ Affiliation at the time of study

BACKGROUND AND OBJECTIVE

- 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 5 health insurers participating in the FDA's Sentinel System.
- The study will use a matched cohort design to compare the incidence of 26 safety events of interest in BNT162b2 recipients to the incidence in concurrent, unexposed comparators.
- As part of an interim analysis, incidence rates (IRs) of safety events of interest were estimated in a combined population of BNT162b2 vaccinees and unvaccinated comparators.

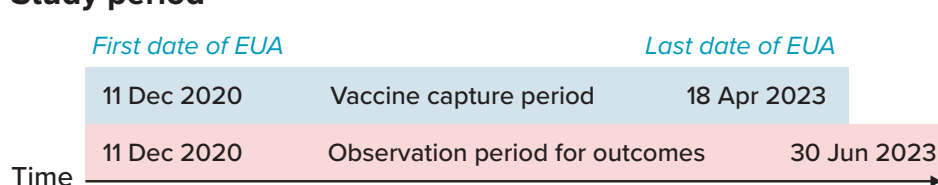
METHODS

Data Sources, Setting, and Variables

Data sources

Claims data from 5 research partners who participate in the FDA's Sentinel System (4 national insurers [CVS Health/Aetna, Celeron Research, Humana, and Optum] and 1 regional insurer [HealthPartners]), supplemented with immunization registry data (where available).

Study period

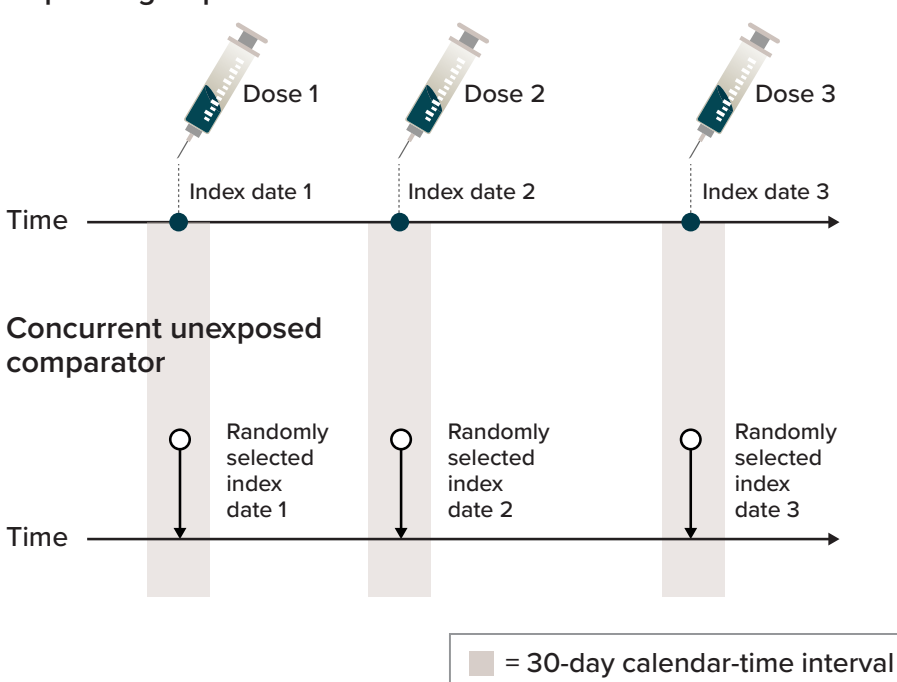


Study population

Individuals aged ≥ 6 months who received a first, second, and/or third dose (within 60 days of second dose) of BNT162b2 in a homologous series and concurrent unvaccinated individuals.

Individuals receiving an eligible dose of BNT162b2 were matched to unexposed comparators (in a variable ratio of up to 1:2) on age, sex, US state, calendar time, and propensity score.

Exposed group



Eligibility criteria (evaluated at each index date)

- Had at least 12 months of continuous medical and prescription drug coverage before the index date [or from birth, if < 12 months of age] AND
- Were enrolled from the first date they were eligible to receive the vaccine, based on age AND
- Were within the age-authorized range for vaccination.

EUA = emergency use authorization.

- Covariates:** Calendar time, demographics on the index date (age, sex, state), comorbidities, comedications, vaccines targeting infections other than SARS-CoV-2, and healthcare use.
- Subgroups**
 - Immunocompromised (IC) individuals: IC status was identified with diagnosis, procedure, and medication dispensing codes, based on an adaptation of a published algorithm.¹
 - Individuals with a history of COVID-19: Defined as having ≥ 1 diagnosis code for COVID-19 in any medical care setting or ≥ 1 positive test for SARS-CoV-2 any time before the index date.
- Safety events of interest:** Safety events of interest were selected based on outcomes included in COVID-19 vaccine safety surveillance in the FDA's Biologics Effectiveness and Safety (BEST) System and CDC's Vaccine Safety Datalink.^{2,3} Safety events of interest were assessed in pre-defined risk intervals after the index date, using diagnosis codes.
- Follow-up:** Individuals were followed from the index date until the earliest of the following: safety event of interest; end of the outcome-specific risk interval; receipt of another brand of COVID-19 vaccine, Pfizer-BioNTech bivalent vaccine, or unknown brand of COVID-19 vaccine; disenrollment from the health plan, receipt of a later dose before the recommended dosing spacing, or death.

Statistical Analysis

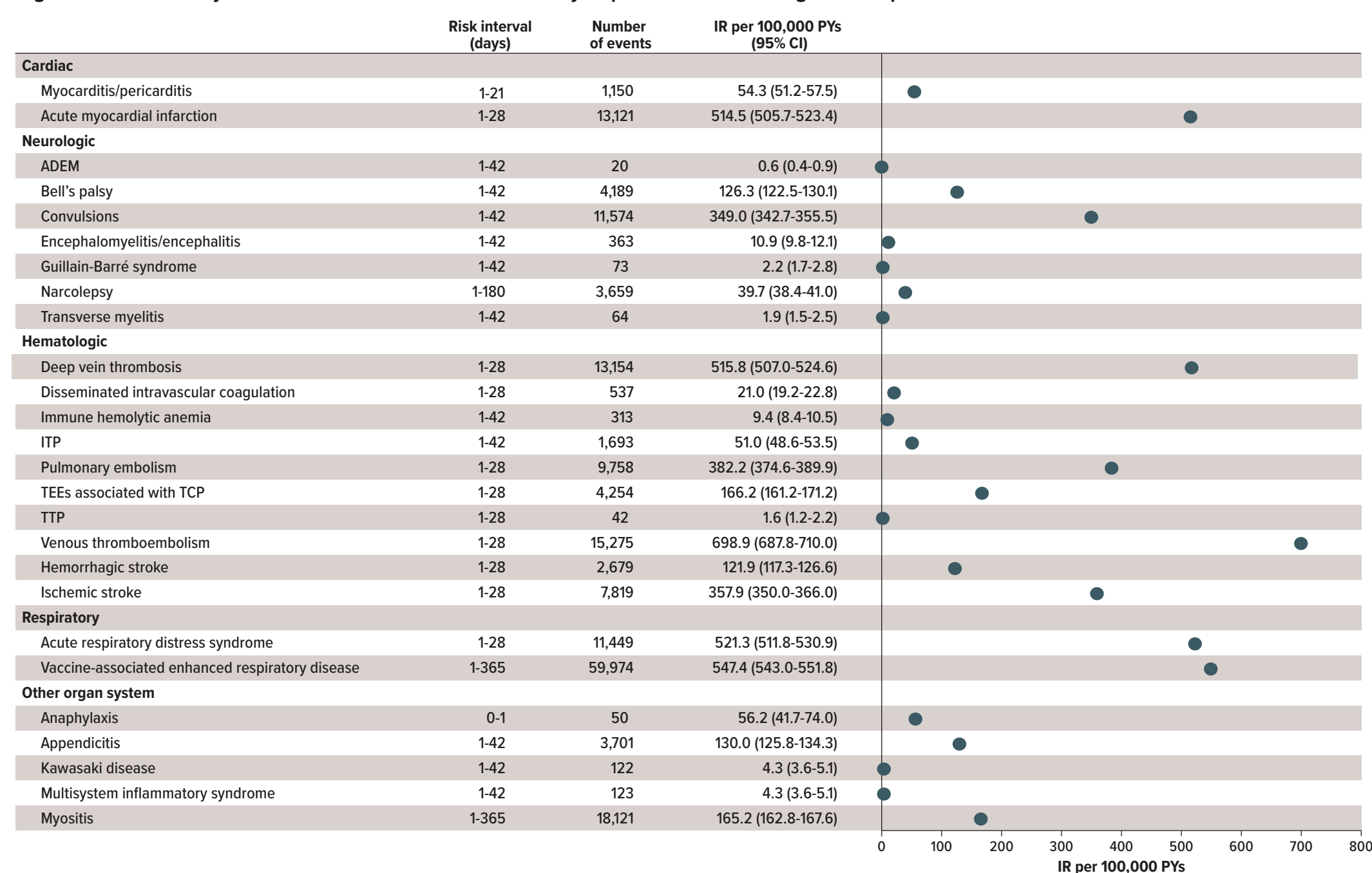
- IRs per 100,000 person-years (PYs) were estimated in the matched, overall study population by dividing the number of events by the total person-time accrued, after combining the exposed and unexposed groups across the dose 1, dose 2, and dose 3 cohorts. IRs were estimated similarly among subgroups (IC individuals and individuals with a history of COVID-19).

RESULTS

Number of Doses and Matched Comparator Episodes Eligible for the Study Population



Figure 1. IR of Safety Events of Interest in the Overall Study Population Without Regard to Exposure Status



ADEM = acute disseminated encephalomyelitis; CI = confidence interval; ITP = immune thrombocytopenia; TEE = thromboembolic event; TCP = thrombocytopenia; TTP = thrombotic thrombocytopenic purpura.

Figure 2. IR of Safety Events of Interest Among Immunocompromised Individuals and Individuals With a History of COVID-19 Without Regard to Exposure Status



DISCUSSION

- IRs of safety events of interest in this interim analysis are generally within the range of background IRs reported by the BEST Initiative, which used administrative claims data from Medicare Fee-For-Service, Blue Health Intelligence, CVS Health (Aetna), Celeron Research, MarketScan, and Optum in 2019-2020.⁴
- At least 20 events of each safety event of interest were observed in the overall study population, which suggests the ability to estimate hazards with adequate precision in the final analysis.
- However, because fewer than 20 cases of some events (ADEM, transverse myelitis, TTP, anaphylaxis) were observed in IC individuals and/or individuals with a history of COVID-19, hazard ratios (HRs) for these events will have limited precision in these subgroups in the final analysis.

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 Celeron 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.

CONCLUSIONS

The results of this interim analysis support the feasibility of evaluating each safety event of interest in the final comparative analysis, including in the overall study population and among IC individuals and individuals with a history of COVID-19. However, due to the rareness of some safety events of interest (e.g., ADEM, transverse myelitis, TTP, and anaphylaxis), HRs for these outcomes may be estimated with limited precision in subgroup analyses.

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Contact Information

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

