Safety Monitoring of COVID-19 Vaccines
FDA BEST Initiative

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Disclaimer

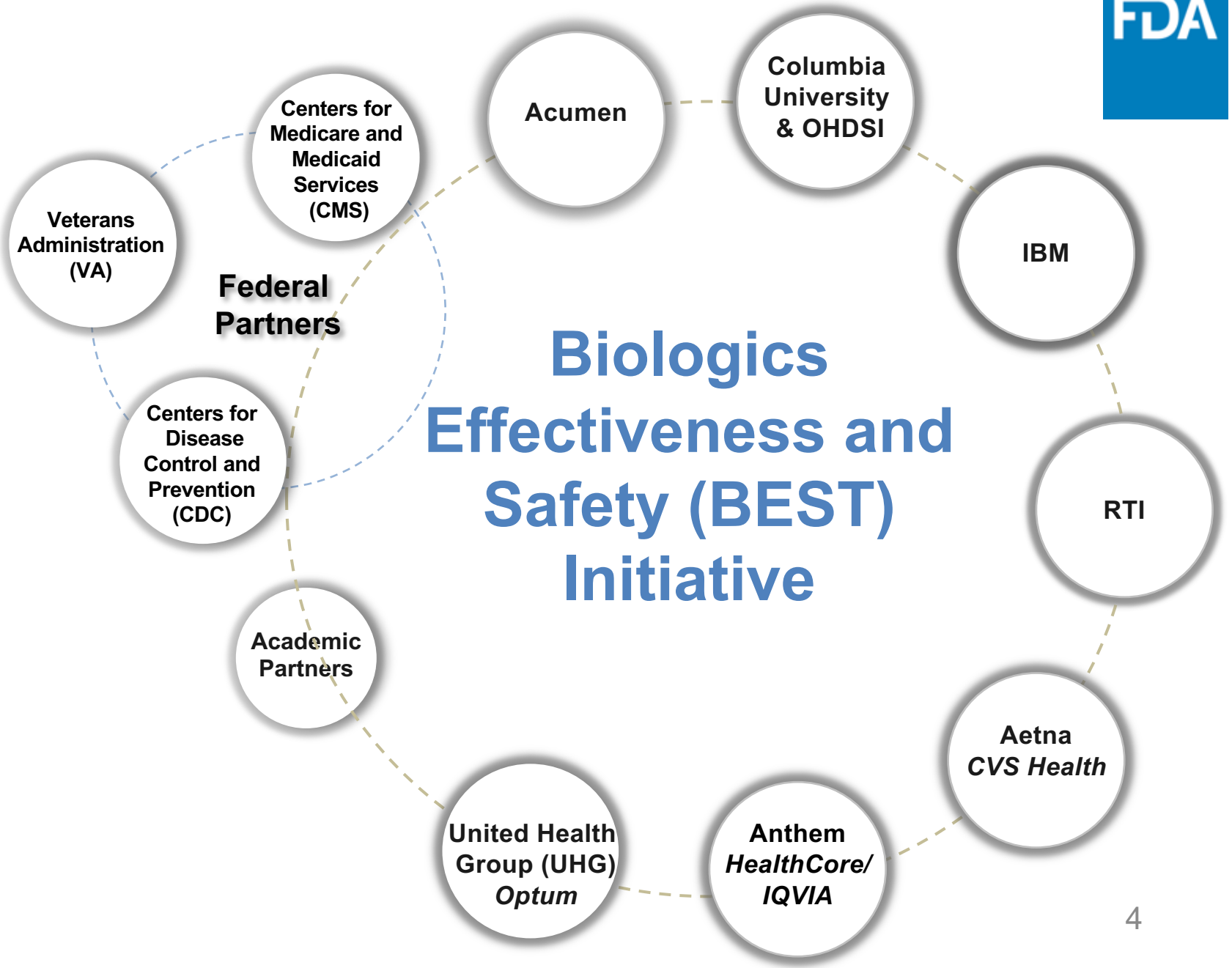
This presentation reflects the views of the authors and should not be construed to represent views or policies of the U.S. Food and Drug Administration.

CBER Regulated Products

- Vaccines (preventative and therapeutic)
- Blood (components and derived)
- Human Tissues and Cellular Products
- Gene Therapies
- Xenotransplantation Products

Center for Biologics Evaluation and Research (CBER) regulates biologic products[3]

FDA CBER Active Surveillance Program Collaborative

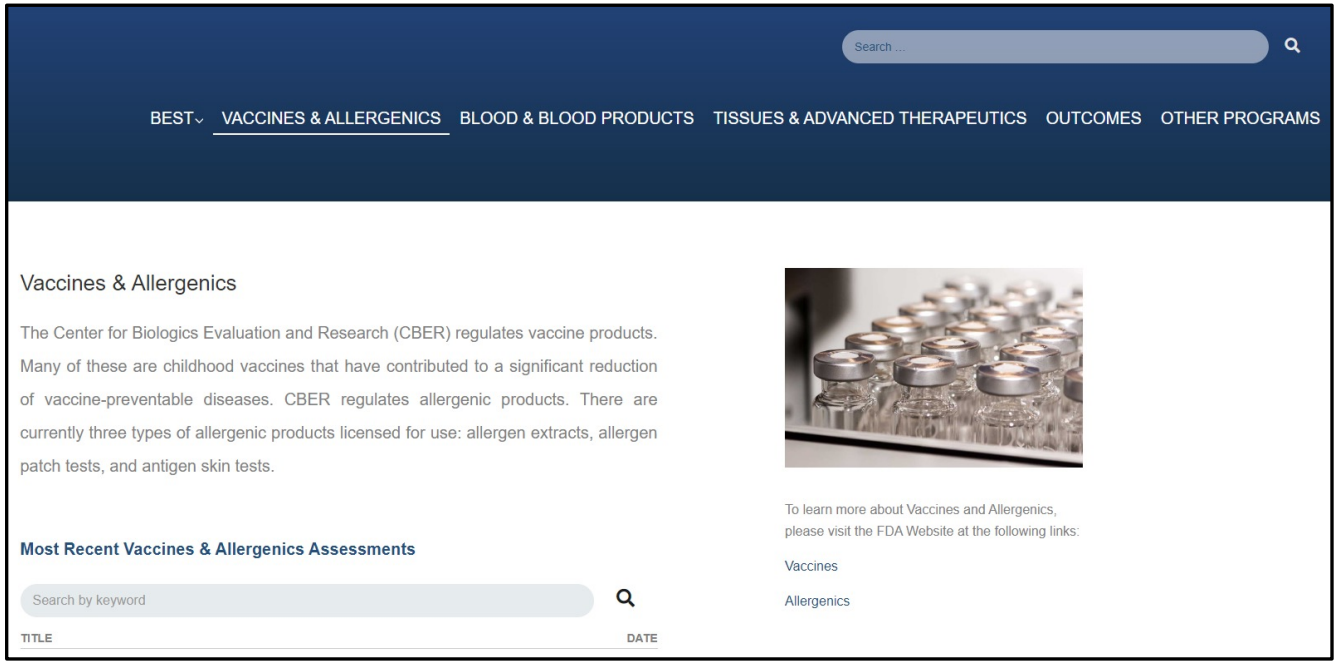


BEST Data Sources

BEST Initiative Data Source*	Database Type	No. Patients Covered (Millions)	Time Period Covered
CMS – Medicare	Claims	105	2005 - present
MarketScan Commercial and Medicare Supplemental	Claims	254	1999 - 2019
MarketScan Medicaid	Claims	48	1999 - 2019
Blue Health Intelligence	Claims	33.6	2012 - present
Optum – Adjudicated	Claims	66	1993 - present
Optum – Pre adjudicated	Claims	22	2017 - present
HealthCore	Claims	76	2006 - present
CVS Health	Claims	26	2014 - present
OneFlorida Clinical Research Consortium – Medicaid	Claims	6.7	2012 - present
OneFlorida Clinical Research Consortium – EHR	EHR	5.6	2012 – present
Optum EHR	EHR	102	2007 - 2020
MedStar Health Research Institute	EHR	6.0	2009 - present
PEDSnet	EHR	6.2	2009 - present
IBM CED	Linked EHR Claims	5.4	2000 - present
Optum Integrated Claims – EHR	Linked EHR Claims	25	2007 - 2020
OneFlorida Clinical Research Consortium – Linked EHR Claims	Linked EHR Claims	1.5	2012 - present

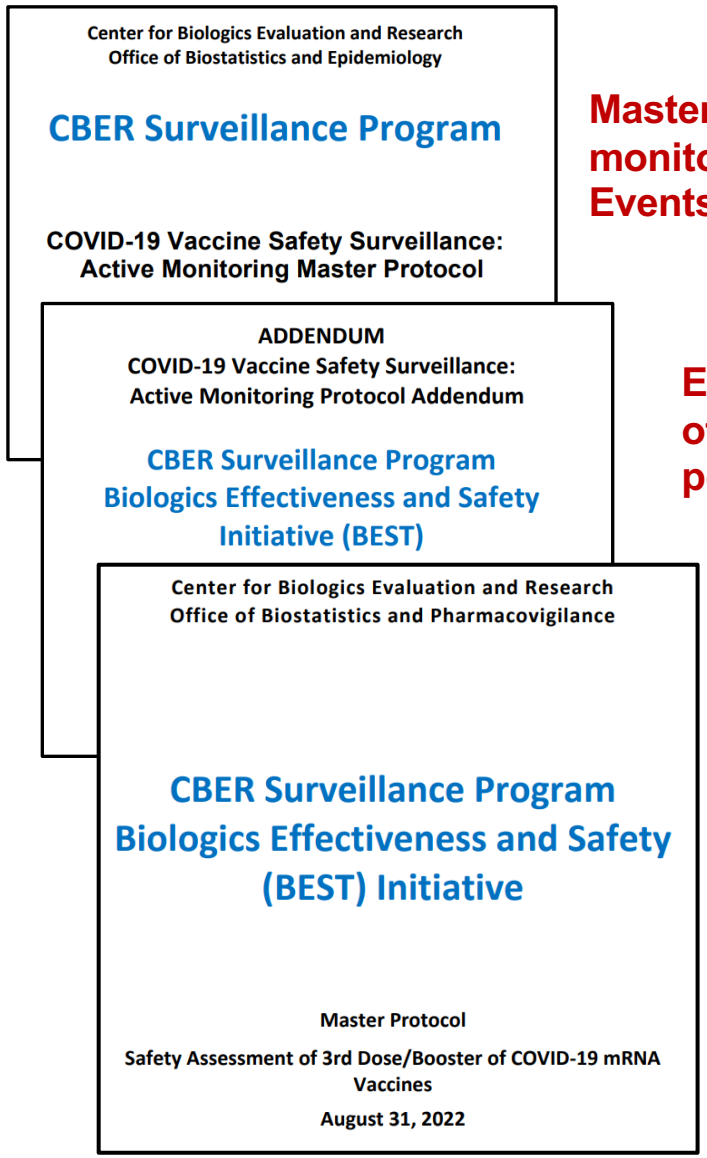
*Data lag varies for different databases from a few days to a few months.

COVID-19 Vaccines Safety Signal Detection



https://bestinitiative.org/vaccines-and-allergenics

BEST Program website provides the active monitoring master protocol and related addendums.



Master Protocol for monitoring Adverse Events (AEs)

Expands monitoring of AEs to pediatric population

Protocol for the 3rd dose/Booster study of COVID-19 mRNA vaccines

COVID-19 Vaccine Safety Monitoring

- **FDA-CMS Medicare**
  - >92% of US elderly use Medicare
  - Data cover very large population of >50 million US beneficiaries ≥ 65 years of age
  - Consists of claims data with access to medical charts

- **FDA Biologics Effectiveness and Safety (BEST) Initiative**
  - Use of commercial claims data for vaccine safety:
    - 3 major partners: Optum, CVS Health, HealthCore
  - Data includes individuals aged 0 – 64 years
  - Emphasis on detection of rare vaccine AEs (<1/100,000 doses)

COVID-19 Vaccine Safety Monitoring

List of Potential Adverse Events*

Adults
Acute Myocardial Infarction (AMI)
Anaphylaxis
Appendicitis
Disseminated Intravascular Coagulation (DIC)
Deep Vein Thrombosis (DVT)
Bell's Palsy
Encephalomyelitis/Encephalitis
Guillain-Barré Syndrome (GBS)
Hemorrhagic Stroke
Myocarditis/Pericarditis
Narcolepsy
Non-hemorrhagic Stroke (NHS)
Pulmonary Embolism (PE)
Transverse Myelitis
Immune Thrombocytopenia (ITP)
Thrombosis with Thrombocytopenia Syndrome (TTS) (unusual, common site)

Pediatrics	
Acute Myocardial Infarction (AMI)	Seizures
Anaphylaxis	Kawasaki Disease
Appendicitis	Multisystem Inflammatory Syndrome in children (MIS-C)
Disseminated Intravascular Coagulation (DIC)	
Deep Vein Thrombosis (DVT)	
Bell's Palsy	
Encephalomyelitis/Encephalitis	
Guillain-Barré Syndrome (GBS)	
Hemorrhagic Stroke	
Myocarditis/Pericarditis	
Narcolepsy	
Non-hemorrhagic Stroke (NHS)	
Pulmonary Embolism (PE)	
Transverse Myelitis	
Immune Thrombocytopenia (ITP)	
Thrombosis with Thrombocytopenia Syndrome (TTS) (unusual, common site)	

* These AESIs have not been associated with COVID-19 vaccines based on available pre-licensure evidence.

COVID-19 Vaccine Safety Monitoring

Signal detection and/or Rapid Cycle Analysis (RCA)

- Primary series RCA (Medicare ≥ 65 years); initiation date: **Feb 2021**
- Primary series RCA (12-64 years); initiation date: **Jun 2021**
- Primary series pediatric RCA (6 month-17 years); initiation date: **Jun 2022**
- Monovalent Booster Analysis (Medicare ≥ 65 years); initiation date: **Mar 2022**
- Monovalent Booster Analysis (18-64 years); initiation date: **Jun 2022**
- Bivalent Booster RCA; initiation date: **Nov 2022**

COVID-19 Vaccine Safety Monitoring

Signal evaluation and/or fully adjusted studies

- Vascular outcomes, primary series, self-controlled design; completion date: **Aug 2022**
- Myocarditis/pericarditis; completion date: **Dec 2021**
- Monovalent Booster Self-Controlled Case Series (SCCS); *In progress*

COVID-19 Vaccine Safety Studies

Key outcomes and communication

Vascular outcomes (RCA)[1]

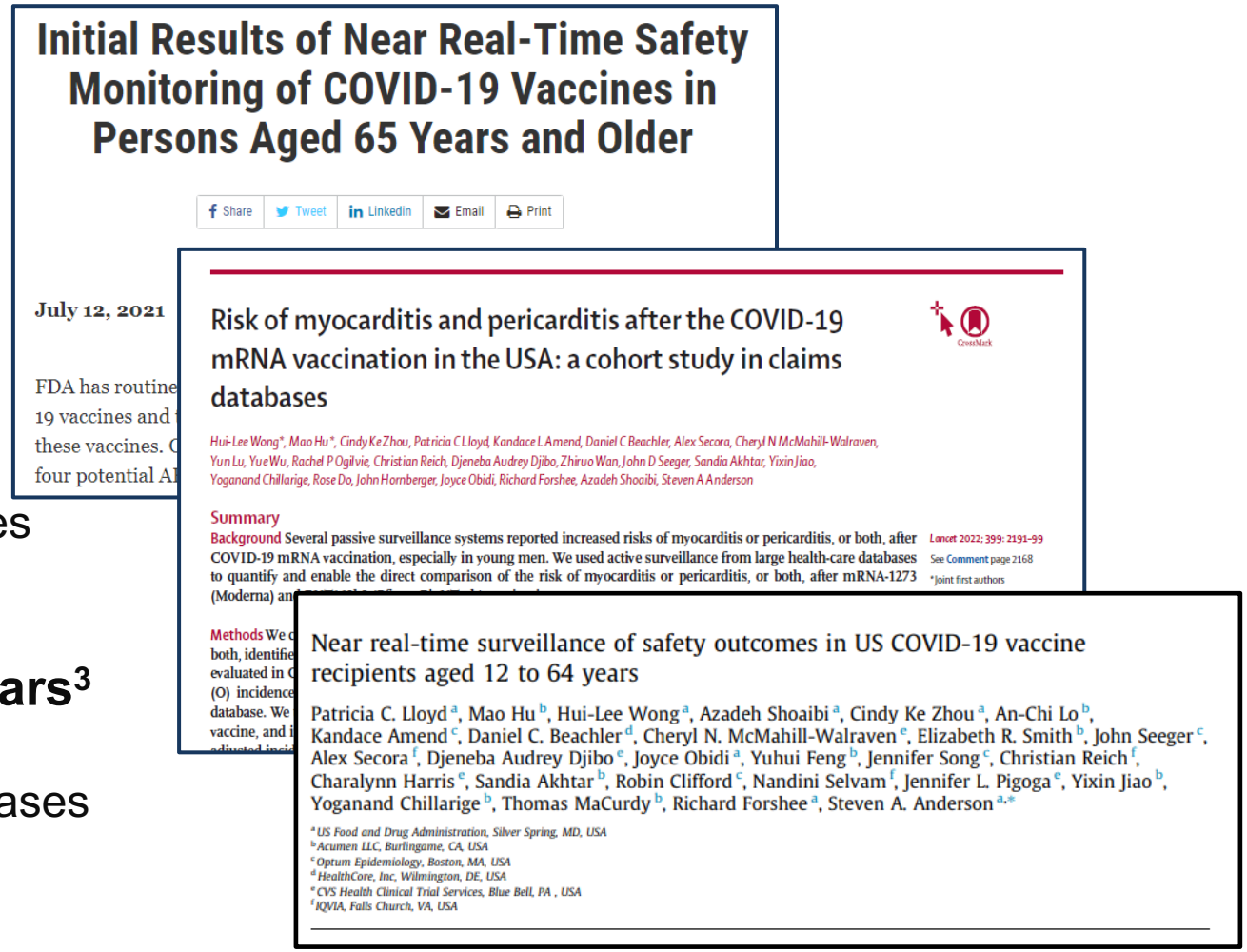
- Four potential AESIs detected
- Adults 65 years and older
- Post-vaccination with Pfizer-BioNTech COVID-19 vaccines
- FDA safety communication – **Jul 2021**

Myocarditis/Pericarditis[2]

- Potential signal in young, male adults
- Post-vaccination with mRNA COVID-19 vaccines
- Study completion – **Dec 2021**

RCA in adolescents and adults aged 12-64 years[3]

- 17 outcomes monitored in 3 databases
- Myocarditis/pericarditis signaled in 2 of 3 databases
- Anaphylaxis signaled in all databases
- Study completion – **Apr 2022**



Initial Results of Near Real-Time Safety Monitoring of COVID-19 Vaccines in Persons Aged 65 Years and Older

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July 12, 2021

FDA has routine
19 vaccines and
these vaccines.
four potential A

Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases

Hui-Lee Wong*, Mao Hu*, Cindy Ke Zhou, Patricia C Lloyd, Kandace L Amend, Daniel C Beachler, Alex Secora, Cheryl N McMahill-Walraven, Yun Lu, Yue Wu, Rachel P Ogilvie, Christian Reich, Djeneba Audrey Djibo, Zhiruo Wan, John D Seeger, Sandia Akhtar, Yixin Jiao, Yoganand Chillarige, Rose Do, John Hornberger, Joyce Obidi, Richard Forshee, Azadeh Shoaibi, Steven A Anderson

Summary

Background Several passive surveillance systems reported increased risks of myocarditis or pericarditis, or both, after COVID-19 mRNA vaccination, especially in young men. We used active surveillance from large health-care databases to quantify and enable the direct comparison of the risk of myocarditis or pericarditis, or both, after mRNA-1273 (Moderna) an

Lancet 2022; 399: 2191–99

See Comment page 2168

*Joint first authors

Methods We
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Near real-time surveillance of safety outcomes in US COVID-19 vaccine recipients aged 12 to 64 years

Patricia C. Lloyd [a], Mao Hu [b], Hui-Lee Wong [a], Azadeh Shoaibi [a], Cindy Ke Zhou [a], An-Chi Lo [b], Kandace Amend [c], Daniel C. Beachler [d], Cheryl N. McMahill-Walraven [e], Elizabeth R. Smith [b], John Seeger [c], Alex Secora [f], Djeneba Audrey Djibo [e], Joyce Obidi [a], Yuhui Feng [b], Jennifer Song [c], Christian Reich [f], Charalynn Harris [e], Sandia Akhtar [b], Robin Clifford [c], Nandini Selvam [f], Jennifer L. Pigoga [e], Yixin Jiao [b], Yoganand Chillarige [b], Thomas MaCurdy [b], Richard Forshee [a], Steven A. Anderson [a,*]

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[d] HealthCore, Inc, Wilmington, DE, USA
[e] CVS Health Clinical Trial Services, Blue Bell, PA , USA
[f] IQVIA, Falls Church, VA, USA

1. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/initial-results-near-real-time-safety-monitoring-covid-19-vaccines-persons-aged-65-years-and-older
2. Wong, Hui-Lee et al., Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases. The Lancet, Volume 399, Issue 10342, 2191 – 2199
3. Lloyd PC, Hu M, Wong HL, Shoaibi A, Ke Zhou C, Lo AC, Amend K, Beachler DC, McMahill-Walraven CN, Smith ER, Seeger J, Secora A, Audrey Djibo D, Obidi J, Feng Y, Song J, Reich C, Harris C, Akhtar S, Clifford R, Selvam N, Pigoga JL, Jiao Y, Chillarige Y, MaCurdy T, Forshee R, Anderson SA. Near real-time surveillance of safety outcomes in US COVID-19 vaccine recipients aged 12 to 64 years. Vaccine. 2022 Sep 27:S0264-410X(22)01167-7. doi: 10.1016/j.vaccine.2022.09.060. Epub ahead of print. PMID: 36195472; PMCID: PMC9513329.

Thank you

Website: https://bestinitiative.org/
Email: fdabest@fda.hhs.gov