Vaccines and Related Biological Products Advisory Committee Meeting

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Safety Surveillance of COVID-19 Vaccines in Children and Adolescents

Vaccines and Related Biological Products Advisory Committee
June 14, 2022

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Outline

- Evaluation of Evidence for Myocarditis/Pericarditis Risk in Young Males following Second Dose of Moderna vs. Pfizer-BioNTech COVID-19 Vaccines

- FDA Biologics Effectiveness and Safety (BEST) Initiative Results: Comparative Risk of Myocarditis/Pericarditis between Moderna (mRNA-1273) versus Pfizer-BioNTech (BNT162b2) COVID-19 Vaccines in Males 18-25 Years of Age

- Safety Surveillance in Vaccine Recipients 5-17 Years of Age in FDA BEST

Evaluation of Myocarditis/Pericarditis Risk in Young Males following Second Dose of Moderna vs. Pfizer-BioNTech COVID-19 Vaccines

Comparison of myocarditis/pericarditis risk for Moderna vs Pfizer-BioNTech COVID-19 vaccines in young males post dose 2

Data through October 2021

Reports concluding lack of evidence for significant differential risk	Reports concluding higher myocarditis/pericarditis rates in Moderna COVID-19 vaccine
Passive Surveillance: 1.3x higher • US VAERS[a] (18-24 years)	**Passive Surveillance: 1.7x – 6.6x higher** • Medicines and Healthcare products Regulatory Agency (18-29 years) • European Medicines Agency (18-24 years) • Public Health Agency of Canada (18-29 years) • Public Health Ontario, Canada (18-24 years)
Active Surveillance: 1.2x higher • US FDA BEST[b] (18-25 years)	**Active Surveillance: 2.3x – 3.1x higher** • US CDC VSD[c] (18-39 years) • Denmark/Norway/Finland/Sweden (16-24 years)

Based on the available evidence, FDA did not take regulatory action on the EUA amendment for use of Moderna COVID-19 vaccine in adolescents

Sources: Results either shared with FDA under confidentiality agreements or FDA studies

[a] US Vaccine Adverse Event Reporting System ; [b] Food and Drug Administration Biologics Effectiveness and Safety System; [c] Centers for Disease Control and Prevention (CDC) Vaccine Safety Datalink

Note : Risk windows were within 7 days for all reports/publications except for European Medicines Agency (0-14 days)

Comparison of myocarditis/pericarditis risk for Moderna vs Pfizer-BioNTech COVID-19 vaccines in young males post dose 2

Data through May 2022

Reports concluding lack of evidence for significant differential risk	Reports concluding higher myocarditis/pericarditis rates in the Moderna COVID-19 vaccine
Passive Surveillance: 1.1x higher • US VAERS[a] (18-24 years)	**Passive Surveillance: 1.7x – 6.6x higher** • Medicines and Healthcare products Regulatory Agency (18-29 years) • European Medicines Agency (18-24 years) • Public Health Agency of Canada (18-29 years) • Public Health Ontario, Canada (18-24 years)
Active Surveillance: 1.3x – 1.5x higher • US FDA BEST[b] (18-25 years) • US CDC VSD[c] (18-39 years)	**Active Surveillance: 3.1x – 7.3x higher** • Denmark/Norway/Finland/Sweden (16-24 years) • Denmark (12-39 years) • United Kingdom (13-39 years) • France (12-29 years) • Italy (12-39 years)

As of May 2022, US surveillance data do not support a statistically significant higher myocarditis/pericarditis risk of Moderna COVID-19 vaccine relative to Pfizer-BioNTech COVID-19 vaccine

Sources: Per Appendix

[a] US Vaccine Adverse Event Reporting System ; [b] Food and Drug Administration Biologics Effectiveness and Safety System; [c] Centers for Disease Control and Prevention Vaccine Safety Datalink

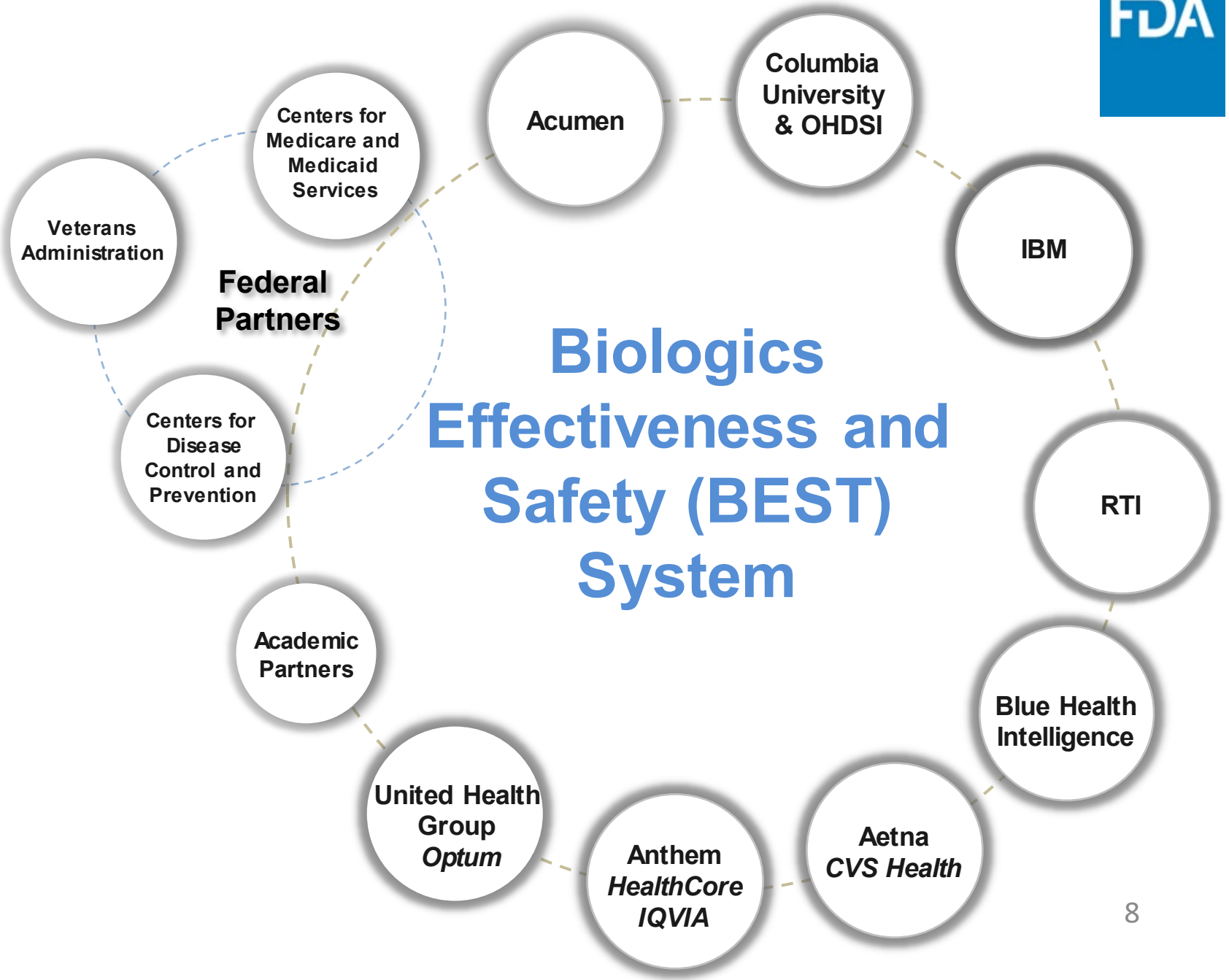
Note : Risk windows were within 7 days for all reports/publications except for except for European Medicines Agency (0-14 days) , Husby 2021(0-28 days) and Patone 2021 (1-28 days)

Summary

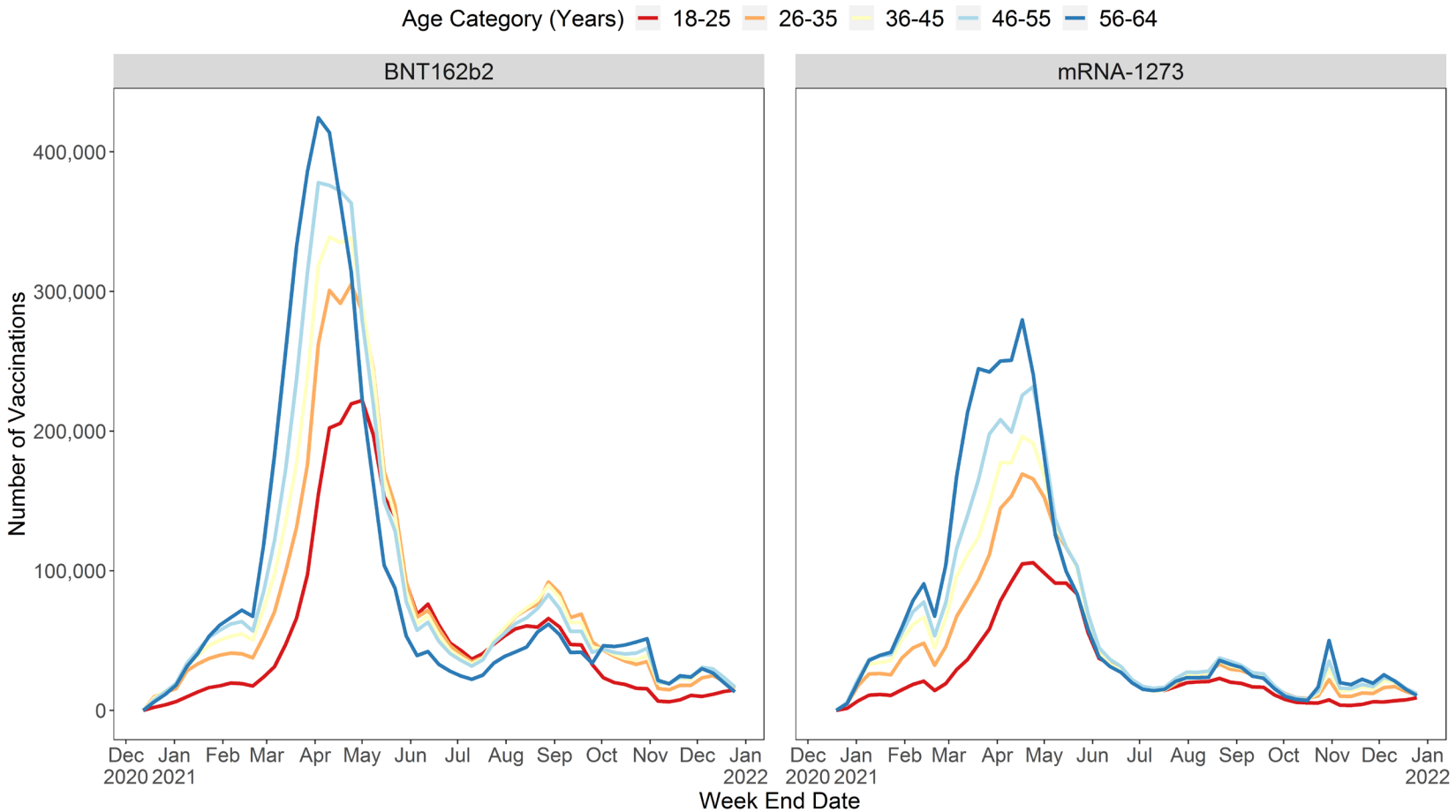
- International passive and active surveillance data sources suggest a higher myocarditis/pericarditis risk following vaccination with Moderna COVID-19 vaccine relative to Pfizer-BioNTech COVID-19 vaccine
- Based on the totality of evidence available previously, FDA did not take regulatory action on the EUA amendment for use of the Moderna COVID-19 vaccine in adolescents
- More recent evidence from US surveillance did not identify a significantly higher myocarditis/pericarditis risk in the Moderna COVID-19 vaccine recipients compared to Pfizer-BioNTech COVID-19 vaccine recipients among males 18-25 years of age post-dose 2
- Results may be limited by: small case counts, lack of adjustments for confounders, self-reported data

FDA BEST Results:
Comparative Risk of Myocarditis/Pericarditis between Moderna (mRNA-1273) versus Pfizer-BioNTech (BNT162b2) COVID-19 Vaccines in Males 18-25 Years of Age

FDA CBER Active Surveillance Program Collaborative



mRNA COVID-19 Vaccine Doses* in FDA BEST Claims Data Sources, 18-64 years

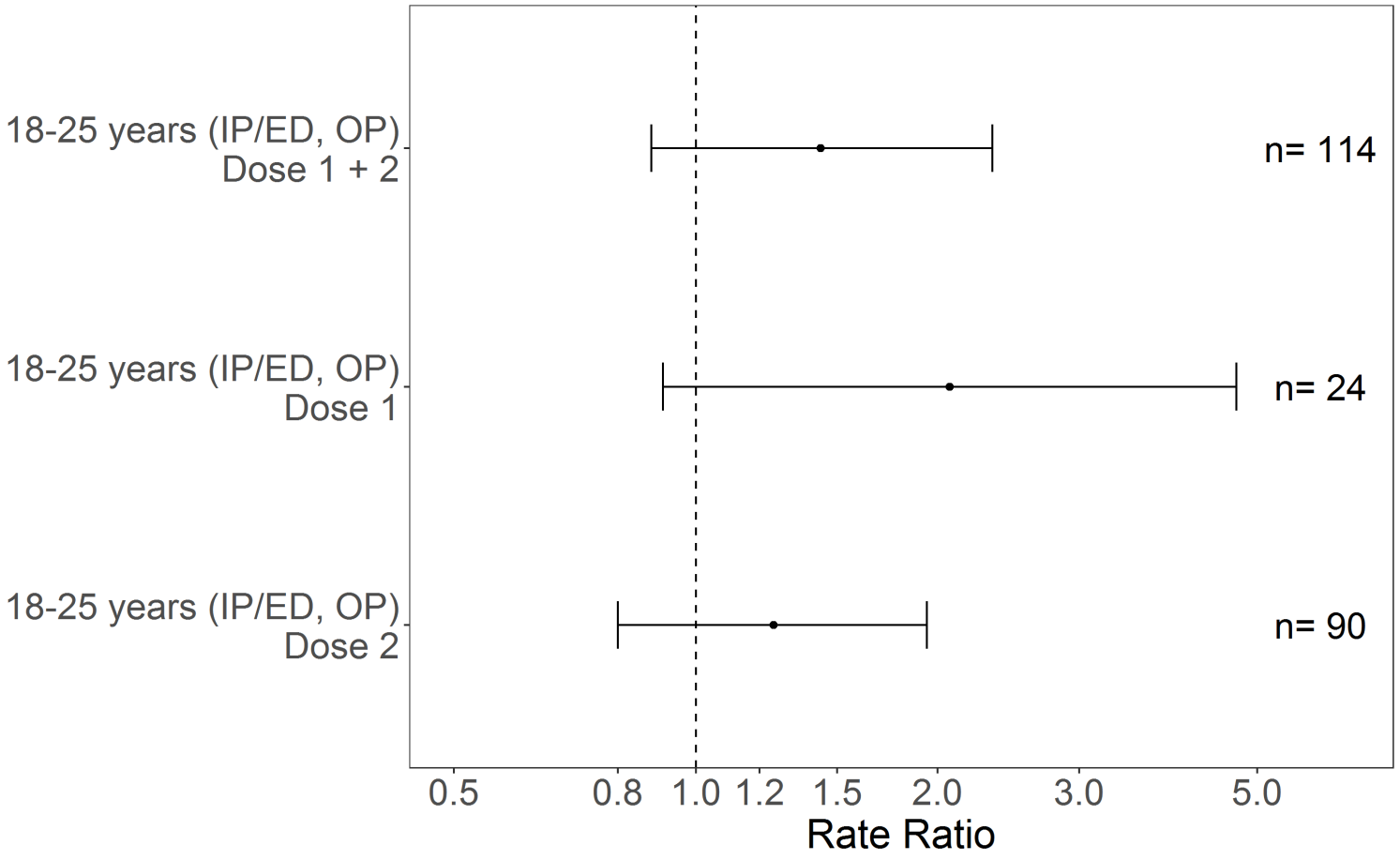


Total Doses

Pfizer-BioNTech	Moderna
16,912,716	10,631,554

*Dose 1, Dose 2, and other doses. Vaccine counts for recent dates may be underestimated due to data delay
Data cutoff date: Data Partner 1 (9/30/2021), Data Partner 2 (10/31/2021), Data Partner 3 (11/4/2021), Data Partner 4 (12/25/2021)

Direct comparisons of myocarditis/pericarditis risk within 7 days of receipt of Moderna versus Pfizer-BioNTech COVID-19 vaccines among males 18-25 years of age, by dose



Source: Wong HL, Hu M, Zhou CK 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;399:2191-2199.
Rate ratios adjusted for age, age by vaccine brand interaction, study week of vaccination, COVID-19 diagnosis prior to vaccination, urban/rural residency

Limitations

- Chart review for events are on-going
  - Interim positive predictive values were estimated
- Partial adjustment for potential confounders
  - Cannot rule out biased estimates
- Large uncertainty incidence rate ratios
  - Small number of events, wide confidence intervals

Summary

- FDA BEST study results **did not** identify a significantly higher myocarditis/pericarditis risk following vaccination with dose 2 of Moderna COVID-19 vaccine compared to Pfizer-BioNTech COVID-19 vaccine among males 18-25 years of age

- Results were compatible with a **20%-lower to 94%-higher** myocarditis/pericarditis rates in Moderna COVID-19 vaccine recipients compared to Pfizer-BioNTech COVID-19 vaccine recipients

Safety Surveillance in Vaccine Recipients 5-17 Years of Age in FDA BEST

Pediatric Data Sources in FDA BEST

- Data Sources
  - Administrative Claims Databases*
  - Immunization Information System**
- Enrollment and Vaccine Counts

Age group, year	Patients covered, million	Total Vaccines Doses, million
5-11	4.7	2.0
12-15	3.1	2.2
16-17	1.6	1.8
Total	**9.4**	**5.4**

*CVS Health (data through 2/28/2022), Optum, (data through 4/30/2022), HealthCore; (data through 3/1/2022)** 23 jurisdictions

Pre-specified Adverse Events of Interest

These potential adverse events of special interest have not been associated with COVID-19 vaccines based on pre-authorization studies

Descriptive monitoring Only

- Guillain-Barré syndrome
- Multisystem inflammatory syndrome in children
- Transverse myelitis
- Unusual site (cerebral and abdominal) thrombosis with thrombocytopenia
- Kawasaki disease
- Hemorrhagic stroke
- Acute myocardial infarction

Sequential Testing

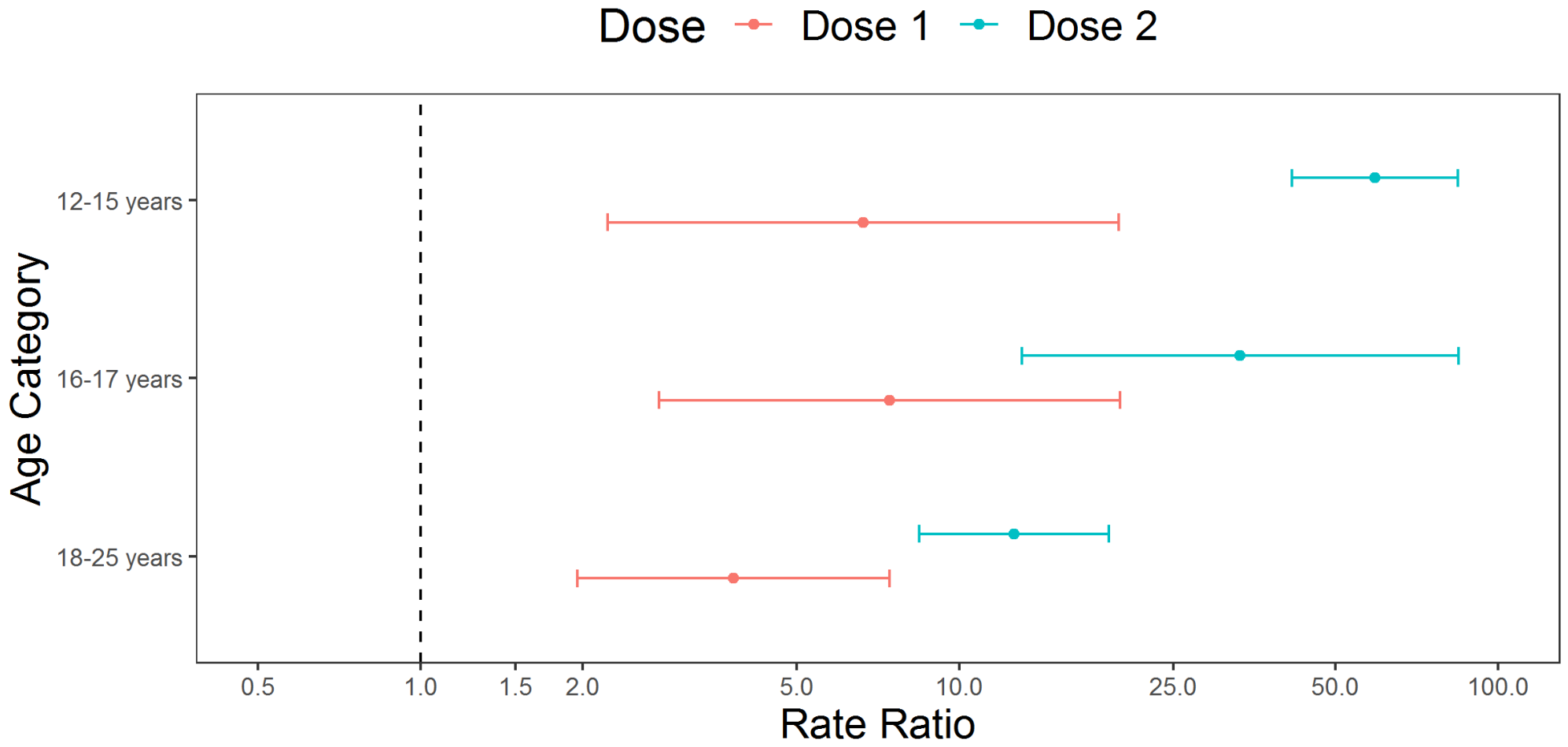
- Bell's Palsy
- Anaphylaxis
- Encephalitis / myelitis / encephalomyelitis
- Narcolepsy
- Appendicitis
- Non-hemorrhagic stroke
- Myocarditis/pericarditis
- Deep vein thrombosis
- Pulmonary embolism
- Disseminated intravascular coagulation
- Immune thrombocytopenia
- Common site thrombosis with thrombocytopenia
- Seizures/convulsions

Sequential Testing Results for Primary Series & Third/Booster Doses in 5-17 years of age, FDA BEST System

AESI	Ages 5-11	Ages 12-15	Ages 16-17
Anaphylaxis	No signal	No signal	No signal
Appendicitis	No signal	No signal	No signal
Bell's palsy	No signal	No signal	No signal
Common thromboses with thrombocytopenia	No signal	No signal	No signal
Deep vein thrombosis	No signal	No signal	No signal
Disseminated intravascular coagulation	No signal	No signal	No signal
Encephalitis / myelitis / encephalomyelitis	No signal	No signal	No signal
Immune thrombocytopenia	No signal	No signal	No signal
Myocarditis/Pericarditis	No signal	Primary Series Signal[1,2,3]	Primary Series Signal[1,2,3]
Narcolepsy	No signal	No signal	No signal
Seizures/convulsions*	No Signal	No signal	No signal
Non-hemorrhagic stroke	No signal	No signal	No signal
Pulmonary embolism	No signal	No signal	No signal

[1] In Optum (SAF data through 4/30)
[2] In HCI (data through 3/1/2022)
[3] In CVS (data through 2/28/2022)
*Analyses for seizures/convulsions have not been conducted in Optum

Observed/Expected Rate Ratio of Myocarditis/Pericarditis Risk after Receipt of Pfizer-BioNTech COVID-19 vaccine in Males 12-25 years of age, by dose



Note: Observed rates adjusted for observation delay estimated from historical data. Expected rates adjusted for age and sex where background rates permit.
O/E rate ratios : the rate of observed events divided by the rate of expected events. 95% exact Poisson confidence intervals are calculated.

Summary

- Myocarditis/Pericarditis was identified as a safety signal in vaccine recipients 12 – 15 years of age and 16 – 17 years of age following dose 1 and 2
- Myocarditis/pericarditis did not signal in 5 – 11 years old vaccine recipients
- No other safety signals were identified in any of the three age groups or for booster analyses

Conclusions

Conclusions

- FDA BEST study results did not identify a significantly higher myocarditis/pericarditis risk in the recipients of Moderna COVID-19 vaccine compared to Pfizer-BioNTech COVID-19 vaccine among males 18-25 years of age post-Dose 2
- Myocarditis/Pericarditis signaled for vaccine recipients 12-17 years of age, post-dose 1 and 2; no other signals were identified
- FDA continues to monitor myocarditis/pericarditis risk and the safety of COVID-19 vaccines in the pediatric population

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- Xinyi Ng, Marisabel Rodriguez, Whitney Steele

www.bestinitiative.org

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