NON-INTERVENTIONAL/LOW-INTERVENTIONAL STUDY TYPE 1 STUDY REPORT ABSTRACT

Title: A Non-Interventional Post-Approval Safety Study of Pfizer-BioNTech BNT162b2 (original monovalent) COVID-19 Vaccine in the United States

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Name and affiliation of the main author: Alison Kawai, ScD, RTI Health Solutions

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Rationale and background: From 11 December 2020 until 18 April 2023, original monovalent Pfizer-BioNTech coronavirus disease 2019 (COVID-19) Vaccine (Comirnaty) was authorized for primary series vaccination and booster vaccination in the United States (US). Following the initial authorization, a potential increased risk of myocarditis/pericarditis was identified following receipt of the vaccine. Study C4591009 is an observational study designed to assess safety events of interest (including myocarditis and pericarditis) among recipients of original monovalent Pfizer-BioNTech COVID-19 Vaccine, using data from administrative claims and electronic health records from research partners (RPs) participating in the Sentinel System. The study also assessed pregnancy and birth outcomes. This non-interventional study was designated as a postmarketing requirement to the Food and Drug Administration (FDA) and a Category 3 commitment to the European Medicines Agency (EMA) as noted in the risk management plan.

Research question and objectives

The primary objectives were as follows.

Among the overall study population and subgroups of pregnant women, immunocompromised individuals, and individuals with a history of COVID-19:

1. In individuals aged 5 years and older: To estimate the relative risk (RR) of safety events of interest (including myocarditis/pericarditis) following receipt of a first, second, or third (if received within 2 months of the second dose) dose in a primary series[1] of original monovalent Pfizer-BioNTech COVID-19 Vaccine compared with that among individuals with no receipt of any COVID-19 vaccine

[1] Primary series vaccination was administered in a 2-dose series in individuals aged 5 years and older who were not immunocompromised, in a 3-dose series in individuals aged 5 years and older who were immunocompromised, and in a 3-dose series in individuals aged 6 months through 4 years.

2. In individuals aged 6 months through 4 years: To estimate the RR of safety events of interest (including myocarditis/pericarditis) following receipt of a first, second, or third dose in a primary series[1] of original monovalent Pfizer-BioNTech COVID-19 Vaccine compared with that among individuals with no receipt of any COVID-19 vaccine[2]

3. In individuals aged 5 years and older who have received 2 doses in a primary series[1] of original monovalent Pfizer-BioNTech COVID-19 Vaccine: To estimate the RR of safety events of interest (including myocarditis/pericarditis) following a third dose (as an additional dose in a primary series[1] or as a booster dose) of original monovalent Pfizer-BioNTech COVID-19 Vaccine received > 2 months after the second dose compared with that among individuals without a third dose of any COVID-19 vaccine[2]

Among pregnant women:

4. To estimate the birth prevalence and prevalence ratio of birth outcomes among infants born to pregnant women vaccinated with original monovalent Pfizer-BioNTech COVID-19 Vaccine compared with that among infants born to unvaccinated pregnant women.

Study design: This primary study design was a retrospective cohort design with concurrent unexposed comparators. In the general population, immunocompromised individuals, individuals with a history of COVID-19, and pregnant women, the study compared the incidence of 26 safety events of interest ("general safety events," including myocarditis/pericarditis) among those who had received a first, second, or third dose in a primary series of original monovalent Pfizer-BioNTech COVID-19 Vaccine with the incidence among those who had no record of any COVID-19 vaccine in a concurrent time period. Primary series analyses included first and second doses as well as third doses received ≤ 2 months (≤ 60 days) after the second dose.

A separate booster dose analysis of general safety events was also performed within the general population, immunocompromised individuals, individuals with a history of COVID-19, and pregnant women. Among individuals who had received 2 doses of a primary series of original monovalent Pfizer-BioNTech COVID-19 Vaccine, the incidence of general safety events among those receiving an initial booster dose of original monovalent Pfizer-BioNTech COVID-19 Vaccine was compared with the incidence among those not receiving a subsequent dose of any COVID-19 vaccine. Initial booster doses were defined as third doses received > 2 months (> 60 days) after the second dose.

In addition to assessing general safety events, the study compared the incidence of pregnancy outcomes among pregnant women exposed to original monovalent Pfizer-

[2] As specified in the statistical analysis plan, the third dose was analyzed as part of the primary series with the first and second doses if received within 2 months of the second dose; the third dose was considered a booster dose if received > 2 months after the second dose in individuals aged 6 months through 4 years and all other age groups. The rationale for this differentiation (which was applied for all age groups) was that the safety of the third dose may depend on the timing between the second and third doses.

BioNTech COVID-19 Vaccine with the incidence among pregnant women not exposed to any COVID-19 vaccine, in separate analyses for the primary series and for initial booster doses. Finally, the study compared the prevalence of birth outcomes among infants born to pregnant women who had received at least 1 dose of original monovalent Pfizer-BioNTech COVID-19 Vaccine during an exposure window of interest with that among infants born to pregnant women who had not received any COVID-19 vaccine during the same exposure window.

For safety analyses in the general population, immunocompromised individuals, and individuals with a history of COVID-19, individuals in the exposed cohorts were matched to individuals in the unexposed or comparator cohorts (in a variable ratio of up to 1:2) within data source on age, sex, US state, calendar time, and propensity score. For safety analyses in pregnant women, women in the exposed cohort were matched to the unexposed or comparator cohorts (in a ratio of 1:1) on maternal age, US geographic region, and estimated pregnancy start.

Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of general safety events and pregnancy outcomes. Modified Poisson regression was used to estimate prevalence ratios and 95% CIs of birth outcomes. Regression models were not adjusted for covariates, as confounding bias was addressed via propensity score matching (for analysis within the general population and subgroup analysis among immunocompromised individuals and individuals with a history of COVID-19) or inverse probability treatment (IPT) weighting (for analysis among pregnant women).

Setting: To be eligible for the study, exposures and comparator index dates were required to occur between 11 December 2020 (the first date of the Emergency Use Authorization [EUA] for original monovalent Pfizer-BioNTech COVID-19 Vaccine) and 18 April 2023 (the last date of the EUA for original monovalent Pfizer-BioNTech COVID-19 Vaccine).

The follow-up period for general safety events started on 11 December 2020 and ended on 18 April 2024 (1 year after the last date that original monovalent Pfizer-BioNTech COVID-19 Vaccine was authorized for use in the US). The follow-up period for pregnancy outcomes was from 12 December 2020 until 12 March 2024 (the pregnancy end date for the last eligible pregnancy), and the observation period for identifying birth outcomes was from 11 December 2020 until the last date of data available in each data source at the time of the final analysis (ranging from 04 April 2024 to 31 August 2024).

Subjects and study size, including dropouts: Safety analyses were limited to individuals who were within the ages authorized by the FDA to receive original monovalent Pfizer-BioNTech COVID-19 Vaccine. The age-based eligibility criteria were updated each time the EUA was amended to authorize younger individuals to be vaccinated.

For all safety analyses, individuals were required to be aged ≥ 6 months on the index date (i.e., date of cohort entry) and to be enrolled with continuous medical and pharmacy coverage for the longer of the following time periods: (1) from the first date that they were

eligible to receive the vaccine (based on age) until the index date or (2) from 12 months before the index date until the index date.[3]

Additional eligibility criteria were required for safety analyses in pregnant women. For all safety analyses, pregnant women were required to have an end-of-pregnancy event (i.e., live birth, stillbirth, spontaneous abortion, or ectopic pregnancy) recorded in the data sources, be aged between 12 and 55 years at the time of the end-of-pregnancy event, and have continuous health plan enrollment until the end of pregnancy.

For analyses of birth outcomes, pregnant women were also required to have a singleton live delivery that could be successfully linked to an infant and to have 30 days of continuous health plan enrollment after delivery. For analysis of major congenital malformations, ≥ 90 days of continuous enrollment from birth (or from birth until death, if the infant died before 90 days after birth) was required for linked infants. No minimum enrollment was required for linked infants for analysis of small size for gestational age.

For primary series and booster dose analyses in the general population, immunocompromised individuals, and individuals with a history of COVID-19, Table 1 and Table 2 present the numbers of individuals included in the matched, outcome-specific cohorts. Ranges are provided to summarize the cohort sizes across the outcome-specific cohorts, which were formed by excluding individuals with a history of each specific outcome before the index date.

Table 1. Number of individuals included in outcome-specific cohorts in primary series analysis in the general population, immunocompromised individuals, and individuals with a history of COVID-19

Population	Dose 1		Dose 2		Dose 3	
	Exposed (range N)	Unexposed (range N)	Exposed (range N)	Unexposed (range N)	Exposed (range N)	Unexposed (range N)
General population	6,982,505 to 7,036,223	13,316,402 to 13,431,771	5,658,225 to 5,702,994	10,727,955 to 10,821,065	31,531 to 31,752	63,049 to 63,491
Immunocompromised individuals	1,144,485 to 1,172,279	2,215,003 to 2,268,895	891,915 to 913,076	1,708,271 to 1,749,317	4,775 to 4,908	9,529 to 9,796
Individuals with a history of COVID-19	684,377 to 715,744	1,334,460 to 1,397,184	574,854 to 600,418	1,115,476 to 1,166,143	4,721 to 4,857	9,426 to 9,698

COVID-19 = coronavirus 2019.

[3] Individuals aged < 1 year as of the index date were required to be enrolled with continuous medical and pharmacy coverage from birth until the index date.

Table 2. Number of individuals included in outcome-specific cohorts in booster dose analysis in the general population, immunocompromised individuals, and individuals with a history of COVID-19

Population	Exposed cohort (range N)	Comparator cohort (range N)
General population	2,074,831 to 2,092,944	3,405,758 to 3,438,945
Immunocompromised individuals	343,398 to 351,961	543,156 to 557,061
Individuals with a history of COVID-19	246,632 to 253,267	407,339 to 417,826

COVID-19 = coronavirus 2019.

For primary series and booster dose analysis of general safety events and pregnancy outcomes among pregnant women, Table 3 and Table 4 present ranges for the numbers of pregnancies included in the matched, outcome-specific cohorts. For analysis of general safety events, the sizes of the outcome-specific cohorts varied due to excluding individuals with a history of the outcome of interest before the index date. For analysis of pregnancy outcomes, the sizes of the outcome-specific cohorts varied due to differences in the outcome-specific exposure windows, as women who were vaccinated after the exposure window for the outcome of interest were not eligible for the exposed cohort.

Table 3. Number of pregnancies included in outcome-specific cohorts for primary series analysis of general safety events and pregnancy outcomes

Outcome	Dose 1		Dose 2		Dose 3	
	Exposed (range N)	Unexposed (range N)	Exposed (range N)	Unexposed (range N)	Exposed (range N)	Unexposed (range N)
General safety events	38,738 to 38,932	38,738 to 38,932	33,897 to 34,071	33,897 to 34,071	79 to 81	79 to 81
Pregnancy outcomes	32,559 to 55,416	32,559 to 55,416	13,096 to 30,460	13,096 to 30,460	20 to 45	20 to 45

COVID-19 = coronavirus 2019.

Table 4. Number of pregnancies included in outcome-specific cohorts for booster dose analysis of general safety events and pregnancy outcomes

Outcome	Exposed (range N)	Comparator (range N)
General safety events	15,001 to 15,079	15,001 to 15,079
Pregnancy outcomes	10 to 1,944	10 to 1,944

COVID-19 = coronavirus 2019.

For analysis of birth outcomes, the number of mother-infant pairs included in each of the exposed and unexposed cohorts after matching (in a 1:1 ratio) was 13,201 for analysis of major congenital malformations and 34,683 for analysis of small size for gestational age.

Variables and data sources: This study included secondary data from 5 RPs, all of which are participants in the FDA Sentinel System. For analyses of birth outcomes, data from only 4 RPs were included, as the fifth RP did not have mother-infant linkage available.

Receipt of the monovalent Pfizer-BioNTech COVID-19 Vaccine and other monovalent COVID-19 vaccines that were authorized or approved for use in the US during the study observation period were identified in data from claims, electronic health records (where available), and immunization registry data (where available), using procedure codes, pharmacy dispensing codes, or Centers for Disease Control Vaccine Administered codes.

General safety events, pregnancy outcomes, and birth outcomes were identified in claims and electronic health records data using diagnosis codes.

The following general safety events were assessed in the general population and among subgroups of interest:

- Cardiac events: myocarditis/pericarditis and acute myocardial infarction
- Neurologic events: acute disseminated encephalomyelitis, Bell's palsy, convulsions,[4] encephalomyelitis/encephalitis, Guillain-Barré syndrome, narcolepsy, and transverse myelitis
- Hematologic events: deep vein thrombosis, disseminated intravascular coagulation, immune hemolytic anemia, immune thrombocytopenia, pulmonary embolism, thromboembolic events associated with thrombocytopenia, thrombotic thrombocytopenic purpura, venous thromboembolism, hemorrhagic stroke, and ischemic stroke

[4] Convulsions and Kawasaki disease were assessed only in individuals aged < 5 years and were not assessed in the subgroup analysis of pregnant women.

- Respiratory events: acute respiratory distress syndrome and vaccine-associated enhanced respiratory disease

- Other organ system events: anaphylaxis, appendicitis, Kawasaki disease,[4] multisystem inflammatory syndrome,[5] and myositis

Pregnancy outcomes (i.e., spontaneous abortion, stillbirth, and preterm birth) were identified in data from pregnant women. Birth outcomes (i.e., small size for gestational age and major congenital malformations) were identified in data from pregnant women and in linked infant data.

Within the general population and the subcohorts, baseline characteristics of individuals eligible for the study were identified using diagnosis and procedure codes. These characteristics were included as variables in propensity scores. Such variables included demographic characteristics (e.g., age, sex), comorbidities (e.g., diabetes, hypertension, cardiovascular disease, history of COVID-19, immunocompromised status, obesity, pregnancy status), receipt of other vaccines, and healthcare utilization.

Results

Myocarditis/pericarditis

In the primary series analysis within the general population, the HR of myocarditis/pericarditis was 1.15 (95% CI, 1.03-1.30). In subgroup analysis by age, sex, and dose number, the highest HR estimates were observed after dose 2 among males aged 12 to 17 years (HR = 12.22; 95% CI, 5.51-27.11), males aged 18 to 24 years (HR = 3.63; 95% CI, 1.94-6.80), and females aged 18 to 24 years (HR = 4.33; 95% CI, 1.65-11.40). The incidence rate (IR) of myocarditis/pericarditis after receipt of a second dose was 286.38 cases per 100,000 person-years (16.28 per 100,000 doses) in males aged 12 to 17 years, 242.82 cases per 100,000 person-years (13.84 cases per 100,000 doses) in males aged 18 to 24 years, and 101.90 cases per 100,000 person-years (5.80 cases per 100,000 doses) in females aged 18 to 24 years.

In the booster dose analysis within the general population, the HR of myocarditis/pericarditis was 1.09 (95% CI, 0.77-1.54). In subgroup analysis by age and sex, the highest HR estimates were observed among males aged 12 to 17 years (HR = 4.92; 95% CI, 1.01-24.09), 18 to 24 years (HR = 5.16; 95% CI, 1.39-19.24), and 30 to 39 years (HR = 8.22; 95% CI, 0.95-71.27). Among males, IRs of myocarditis/pericarditis following booster dose vaccination were 120.84 cases per 100,000 person-years (6.76 cases per 100,000 doses) among those aged 12 to 17 years, 249.37 cases per 100,000 person-years (13.73 cases per 100,000 doses) among those aged 18 to 24 years, and 80.38 cases per 100,000 person-years (4.42 cases per 100,000 doses) among those aged 30 to 39 years.

[5] Multisystem inflammatory syndrome was assessed in individuals aged ≥ 6 months. Additionally, multisystem inflammatory syndrome in children (MIS-C) was assessed in individuals aged < 21 years and was not assessed in the subgroup analysis of pregnant women.

In subgroup analysis among immunocompromised individuals, the HR of myocarditis/pericarditis in the primary series analysis was 0.87 (95% CI, 0.71-1.08) and in the booster dose analysis was 0.66 (95% CI, 0.33-1.31). Among individuals with a history of COVID-19, the HR in the primary series analysis was 0.85 (95% CI, 0.64-1.13) and in the booster dose analysis was 0.76 (95% CI, 0.33-1.71). In the primary series and booster dose analysis among pregnant women, no cases of myocarditis/pericarditis were observed in the exposed cohorts.

Other general safety events

General population

For analysis within the general population, Table 5 presents HRs for general safety events that were > 1.0 in the primary series and/or booster dose analysis. HR estimates for all other general safety events were ~1.0 or < 1.0 in both the primary series and booster dose analysis within the general population.

Table 5. HRs of general safety events that were > 1.0 in the primary series and/or booster dose analysis within the general population

General safety event	Primary series analysis HR (95% CI)	Booster dose analysis HR (95% CI)
Anaphylaxis	11.65 (5.51-24.65)	1.69 (0.23-12.23)
Guillain-Barré syndrome	1.19 (0.75-1.89)	0.46 (0.12-1.71)
Acute disseminated encephalomyelitis	0.92 (0.34-2.47)	1.41 (0.08-23.57)
Convulsions	0.90 (0.71-1.13)	1.14 (0.42-3.05)
Appendicitis	0.98 (0.92-1.04)	1.06 (0.90-1.24)
Kawasaki disease	0.59 (0.19-1.81)	2.00 (0.13-31.98)

CI = confidence interval; HR = hazard ratio

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Immunocompromised individuals

For subgroup analysis among immunocompromised individuals, Table 6 presents HRs for general safety events that were > 1.0 in the primary series and/or booster dose analysis. HR estimates for all other general safety events were ~ 1.0 or < 1.0 in both the primary series and booster dose analysis among immunocompromised individuals.

Table 6. HRs of general safety events that were > 1.0 in the primary series and/or booster dose analysis among immunocompromised individuals

General safety event	Primary series analysis HR (95% CI)	Booster dose analysis HR (95% CI)
Anaphylaxis	10.27 (3.52-29.95)	5.16 (0.53-50.41)
Convulsions	1.23 (0.64-2.34)	Not estimable due to zero events
Transverse myelitis	1.33 (0.55-3.26)	0.55 (0.06-5.39)
Guillain-Barré syndrome	0.31 (0.11-0.92)	1.33 (0.22-7.98)
Appendicitis	0.92 (0.79-1.06)	1.33 (0.93-1.91)

CI = confidence interval; HR = hazard ratio.

Individuals with a history of COVID-19

For subgroup analysis among individuals with a history of COVID-19, Table 7 presents HRs for general safety events that were > 1.0 in the primary series and/or booster dose analysis. HR estimates for all other general safety events were ~ 1.0 or < 1.0 in both the primary series and booster dose analysis among individuals with a history of COVID-19.

Table 7. HR of general safety events that were > 1.0 in the primary series and/or booster dose analysis among individuals with a history of COVID-19

General safety event	Primary series analysis HR (95% CI)	Booster dose analysis HR (95% CI)
Guillain-Barré syndrome	1.21 (0.43-3.43)	1.41 (0.08-23.57)
Anaphylaxis	4.67 (1.21-18.05)	Not estimable with 1 case in exposed and 0 cases in comparator
Kawasaki disease	1.33 (0.22-7.98)	Not estimable due to zero counts
Bell's palsy	0.93 (0.77-1.11)	1.33 (0.92-1.93)
Narcolepsy	0.88 (0.73-1.08)	1.42 (0.97-2.08)
Transverse myelitis	0.67 (0.18-2.46)	1.41 (0.08-23.57)

CI = confidence interval; HR = hazard ratio.

Pregnant women

In the primary series and booster dose analysis among pregnant women, no cases or few cases of several general safety events were observed. For subgroup analysis among pregnant women, Table 8 presents HRs for general safety events that were > 1.0 in the primary series and/or booster dose analysis.

Table 8. HRs of general safety events that were > 1.0 in the primary series and/or booster dose analysis among pregnant women

General safety event	Primary series analysis HR (95% CI)	Booster dose analysis HR (95% CI)
Narcolepsy	1.56 (0.55-4.40)	Not estimable with 1 event in exposed and no events in comparator
Immune thrombocytopenia	1.73 (0.83-3.59)	4.35 (0.42-44.71)
Pulmonary embolism	1.26 (0.52-3.07)	1.28 (0.12-13.84)
Myositis	1.23 (0.85-1.78)	0.50 (0.17-1.47)
Appendicitis	0.55 (0.23-1.35)	1.93 (0.21-17.76)

CI = confidence interval; HR = hazard ratio.

Age groups

In subgroup analysis by age, HR estimates for most general safety events were generally consistent across all age groups. However, some variation across age groups was observed for the following outcomes in either the primary series or booster dose analysis: acute myocardial infarction, Bell's palsy, Guillain-Barré syndrome, narcolepsy, hemorrhagic stroke, transverse myelitis, acute respiratory distress syndrome, anaphylaxis, and vaccine-associated enhanced respiratory disease. Notably, in the primary series analysis, the HR of acute myocardial infarction among individuals aged 12 to 17 years was 5.58 (95% CI, 1.12-27.79), with 6 cases in the exposed cohort. In contrast, HR estimates were < 1.0 for individuals aged 18 to 64 years (HR = 0.63; 95% CI, 0.58-0.68) and those aged ≥ 65 years (HR = 0.60; 95% CI, 0.57-0.63). HRs were inestimable for individuals aged 6 months through 4 years and 5 to 11 years due to zero counts.

Pregnancy and birth outcomes

In the primary series analysis and booster dose analysis, IPT-weighted HR estimates of spontaneous abortion, stillbirth, and preterm birth were < 1.0. The IPT-weighted prevalence ratio (PR) of major congenital malformations was 1.02 (95% CI, 0.88-1.18), and the IPT-weighted PR of small size for gestational age was 1.12 (95% CI, 1.07-1.17).

Discussion: Consistent with published observational studies, the US prescribing information, and the European Union summary of product characteristics for Comirnaty, increased risks of myocarditis/pericarditis and anaphylaxis were observed after receipt of original monovalent Pfizer-BioNTech COVID-19 Vaccine. In the primary series analysis among subgroups defined by age, sex, and dose number, the highest increased risks of myocarditis/pericarditis in the 1-21 days after vaccination were observed for dose 2 among males aged 12 to 17 years, males aged 18 to 24 years, and females aged 18 to 24 years. In the booster dose analysis, the highest HR estimates of myocarditis/pericarditis were observed among males aged 12 to 17 years, 18 to 24 years, and 30 to 39 years. Sensitivity analyses utilizing alternative risk interval definitions (1-7 days and 1-14 days) also yielded HR estimates that were > 1.0; however, the highest HR estimates were observed using the 1-7 days risk interval definition.

The increased risks of myocarditis/pericarditis and anaphylaxis should be interpreted in the context of the benefits of vaccination for prevention of SARS-CoV-2 infection. Prior observational studies have reported increased risks of myocarditis and pericarditis in association with SARS-CoV-2 infection, with the risks following SARS-CoV-2 infection greater than the risks following vaccination. Importantly, the incidence of anaphylaxis following receipt of original monovalent Pfizer-BioNTech COVID-19 Vaccine was extremely rare, equating to 3.76 cases per million doses in the primary series analysis and 0.96 cases per million doses in the booster dose analysis.

In analysis of birth outcomes, a slightly elevated prevalence of small size for gestational age was observed among infants born to pregnant women who had been exposed to original monovalent Pfizer-BioNTech COVID-19 Vaccine (PR = 1.12; 95% CI, 1.07-1.17). However, no association between original monovalent Pfizer-BioNTech COVID-19 Vaccine and small size for gestational age has been reported in prior studies that have identified this outcome

using clinical data on birthweight and gestational age, and residual confounding may have been present in this study. In the present study, small size for gestational age was identified in claims data only, using an *International Classification of Diseases, Tenth Revision* (ICD-10)-based algorithm adapted from an *International Classification of Diseases, Ninth Revision* (ICD-9)-based algorithm that was validated in another study. Although several baseline characteristics were accounted for via propensity score weighting, some confounders (e.g., race/ethnicity, socioeconomic status, prenatal care, obesity) were not available or were incompletely captured in the data sources. The increased prevalence of small size for gestational age should be interpreted within the context of these limitations, as well as the benefits of vaccination for pregnant women, as SARS-CoV-2 infection has been previously associated with increased risks of maternal morbidity and mortality from obstetric complications.

The incidences of certain general safety events were numerically higher among Pfizer-BioNTech COVID-19 Vaccine–exposed individuals in subgroup analyses among immunocompromised individuals (i.e., convulsions, transverse myelitis, Guillain-Barré syndrome, and appendicitis), individuals with a history of COVID-19 (i.e., Guillain-Barré syndrome, Kawasaki disease, Bell's palsy, narcolepsy, and transverse myelitis), pregnant women (i.e., narcolepsy, immune thrombocytopenia, pulmonary embolism, myositis, and appendicitis), and specific age groups (i.e., acute myocardial infarction, Bell's palsy, Guillain-Barré syndrome, narcolepsy, hemorrhagic stroke, transverse myelitis, acute respiratory distress syndrome, anaphylaxis, and vaccine-associated enhanced respiratory disease). However, sample sizes were limited and estimates were imprecise in many of the subgroup analyses; thus, associations with these outcomes cannot be confirmed. The results of other general safety events, pregnancy outcomes, and birth outcomes did not suggest increased risks associated with receipt of original monovalent Pfizer-BioNTech COVID-19 Vaccine.

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Names and affiliations of principal investigators: Nana Koram, PhD, MPH, Pfizer Inc.; Alison Kawai, ScD, RTI Health Solutions (RTI-HS); Candace C. Fuller, PhD, MPH, Harvard Medical School (HMS) and Harvard Pilgrim Health Care Institute (HPHCI); Bradley Layton, PhD, FISPE, RTI-HS; Alicia Gilsenan, PhD, FISPE, RTI-HS; Brian Calingaert, MS, RTI-HS; Sapna Rao, PhD, RTI-HS; Sophie E. Mayer, PhD, HMS and HPHCI; Elizabeth Bell, PhD, HMS and HPHCI; Mayura Shinde, PhD, HMS and HPHCI; Jennifer Lyons, PhD, HMS and HPHCI; Geetha Iyer, PhD, HMS and HPHCI; Richard Platt, MD, MSc, HMS and HPHCI; Audrey Djibo, PhD, CVS Health; Kimberly Daniels, PhD, MS, Carelon Research; Shelly-Ann Love, PhD, MS, Carelon Research; Margaret Nolan, MD, MS, HealthPartners Institute; Andrea DeVries, PhD, Humana; Brandon Diessner, PhD, MPH, Optum; Najat Ziyadeh, MPH, Optum

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