Post-licensure safety monitoring of respiratory syncytial virus (RSV) vaccines in adults aged ≥60 years

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On behalf of the Immunization Safety Office, CDC

Advisory Committee on Immunization Practices (ACIP)
February 29, 2024

Topics

- Background
- CDC vaccine safety monitoring for RSV vaccines in adults aged ≥60 years
  - V-safe
  - Vaccine Adverse Event Reporting System (VAERS) (co-managed with FDA)
  - Vaccine Safety Datalink (VSD)
- Summary

Background

- In May 2023, the U.S. Food and Drug Administration licensed two RSV vaccines with approvals for use in adults aged ≥60 years
  - GSK RSV vaccine (trade name Arexvy)*
  - Pfizer RSV vaccine (trade name Abrysvo)†
- In June 2023, the Advisory Committee on Immunization Practices (ACIP) voted to recommend that adults aged ≥60 years may receive a single dose of an RSV vaccine using shared clinical decision-making‡

* Package Insert - AREXVY (fda.gov)

† Package Insert - ABRYSVO (STN 125769/26) (fda.gov); Abrysvo was also authorized on August 21, 2023, for use in pregnant people to prevent lower respiratory tract disease caused by RSV in infants from birth through six months of age.

‡ Melgar et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. MMWR Morb Mortal Wkly Rep. 2023;72(29):793-801.

Background, cont.

- The most common reactions in prelicensure studies among adults aged ≥60 years receiving RSV vaccine were:
  - GSK (Arexvy)[*] RSV vaccine: pain at the injection site (61%), fatigue (34%), and myalgia (29%)
  - Pfizer (Abrysvo)[†] RSV vaccine: fatigue (16%), headache (13%), and pain at the injection site (11%)
- In prelicensure studies[‡] of Pfizer (Abrysvo) RSV vaccine among 20,255 vaccine recipients aged ≥60 years, 2 cases of Guillain-Barré syndrome (GBS) were observed within 42 days of vaccination
- In prelicensure studies[‡,¶] of GSK (Arexvy) RSV vaccine among 18,304 vaccine recipients aged ≥60 years, 1 case of GBS was observed within 42 days of vaccination

[*] Package Insert - AREXVY (fda.gov)

[†] Package Insert - ABRYSVO (STN 125769/26) (fda.gov)

[‡] Melgar et al. Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023. MMWR Morb Mortal Wkly Rep. 2023;72(29):793-801

[¶] Gerber S. ACIP presentation slides, October 25, 2023 (1 - GSK RSV - ACIP Core Presentation_CO (cdc.gov))

Background, cont.

- Clinical trials generally are too small to assess risk for rare adverse events
- Due to the small number of GBS cases and size of the prelicensure studies, it is not known at this time whether these GBS cases or other neuroinflammatory events occurred due to random chance, or whether RSV vaccination might increase the risk of these events
- Post-licensure safety monitoring* of the RSV vaccines is currently ongoing in:
  - V-safe
  - Vaccine Adverse Reporting System (VAERS)†
  - Vaccine Safety Datalink (VSD)
  - Non-CDC systems

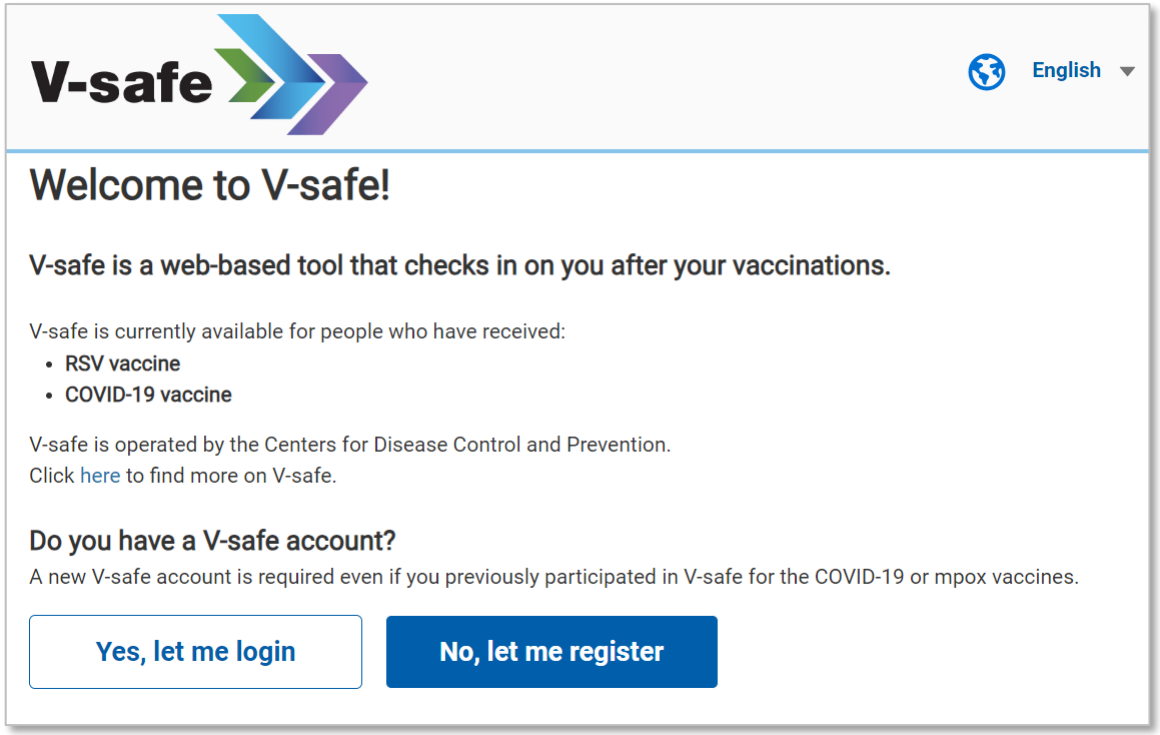
* Vaccine Safety Monitoring | Vaccine Safety | CDC

† Clinical Immunization Safety Assessment (CISA) Project contributing expertise to VAERS report reviews

V-safe

New version of V-safe is now available

- System requires both previous and new users to create an account
- Includes both email and text messaging functionality
- Vaccines currently monitored:
  - RSV vaccines for older adults and pregnant persons
  - COVID-19 vaccines for persons aged 6 months and older



V-safe sends health surveys after vaccination

- After vaccinations, surveys are sent daily during the first week, then weekly through 6 weeks
- Daily surveys solicit adverse events and health impacts after vaccination
  - Local reactions (e.g., pain, redness, swelling)
  - Systemic reactions (e.g., fatigue, headache, muscle pain)
  - Health impacts (e.g., unable to perform normal daily activities, missed school or work, or received medical care)
  - Additional questions for persons who reported immunocompromise at vaccination
- Weekly surveys solicit new symptoms or conditions after vaccination
- Participants reporting medically attended health impacts are encouraged to complete a VAERS report

Demographic characteristics of adults aged ≥60 years who reported RSV vaccination*

Characteristic	Vaccine manufacturer (%)			
	GSK (Arexvy) N=6,227	Pfizer (Abrysvo) N=3,746	Manuf not known N=5,772	Total N=15,745
Female sex assigned at birth	59.5	58.0	61.1	59.7
Median age (min, max), years	70 (60, 93)	70 (60, 94)	70 (60, 94)	70 (60, 94)
Ethnicity				
Hispanic, Latino, or Spanish	2.7	3.8	3.0	3.1
Race				
American Indian or Alaska Native	0.2	0.2	0.3	0.3
Asian	2.9	2.7	2.2	2.6
Black or African American	4.4	7.2	4.6	5.2
Native Hawaiian or Pacific Islander	0.2	0.1	0.1	0.1
White	89.2	85.9	88.7	88.2
Other	0.7	1.2	1.0	1.0
Unknown/prefer not to answer	1.0	1.4	1.5	1.3
Multiracial	1.3	1.2	1.6	1.4

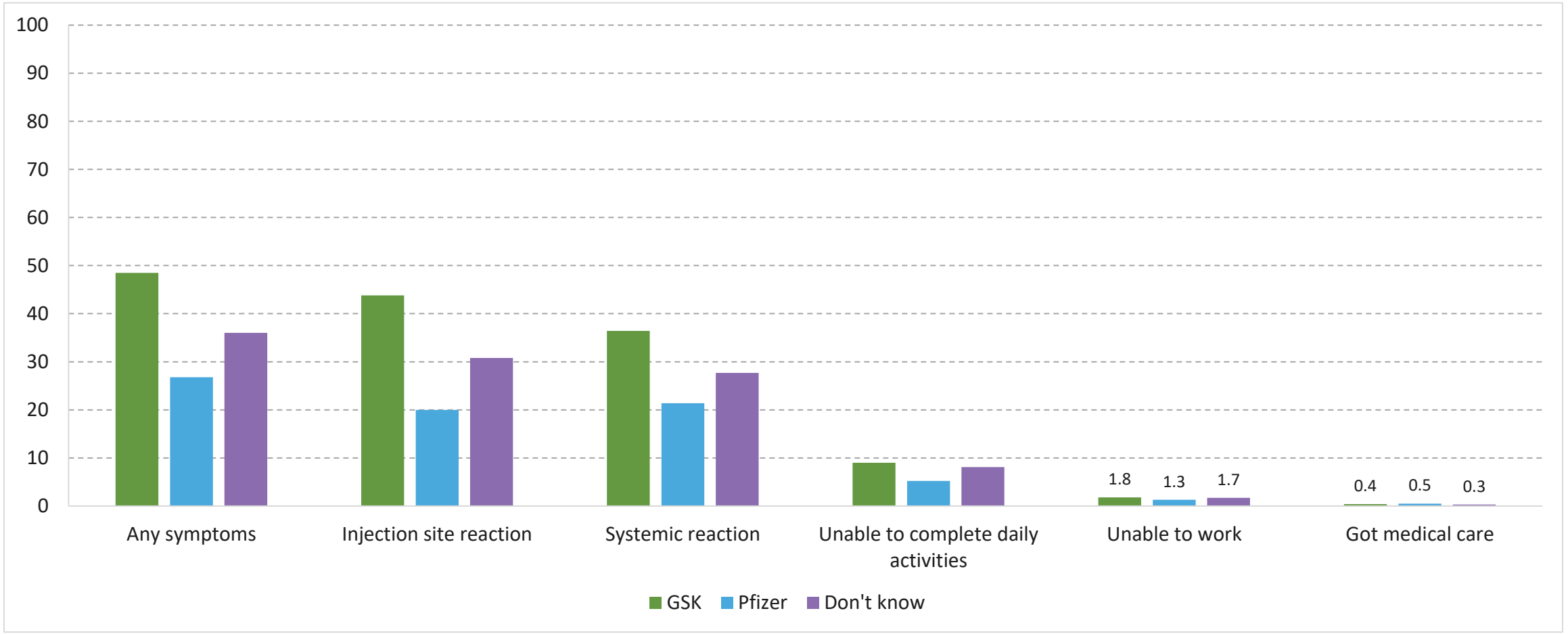
* For 15,745 V-safe participants who enrolled in the RSV 60+ years old protocol and completed ≥1 daily survey during October 20, 2023-January 28, 2024

Additional characteristics of adults aged ≥60 years who reported RSV vaccination*

Characteristic	Vaccine manufacturer (%)			
	GSK (Arexvy) N=6,227	Pfizer (Abrysvo) N=3,746	Manuf not known N=5,772	Total N=15,745
Immunocompromised	**6.8**	**6.6**	**6.4**	**6.6**
State of health				
Excellent	22.7	22.6	21.5	22.2
Very good	46.9	46.0	46.1	46.4
Good	25.1	25.8	26.5	25.8
Fair	4.9	5.3	5.6	5.3
Poor	0.3	0.2	0.4	0.3
Vaccine(s) co-administered	**24.6**	**33.8**	**35.6**	**30.8**
COVID-19	16.0	22.8	23.5	20.4
Influenza	12.6	17.4	20.0	16.5
COVID-19 and influenza	7.3	10.1	11.4	9.5
COVID-19, influenza, and other	0.7	1.1	1.2	1.0
Other	4.9	6.0	5.8	5.5

* For 15,745 V-safe participants who enrolled in the RSV 60+ years old protocol and completed ≥1 daily survey during October 20, 2023-January 28, 2024

Reactions and health impacts reported for adults aged ≥60 years at least once in days 0-7 following RSV vaccination, by manufacturer*



* For 15,745 V-safe participants who enrolled in the RSV 60+ protocol and completed ≥1 daily survey during October 20, 2023-January 28, 2024

Promoting V-safe – We need your help

- Ensure vaccination partners are aware of V-safe
  - Information sheets
  - Social media posts
  - Communications to vaccine recipients

Materials and more information available at:

https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/v-safe/index.html

What is V-safe?

V-safe is an innovative vaccine safety monitoring system that allows you or your dependent to quickly and easily share how you feel after getting a vaccine. It takes just a few minutes to enroll, and then you will receive V-safe notifications through text messages or emails to complete **short, confidential health check-ins.** Your participation in V-safe makes a difference—it helps others know what to expect in the days following vaccination, and it helps CDC monitor the safety of vaccines for everyone.

V-safe features:

- **Receive health check-ins via text or email** after vaccination.
- **Enroll your dependents** and complete check-ins on their behalf.
- **Share** how you feel **after getting a vaccine dose.**

How can I enroll, and how does it work?

V-safe is available for several vaccines. Go to vsafe.cdc.gov to find out if you are eligible to enroll. If you are eligible, follow the prompts to register for V-safe health check-ins. During the first week after vaccination, V-safe will send you a text message or email notification each day to ask how you are feeling. Then you will get check-in messages once a week for up to 5 weeks. Depending on your answers, V-safe may send you a link to submit a report in the Vaccine Adverse Event Reporting System (VAERS).

You can opt out at any time by texting "STOP" when V-safe sends you a text message or by clicking "unsubscribe" when V-safe sends you an email. You can also opt back in by changing your preferred method of contact, found in your user profile. **Your personal information in V-safe is protected so that it stays confidential and private.***

How can I enroll my dependent?

To enroll a dependent in V-safe, **add them to your existing account,** or create a new account if you don't have one yet. Enrolling a dependent does not require you to enter your own vaccination information or complete health check-ins for yourself.

Need step-by-step instructions? Go to: www.cdc.gov/vsafe

*V-safe gathers data employing strict security measures appropriate for the data's level of sensitivity. These measures comply, where applicable, with the following federal laws including the Privacy Act of 1974, standards enacted that are consistent with the Health Insurance Portability and Accountability Act of 1996 (HIPAA), the Federal Information Security Management Act, and the Freedom of Information Act.

V-safe

Sign up with your smartphone, tablet, or computer at
vsafe.cdc.gov

OR

Aim your smartphone's camera at this code

Need help with V-safe?

Call
1-833-748-1979

Email
CARS_HelpDesk@cdc.gov

Visit
www.cdc.gov/vsafe

CS324195-V 10/05/2023

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

Vaccine Adverse Event Reporting System (VAERS)

Strengths

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

Limitations

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Not designed to assess causality

- VAERS accepts all reports from all reporters without making judgments on causality or judging clinical seriousness of the event
- As a hypothesis generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems

VAERS methods

- Signs and symptoms of adverse events are coded using Medical Dictionary for Regulatory Activities (MedDRA)* Preferred Terms (PTs)
  - MedDRA PTs are not mutually exclusive
  - A single report may be assigned more than 1 MedDRA PT
- Individual report review of serious† reports and medical records, if available
- Brighton Collaboration case definitions applied for the neuroinflammatory conditions, Guillain-Barré syndrome and acute disseminated encephalomyelitis‡
- Reporting rate calculations use doses of vaccine administered for each type of RSV vaccine
- Empirical Bayesian datamining used to detect disproportional reporting for the entire post marketing period for each product¶

* Welcome to MedDRA | MedDRA

† Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

‡ Sejvar et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29(3):599-612. Sejvar et al. Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2007 Aug 1;25(31):5771-92.

¶ DuMouchel W. Bayesian data mining in large frequency tables, with an application to the FDA spontaneous reporting system. Am Statistician 1999;53:177–90.

Surveillance of Adverse Events of Special Interest (AESI) after RSV vaccination

- Primary AESIs
  - Selected for historical, theoretical, or observed safety concerns (i.e., observed in clinical trials)
  - Attempts are made to obtain medical records for all primary AESI reports (serious* and non-serious)
  - CDC reviews records and abstracts clinically important information
  - AESIs may be added to or removed from the list as appropriate
- Secondary AESIs
  - Monitored via periodic (e.g., weekly) automated data tables
  - Can be added to primary AESI list if safety concerns identified

* Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

AESI after RSV vaccination

Primary AESI

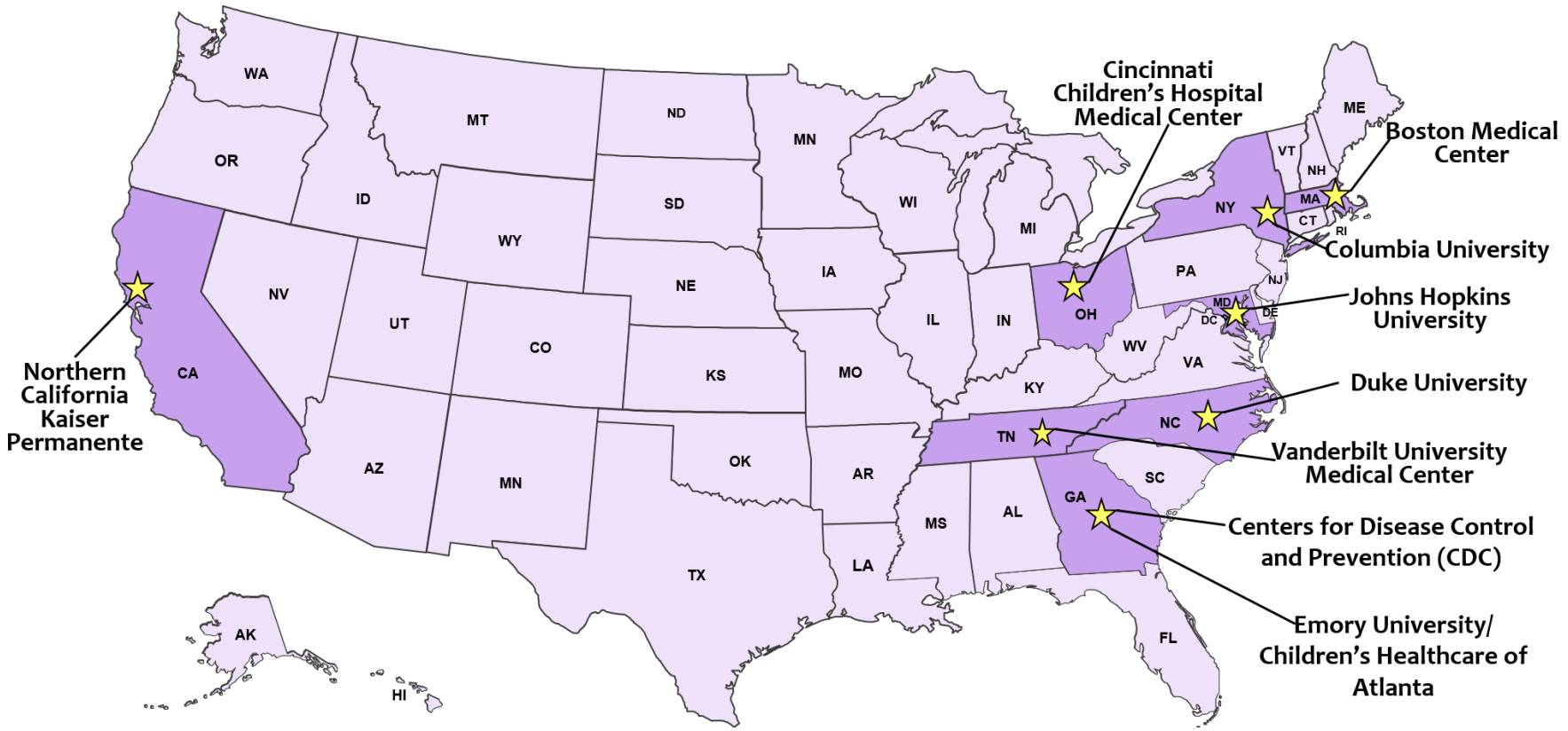
- Outcomes of general interest
  - Death
- Neurologic/neuroinflammatory conditions
  - Guillain-Barré syndrome (GBS), including Miller Fisher variant
  - Acute disseminated encephalomyelitis (ADEM)
  - Transverse myelitis (TM)
  - Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Allergic reactions
  - Anaphylaxis
- Cardiac conditions
  - Atrial fibrillation
  - Other supraventricular tachycardias (SVT)

Secondary AESI

- Neurologic/neuroinflammatory conditions
  - Optic neuritis
  - Multiple sclerosis
  - Bell's palsy
  - Encephalitis/Encephalomyelitis
  - Meningitis/Meningoencephalitis
  - Myelitis
- Other conditions
  - Vaccination errors
  - AEs following simultaneous administration with COVID-19, inactivated influenza, or other adult vaccines

CISA

Clinical Immunization Safety Assessment (CISA) Project



8 participating medical research centers with vaccine safety experts

- clinical consult services*
- clinical expertise for surveillance
- clinical research

*More information about clinical consults available at: Clinical Immunization Safety Assessment (CISA) Project | CISA | Monitoring | Ensuring Safety | Vaccine Safety | CDC

U.S. reports to VAERS following respiratory syncytial virus (RSV) vaccination among adults ages ≥60 years (as of February 16, 2024)

Vaccine	Doses administered (as of Feb 2–3, 2004)*	Median age (IQR†), years	Female N (%)	Non-serious N (%)	Serious‡ N (%)	Total Reports
GSK (Arexvy)	6,587,912	72 (67–77)	1,674 (67)	2,347 (93)	169 (7)	2,516
Pfizer (Abrysvo)	3,063,832	73 (68–78)	618 (59)	954 (91)	91 (9)	1,045
Vaccine brand unknown	Not applicable	73.5 (67-78)	70 (55)	109 (85)	19 (15)	128
Total	**9,651,744**	**72 (67–77)**	**2,362 (64)**	**3,410 (92)**	**279 (8)**	**3,689**

* Doses administered during August 4, 2023, through February 3, 2024, at medical offices from AMA's list of physicians [Data source: Custom IQVIA Custom Medical Claims (Dx)] and during August 12, 2023, through February 2, 2024, at retail pharmacies [Data source: Custom Longitudinal Prescription Claims (LRx)]. IQVIA data do not include vaccinations administered at other medical settings such as public health clinics and other settings including workplaces and community locations. These represent projected doses. Based on a sample of retail pharmacies and medical offices of a sample of AMA physicians, IQVIA projects doses administered in all retail pharmacies and medical offices of all AMA physicians.

† Interquartile range

‡ Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

Most frequently reported MedDRA Preferred Terms* among reports to VAERS following RSV vaccination among adults ages ≥60 years, by manufacturer

(as of February 16, 2024)

Rank	All Reports (N=3,689)†,‡	n (%)	Pfizer (Abrysvo) (N=1,045)†	n (%)	GSK (Arexvy) (N=2,516)†	n (%)
1	Pain in extremity	439 (12)	Fatigue	120 (12)	Pain in extremity	327 (13)
2	Fatigue	432 (12)	Headache	114 (11)	Injection site pain	320 (13)
3	Pain	414 (11)	Pain in extremity	99 (10)	Pain	305 (12)
4	Injection site pain	408 (11)	Pain	97 (9)	Fatigue	290 (12)
5	Headache	404 (11)	Fever	95 (9)	Headache	277 (11)
6	Fever	353 (10)	Arthralgia	86 (8)	Injection site erythema	267 (11)
7	Injection site erythema	338 (9)	Injection site pain	81 (8)	Fever	249 (10)
8	Arthralgia	304 (8)	Chills	75 (7)	Arthralgia	210 (8)
9	Erythema	255 (7)	Nausea	71 (7)	Erythema	193 (8)
10	Injection site swelling	247 (7)	Dizziness	70 (7)	Injection site swelling	191 (8)

* Medical Dictionary for Regulatory Activities Preferred Terms (MedDRA Hierarchy | MedDRA)

† Signs and symptoms are not mutually exclusive

‡ Includes 128 reports with unknown RSV vaccine brand

Most frequently reported MedDRA Preferred Terms* among reports to VAERS following RSV vaccination among adults ages ≥60 years (as of February 16, 2024)

Non-serious reports† (N=3,410)

Rank	MedDRA PT (not mutually exclusive)	n (%)
1	Pain in extremity	416 (12)
2	Injection site pain	395 (12)
3	Fatigue	394 (12)
4	Pain	388 (11)
5	Headache	384 (11)
6	Injection site erythema	333 (10)
7	Fever	319 (9)
8	Arthralgia	284 (8)
9	Erythema	252 (7)
10	Injection site swelling	245 (7)

Serious reports†,‡ (N=279)

Rank	MedDRA PT (not mutually exclusive)	n (%)
1	Dyspnoea	48 (17)
2	Asthenia	47 (17)
3	Fatigue	38 (14)
4	Gait disturbance	35 (13)
5	Fever	34 (12)
6	Muscular weakness	33 (12)
7	Nausea	31 (11)
8	Guillain-Barré syndrome	30 (11)
9	Intensive care	29 (10)
10	Paraesthesia	29 (10)

* Medical Dictionary for Regulatory Activities Preferred Terms (MedDRA Hierarchy | MedDRA)

† Includes 128 reports with unknown RSV vaccine brand (109 non-serious and 19 serious)

‡ Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect

Reports* to VAERS of selected AESIs after RSV vaccination among adults ages ≥60 years (as of February 16, 2024)

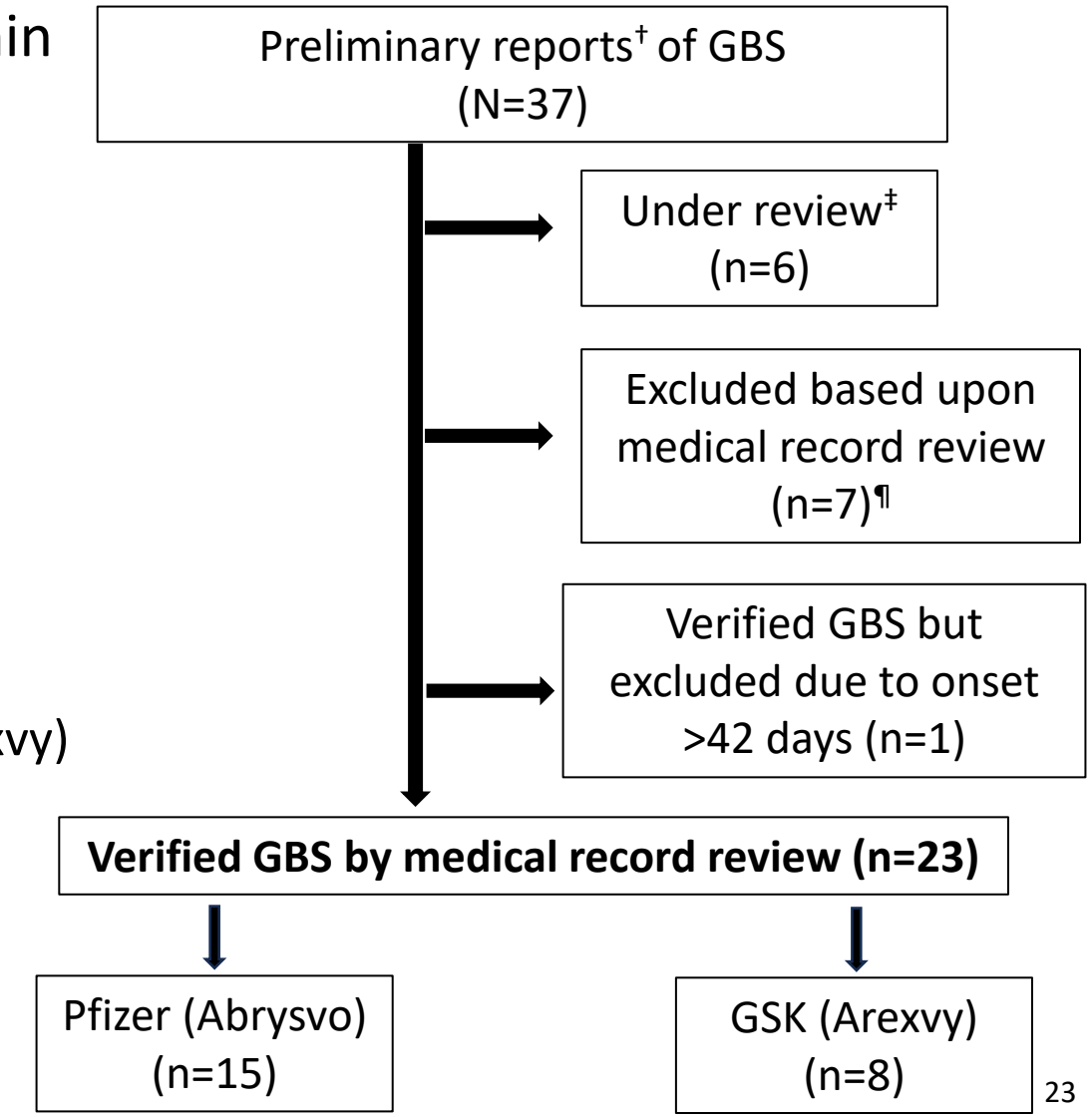
Condition	Pfizer (Abrysvo)	GSK (Arexvy)	No brand name	Total
Death	9	22	3	34
Guillain-Barré syndrome (GBS)	18	16	1	35
Acute disseminated encephalomyelitis (ADEM)	1	0	1	2
Transverse myelitis (TM)	1	2	0	3
Chronic inflammatory demyelinating polyneuropathy (CIDP)	0	1	0	1
Anaphylaxis	1	1	0	2
Atrial fibrillation	15	38	5	58
Supraventricular tachycardia (SVT)	1	2	0	3
Total	**46**	**82**	**10**	**138**

- On January 19, 2024, a data mining alert for disproportional reporting was detected in FDA Empirical Bayesian (EB) data mining for Pfizer (Abrysvo) RSV vaccine and GBS
- No data mining alert for GSK (Arexvy) RSV vaccine and GBS has been detected to date
- EB data mining is product-specific and analyzes product-specific vaccine-adverse event pairings compared to the overall VAERS database

*Reports in this table include verified, unverified, ruled out and duplicate reports

Reports to VAERS of Guillain-Barré syndrome (GBS) after respiratory syncytial virus (RSV) vaccination among adults (as of February 16, 2024)

- 23 verified* reports of GBS with symptom onset within 42 days (all within 22 days) of RSV vaccination:
  - Pfizer (Abrysvo) (n=15), GSK (Arexvy) (n=8)
  - Median age: 71 years (IQR: 63,75 years)
  - 1 report in a non-pregnant female patient aged 50s years, received Pfizer (Abyrsvo)
  - Median time to onset: 9 days (range 1,22 days**)
  - 14 males, 9 females
  - None were pregnant
  - 1 death; patient aged 70s years, male, received GSK (Arexvy)



* Based on VAERS report and medical record review and application of GBS definition in: Sejvar et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29(3):599-612.

† Includes reports identified through automated search and clinical review; all vaccinated Aug 29, 2023, through Jan 5, 2024

‡ Awaiting medical records

¶ Includes one report in a pregnant person who received Pfizer (Abyrsvo) RSV vaccine; patient did not meet clinical criteria for Guillain-Barré syndrome following review by independent experts in CISA, including neurologists

** Includes one report after GSK (Arexvy) RSV vaccine with onset at 22 days

Reports to VAERS of Guillain-Barré syndrome after respiratory syncytial virus (RSV) vaccination among adults (as of February 16, 2024)

- All 23 verified reports met Brighton Collaboration criteria for GBS*:
  - 3 were Brighton level 1, 12 were Brighton level 2, and 8 were Brighton level 3
  - 21 of 23 were also classified as GBS cases (Brighton level 1-3) by at least one CISA neurologist†
- 4 reports involving Pfizer (Abrysvo) RSV vaccine had respiratory symptoms within 4 weeks prior to GBS onset
- Other vaccines were given during same visit in 14 of the 23 GBS reports‡:

Pfizer (Abrysvo) RSV vaccine n=9	
Other vaccine	**N**
Bivalent mRNA COVID-19 (Pfizer-BioNTech)	3
Bivalent mRNA COVID-19 (Moderna) 13-valent pneumococcal conjugate vaccine	1
aIIV4 (Fluad)	1
Imovax rabies	1
Tdap (Boostrix)	1
Zoster (Shingrix)	1
RIV4 (Flublok)	1

GSK (Arexvy) RSV vaccine n=5	
Other vaccine	**N**
HD-IIV4 (Fluzone high-dose influenza) Bivalent mRNA COVID-19 (Pfizer-BioNTech) 20-valent pneumococcal conjugate vaccine	1
aIIV4 (Fluad)	1
Covid-19 Moderna	2
Covid-19 Moderna HD-IIV4 (Fluzone high-dose influenza)	1

* Sejvar et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29(3):599-612.

† One GSK report (death report) (Brighton level 4 per CISA) and 1 Pfizer report aged ≥60 years (Brighton level 4 and 5 per CISA) were not classified as GBS by at least one CISA neurologist after review

‡ Other vaccines were given within 4 weeks of symptom onset and not during same visit in 4 of the 23 reports. 1 Pfizer report, Bivalent mRNA COVID-19 vaccine; 1 GSK report, adjuvanted influenza vaccine; 1 GSK report, unspecified influenza vaccine; 1 GSK report, inactivated influenza vaccine and 20-valent pneumococcal conjugate vaccine

Reports to VAERS of other non-GBS neuroinflammatory conditions after respiratory syncytial virus (RSV) vaccination* (as of February 16, 2024)

- Transverse myelitis (n=2)
  - 1 report each after Pfizer (Abrysvo)† and GSK (Arexvy)‡
- Acute Disseminated Encephalomyelitis (n=3)
  - 1 report after Pfizer (Abrysvo)‡ and 2 reports after GSK (Arexvy)¶
- Posterior reversible encephalopathy syndrome (n=1)
  - 1 report after Pfizer (Abrysvo)‡
- Acute encephalitis (n=1)
  - 1 report after Pfizer (Abrysvo) †

* Sejvar et al. Encephalitis, myelitis, and acute disseminated encephalomyelitis (ADEM): case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2007;25(31):5771-92.

† Pending medical records

‡ Case classified as listed diagnosis by at least one CISA neurologist

¶ One case classified as insufficient information to verify diagnosis by CISA neurologists; another case pending review of medical records

Observed VAERS reports and reporting rates of verified Guillain-Barré syndrome (GBS) after respiratory syncytial virus (RSV) vaccination among adults ages ≥60 years

Age group (years)	Risk window	RSV vaccine	Observed verified GBS reports* (as of Feb 16, 2024)	Doses administered† (as of Feb 2–3, 2024)	Observed VAERS reporting rate (per million doses admin)‡
≥60	21-days	Pfizer (Abrysvo)	**14**	3,063,832	**4.6¶**
		GSK (Arexvy)	**7**	6,587,912	**1.1**
≥60	42-days	Pfizer (Abrysvo)	**14**	3,063,832	**4.6¶**
		GSK (Arexvy)	**8**	6,587,912	**1.2**

* Based on VAERS report and medical record review and application of GBS definition in: Sejvar et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29(3):599-612.

† Doses administered during August 4, 2023, through February 3, 2024, at medical offices from AMA's list of physicians [Data source: Custom IQVIA Custom Medical Claims (Dx)] and during August 12, 2023, through February 2, 2024, at retail pharmacies [Data source: Custom Longitudinal Prescription Claims (LRx)]. IQVIA data do not include vaccinations administered at other medical settings such as public health clinics and other settings including workplaces and community locations. These represent projected doses. Based on a sample of retail pharmacies and medical offices of a sample of AMA physicians, IQVIA projects doses administered in all retail pharmacies and medical offices of all AMA physicians.

‡ Assumes complete person-time follow-up

¶ Reporting rate for Pfizer (Abrysvo) increases to 4.9 if patient aged 50s years is included

Using estimated rate of chart confirmed GBS after mRNA COVID-19 vaccination in the Vaccine Safety Datalink (VSD) as a proxy for background rate*

- Safety monitoring of mRNA COVID-19 vaccines in the VSD did **NOT** detect an increased risk of GBS associated with either of the mRNA COVID-19 vaccines
  - Therefore, the rate of GBS following mRNA COVID-19 vaccination can be used as a proxy for the background rate of GBS in a 'vaccine-accepting' population
  - This rate is appropriate because it is relatively current and all GBS cases were a priori chart reviewed
  - However, there are limitations (e.g., different populations, different time periods, different age groups)
- Estimated rate of confirmed cases of GBS in those 65+ years of age following mRNA COVID-19 primary series vaccination in VSD
  - 21-day risk interval: 3.4 (95% CI 1.2–7.3) per 100,000 person-years
  - 42-day risk interval: 4.5 (95% CI 2.4–7.7) per 100,000 person-years
- **Expected cases per 1 million RSV doses administered, assuming complete person-time follow-up**
  - **21-day risk interval: 2.0 cases per million doses admin (range from 95% CI 0.7–4.2)**
  - **42-day risk interval: 5.2 cases per million doses admin (range from 95% CI 2.8–8.9)**

*Hanson et al. Incidence of Guillain-Barré Syndrome After COVID-19 Vaccination in the Vaccine Safety Datalink. JAMA Netw Open. 2022;5(4):e228879 and VSD unpublished data.

Observed VAERS reports and reporting rates of verified Guillain-Barré syndrome (GBS) after respiratory syncytial virus (RSV) vaccination among adults ages ≥60 years and estimated background rates

Age group (years)	Risk window	RSV vaccine	Observed verified GBS reports* (as of Feb 16, 2024)	Doses Admin (as of Feb 2–3, 2024)†	Observed VAERS Reporting rate (per million doses admin)‡	Estimated expected rate (per million doses admin) based on VSD data¶
≥60	21-days	Pfizer (Abrysvo)	14	3,063,832	**4.6**	**2.0 (95% CI 0.7–4.2)**
		GSK (Arexvy)	7	6,587,912	**1.1**	
≥60	42-days	Pfizer (Abrysvo)	14	3,063,832	**4.6**	**5.2 (95% CI 2.8–8.9)**
		GSK (Arexvy)	8	6,587,912	**1.2**	

* Based on VAERS report and medical record review and application of GBS definition in: Sejvar et al. Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. Vaccine. 2011;29(3):599-612.

† Doses administered during August 4, 2023, through February 3, 2024, at medical offices from AMA's list of physicians [Data source: Custom IQVIA Custom Medical Claims (Dx)] and during August 12, 2023, through February 2, 2024, at retail pharmacies [Data source: Custom Longitudinal Prescription Claims (LRx)]. IQVIA data do not include vaccinations administered at other medical settings such as public health clinics and other settings including workplaces and community locations. These represent projected doses. Based on a sample of retail pharmacies and medical offices of a sample of AMA physicians, IQVIA projects doses administered in all retail pharmacies and medical offices of all AMA physicians.

‡ Assumes complete person-time follow-up

¶ Background data (21-day and 42-day risk windows) on Guillain-Barré syndrome after COVID-19 vaccines from the vaccine safety datalink (cases per million doses); estimate of background rate in a vaccine-accepting population and used as proxy because data from VSD did not detect an increased risk of GBS after mRNA COVID-19 vaccines (Source: Hanson et al. Incidence of Guillain-Barré syndrome After COVID-19 Vaccination in the Vaccine Safety Datalink. JAMA Netw Open. 2022;5(4):e228879.) and VSD unpublished data

Observed VAERS reports and reporting rates of verified Guillain-Barré syndrome (GBS) after respiratory syncytial virus (RSV) vaccination among adults ages ≥60 years compared to the VAERS reporting rate for COVID-19 vaccines

Age group (years)	RSV vaccine	GBS reporting rate in VAERS (verified cases) per million doses admin*
≥60	Pfizer (Abrysvo)	**4.6**
≥60	GSK (Arexvy)	**1.1**

21-day risk interval

Table 2. Rates of Verified GBS by Vaccine Type[†,‡]

Vaccine	No. GBS	No. Vaccine doses	GBS reporting rate, No. cases/ 1 000 000 doses
21-d Postvaccination risk interval			
Ages ≥18 y			
Ad26.COV2.S	59	17 944 515	3.29
BNT162b2	77	266 859 784	0.29
mRNA-1273	72	202 847 486	0.35
Ages 18-49 y			
Ad26.COV2.S	13	9 735 496	1.34
BNT162b2	33	132 439 289	0.25
mRNA-1273	14	83 064 308	0.17
Ages 50-64 y			
Ad26.COV2.S	36	5 482 229	6.57
BNT162b2	16	68 858 186	0.23
mRNA-1273	23	54 462 150	0.42
Ages ≥65 y			
Ad26.COV2.S	10	2 726 790	3.67
BNT162b2	28	65 562 309	0.43
mRNA-1273	35	65 321 028	0.54

21-day risk interval

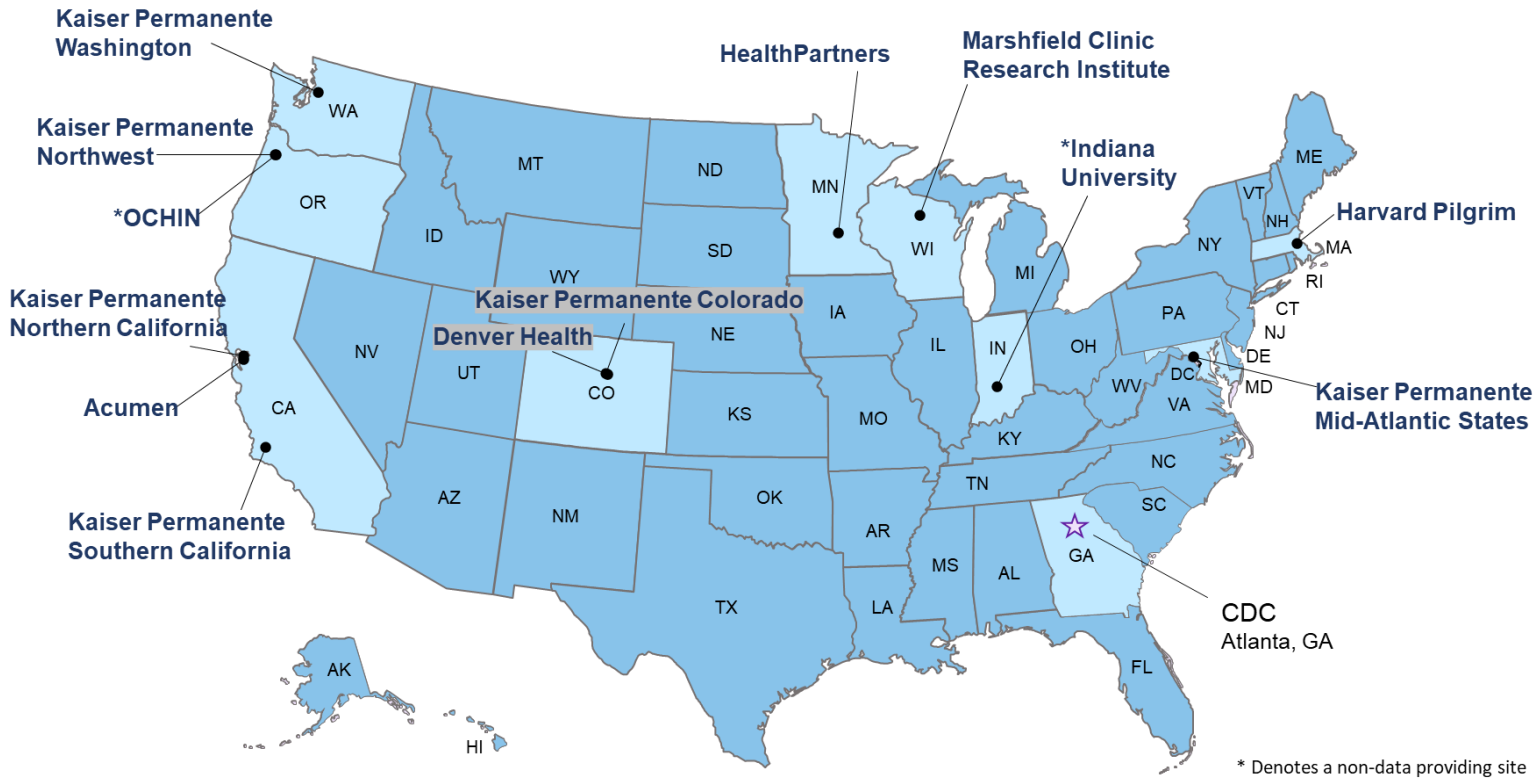
* Assumes complete person-time follow-up

† Reporting rate for GBS (21-day risk window) after mRNA Covid-19 vaccines from VAERS in persons aged ≥65 years during December 2020-January 2022. Source: Abara et al. Reports of Guillain-Barré syndrome After COVID-19 Vaccination in the United States. JAMA Netw Open. 2023;6(2):e2253845.

‡ An association between Ad26 and GBS was observed but not between GBS and mRNA COVID-19 vaccines

Vaccine Safety Datalink (VSD)

- Established in 1990
- Collaborative project between CDC and 13 integrated healthcare organizations
- Includes electronic health data annually on ~13.5 million individuals across all sites which includes ~2.8 million adults aged 60 years or older



Observed VSD GBS rates following RSV vaccination in adults aged ≥60 years through December 30, 2023

- The VSD has identified 4 GBS cases within 1-84 days of GSK (Arexvy) RSV vaccination; all 4 cases have undergone medical record review and have been adjudicated according to Brighton Criteria*

GSK (Arexvy) Chart Confirmed Results – Brighton Levels 1, 2, or 3

Vaccine	Risk window	# GBS cases	# vaccine doses	Rate per million doses admin (95% CI)	Rate per 100,000 person years (95% CI)
GSK (Arexvy)	1-21 days	2	209,653	9.5 (1.2–34.5)	16.6 (2.0–59.9)
GSK (Arexvy)	1-42 days	3	209,653	14.3 (3.0–41.8)	12.4 (2.6–36.4)

- The 4th case, absent from the table above, was classified as Brighton Level 4 and is pending additional medical record review
- Currently no cases of GBS have been observed within 1–42 days after Pfizer (Abrysvo) RSV vaccination in VSD, but only ~10% of all RSV vaccinations in VSD have been with the Pfizer product
- VSD will continue to monitor the safety of RSV vaccines in adults aged ≥60 years and formal sequential safety analysis will begin in March 2024 using a vaccinated concurrent comparison group (similar to COVID-19 vaccine safety monitoring)

* Sejvar et al. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine*. 2011;29(3):599-612.

Summary: Early post-licensure safety monitoring of RSV vaccines in adults aged ≥60 years

- Local and systemic symptoms (e.g., fatigue) were the most commonly reported adverse events following either of the RSV vaccines
- Monitoring in VAERS indicates a higher-than-expected number of GBS reports following Pfizer (Abrysvo) RSV vaccine, but VAERS is subject to the limitations of passive surveillance
  - GBS cases were observed in the pre-licensure clinical trials for both the Pfizer (Abrysvo) and GSK (Arexvy) RSV vaccines and GBS is included as an adverse event in the labels of both vaccines
- Early data from VSD suggest the potential for an increased rate for GBS after GSK (Arexvy) RSV vaccine, but additional analyses are needed to further assess this potential risk; insufficient doses of Pfizer (Abrysvo) RSV vaccine used in VSD to inform risk
- Monitoring for GBS following RSV vaccines in FDA and CDC (VSD) population-based active surveillance systems is in progress
- CDC and FDA will continue to monitor RSV vaccine safety in VAERS and CDC will continue to monitor in V-safe

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- CDC Immunization Safety Office
  - VAERS Team
  - V-safe Team
  - Clinical Immunization Safety Assessment (CISA) Project
  - Vaccine Safety Datalink (VSD)
- Food and Drug Administration
  - Office of Biostatistics and Pharmacovigilance, Center for Biologics Evaluation and Research
- National Center for Immunization and Respiratory Diseases
  - Coronavirus and Other Respiratory Viruses Division

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