Original Research

KANSAS JOURNAL of MEDICINE

Adverse Events Reported Following RSV Prefusion F Protein Vaccines Administration Among Approved Populations: A Cross-Sectional Study

Tyler McLaughlin, MS-3, Dulcinea Rakestraw, Ph.D., MPH, Hayrettin Okut, Ph.D., Elizabeth Ablah, Ph.D.

ABSTRACT

Introduction. Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infections among children and older adults. Two RSV prefusion F protein (RSVpreF) vaccines currently are approved for adults aged 60 years and older. However, little is known about the adverse events reported among individuals in this age group who have received an RSVpreF vaccine. The purpose of this study was to compare adverse events reported by nonpregnant adults (≥60 years old) who received an RSVpreF vaccine.

Methods. This study included individuals who reported a vaccine-related adverse event to the Vaccine Adverse Event Reporting System (VAERS). Data abstracted from VAERS were recoded into standardized adverse event categories for analysis.

Results. A total of 2,321 individuals were included. The three most frequently reported adverse event categories were neurologic, musculoskeletal, and constitutional symptoms. Recipients of Arexvy™ (Respiratory Syncytial Virus Vaccine, Adjuvanted) reported more injection site reactions compared with those who received Abrysvo™ (Respiratory Syncytial Virus vaccine). There were no adverse event categories that were more commonly reported among Abrysvo™ recipients compared with Arexvy™ recipients.

Conclusions. The adverse events observed in this study were consistent with findings from previous Phase II/III trials. The higher frequency of injection site symptoms among Arexvy™ recipients may be attributable to the adjuvant included in Arexvy™ but absent in Abrysvo™. Overall, these findings indicate that both vaccines provide safe protection against RSV for older adults, with minimal side effects, in a population that previously had no vaccination option.

INTRODUCTION

Respiratory Syncytial Virus (RSV) is a major cause of lower respiratory infections among children and older adults.[1,2] In the United States, RSV leads to approximately 1.6 million outpatient pediatric visits each year.[2,3] Older adults also remain at high risk for severe RSV disease due to waning immunity and comorbid conditions.[4] Among this population, RSV is associated with an estimated 10,000 deaths annually, 267 hospitalizations per 100,000 people, and 1.4 million outpatient visits.[5,6] The true burden likely is even greater, as RSV is under-detected when clinicians do not routinely test for it, particularly in older adults.[5]

Historically, RSV treatment strategies have centered on secondary and tertiary prevention, including supportive care, ribavirin, monoclonal antibodies, RSV intravenous immunoglobulin (RSV-IVIG), glucocorticoids, and bronchodilators.[7] Ribavirin, however, is known to cause teratogenic and other adverse effects and is therefore reserved for select cases.[8] Likewise, monoclonal antibodies and RSV-IVIG generally are limited to "high-risk" individuals such as immunocompromised patients, premature infants, and older adults with significant comorbidities.[1,7] Most available treatment approaches provide symptomatic relief but do not prevent infection.

A major advance occurred on May 3, 2023, when the United States Food and Drug Administration (FDA) approved two RSV prefusion F (RSVpreF) protein vaccines (Arexvy™ [Respiratory Syncytial Virus Vaccine, Adjuvanted] and Abrysvo™ [Respiratory Syncytial Virus vaccine]). for adults aged 60 years and older, offering a new primary prevention tool for at-risk populations.[9-11] These vaccines target the RSVpreF protein, which had historically been difficult to isolate and purify.[2,12,13]

Clinical trials for these vaccines reported common adverse events such as injection site pain, muscle pain, joint pain, headache, fatigue, and nausea.[14] Rare but more serious events, including inflammatory neurological conditions like Guillain-Barré syndrome, also were observed.[14] However, real-world data on adverse events reported by individuals who received an RSVpreF vaccine remain limited. Therefore, authors of this study aimed to compare adverse events among nonpregnant adults aged 60 years or older who received an RSVpreF vaccine.

METHODS

Participants. This study included individuals who reported a vaccine-related adverse event to the Health and Human Services Vaccine Adverse Event Reporting System (VAERS).[15] VAERS is an open reporting system that allows anyone to submit post-vaccination adverse events using free-text entries. Eligible participants were adults aged ≥60 years who received one of the two RSVpreF vaccines and reported at least one adverse event between August 1, 2023, and January 31, 2024. Exclusions included missing age, age <60 years, pregnancy, receiving an inappropriate vaccine based on guidelines, or incomplete required information.

Instrument. Extracted variables included demographics (e.g., age, sex), vaccine details (e.g., vaccine name and brand), and adverse event information (e.g., symptoms, disability, vaccination problems). Demographics were used to confirm eligibility, while vaccine details and event characteristics allowed comparison of adverse event profiles between the two RSVpreF vaccines.

Procedures. The study was approved by The University of Kansas Medical Center (KUMC) Institutional Review Board (IRB) and followed STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[16]

De-identified VAERS data were downloaded and stored in REDCap® (CTSA Award # UL1TR002366), electronic data capture tools hosted at The KUMC.[17,18] Because VAERS relies on unstructured free-text reporting, adverse events were recoded into standardized categories based on the affected system. Coding was completed by one researcher and reviewed by four others, with consensus reached through discussion. Categories included vaccine information (e.g., vaccine name, inappropriate administration) and adverse event types (e.g., constitutional symptoms, cardiovascular issues, injection site reactions).

Statistical Analysis. Data were analyzed using SAS® version 9.4 (SAS Institute Inc., Cary, NC). Categorical variables were summarized as frequencies and percentages. Continuous variables were described using means and standard deviations (SD) or medians and interquartile ranges (IQRs), depending on distribution. Associations between categorical variables were tested using likelihood-ratio Chi-square tests in 2×2 tables. Statistical significance was set at $p < 0.0015$ after Bonferroni correction.

RESULTS

A total of 2,764 individuals initially met study criteria. After review, 443 were excluded: 198 lacked age information in their VAERS report, 197 received a vaccine outside the recommended age range or received the incorrect vaccine, and 48 were identified as pregnant after data abstraction. The final sample included 2,321 participants. Of these, 28.5% (n = 662) were male, 71.2% (n = 1,654) were female, and 0.2% (n = 5) did not report sex. Ages ranged from 60 to 102 years, with a mean age of 73 years (SD 7.2). Most participants received Arexvy™ (69.8%, n = 1,620), while 30.2% (n = 701) received Abrysvo™.

The most frequently reported adverse event categories were neurologic (31.6%, n = 733), musculoskeletal (29.1%, n = 676), and constitutional symptoms (28.4%, n = 658; Table 1). Vaccine administration problems, such as incorrect dose, reconstitution issues, or administration errors, accounted for 8.9% (n = 206) of reports. Serious neuroinflammatory events, including Guillain-Barré syndrome, were reported in 0.9% (n = 20) of cases. Mortality was 0.7% (n = 15).

Patients who received Arexvy™ reported injection site symptoms more frequently (29.4%, 477/1,620; χ^2_1=27.7; $p < 0.0001$; Table 2) than those who received Abrysvo™ (18.9%, 133/701; χ^2_1=27.7; $p < 0.0001$; Table 2). Patients who received Abrysvo™ did not report any specific adverse event more often than those who received Arexvy™.

Table 1. Adverse events reported by participants ≥ 60 years.

Reported Adverse Event	Percent (Frequency)
Allergic reaction	3.5% (80)
Autoimmunity	0.5% (11)
Cardiovascular adverse event	8.0% (185)
Clotting problem	0.8% (18)
Constitutional symptoms	28.4% (658)
Death	0.7% (15)
Ear adverse event	1.6% (36)
Edema	10.3% (238)
Genitourinary adverse event	1.2% (27)
GI adverse event	15.8% (367)
Hematological adverse event	0.7% (7)
Infection	2.7% (62)
Injection site symptoms	26.3% (610)
Liver adverse event	0.3% (6)
Metabolic adverse event	0.7% (17)
Musculoskeletal adverse event	29.1% (676)
Nasal adverse event	3.1% (72)
Neurologic adverse event	31.6% (733)
Ocular adverse event	2.5% (59)
Oral adverse event	3.6% (84)
Other	23.8% (552)
Psychiatric adverse event	6.1% (142)
Renal adverse event	0.6% (14)
Respiratory adverse event	9.7% (226)
Serious cardiovascular adverse event	0.4% (9)
Serious neuroinflammatory adverse event	0.9% (20)
Serious neurologic adverse event	0.9% (20)
Serious respiratory adverse event	0.2% (5)
Skin adverse event	19.3% (448)
Vaccine administration problem	8.9% (206)

Table 2. Adverse events reported by vaccine received in adults ≥60 years.

Reported Adverse Event	Abrysvo™	Arexvy™	Chi-square (df)	*P* value
Allergic reaction	4.6% (n = 32)	3.0% (n = 48)	3.8 (1)	0.0521
Autoimmunity	0.7% (n = 5)	0.4% (n = 6)	1.2 (1)	0.2694
Cardiovascular adverse event	8.7% (n = 61)	7.7% (n = 124)	0.7 (1)	0.3923
Clotting problem	1.0% (n = 7)	0.7% (n = 11)	0.6 (1)	0.4204
Constitutional symptoms	27.3% (n = 191)	28.8% (n = 467)	0.6 (1)	0.4380
Death	0.7% (n = 5)	0.6% (n = 10)	0.1 (1)	0.7910
Ear adverse event	1.3% (n = 9)	1.7% (n = 27)	0.5 (1)	0.4932
Edema	9.3% (n = 65)	10.7% (n = 173)	1.1 (1)	0.3051
Genitourinary adverse event	0.6% (n = 4)	1.4% (n = 23)	3.1 (1)	0.0798
GI adverse event	17.4% (n = 122)	15.1% (n = 245)	1.9 (1)	0.1668
Hematological adverse event	0.4% (n = 3)	0.9% (n = 14)	1.3 (1)	0.2578
Infection	3.0% (n = 21)	2.5% (n = 41)	0.4 (1)	0.5237
Injection site symptoms	18.9% (n = 133)	29.4% (n = 477)	27.7 (1)	<0.0001*
Liver adverse event	0.1% (n = 1)	0.3% (n = 5)	0.5 (1)	0.4696
Metabolic adverse event	0.6% (n = 4)	0.8% (n = 13)	0.4 (1)	0.5475
Musculoskeletal adverse event	28.0% (n = 196)	29.6% (n = 480)	0.7 (1)	0.4163
Nasal adverse event	3.4% (n = 24)	3.0% (n = 48)	0.3 (1)	0.5567
Neurologic adverse event	35.52% (n = 249)	29.9% (n = 484)	7.2 (1)	0.0072
Ocular adverse event	2.7% (n = 19)	2.5% (n = 40)	0.1 (1)	0.7346
Oral adverse event	4.6% (n = 32)	3.2% (n = 52)	2.6 (1)	0.1085
Other	23.1% (n = 162)	24.07% (n = 390)	0.3 (1)	0.6164
Psychiatric adverse event	5.9% (n = 41)	6.2% (n = 101)	0.1 (1)	0.7218
Renal adverse event	0.6% (n = 4)	0.6% (n = 10)	0.02 (1)	0.8939
Respiratory adverse event	11.0% (n = 77)	9.2% (n = 149)	1.8 (1)	0.1825
Serious cardiovascular adverse event	0.6% (n = 4)	0.3% (n = 5)	0.9 (1)	0.3511
Serious neuroinflammatory adverse event	1.7% (n=12)	0.5% (n = 8)	8.5 (1)	0.0036
Serious neurologic adverse event	0.7% (n = 5)	0.9% (n = 15)	0.3 (1)	0.6108
Serious respiratory adverse event	0.3% (n = 2)	0.2% (n = 3)	0.2 (1)	0.6329
Skin adverse event	17.8% (n = 125)	19.9% (n = 323)	1.4 (1)	0.2377
Vaccine administration problem	7.7% (n = 54)	9.4% (n = 152)	1.7 (1)	0.1915

*Indicates a statistically significant result (p <.0015). df, Degrees of freedom.

DISCUSSION

In this study, adverse events were grouped by organ system as well as broader categories, such as constitutional symptoms, injection site symptoms, and vaccine administration problems, that emerged during data abstraction. Because VAERS reports consist of unstructured free-text entries, recoding was necessary to standardize symptom categories and enable meaningful analysis. This approach differs from clinical trials, which tracked a narrower set of predefined adverse events such as headache, injection-site pain, and fever.[19,20]

Of all vaccine recipients, about two-thirds reported being female and almost a third reported being male, which aligns with prior research showing that men are less likely to seek medical care or visit their primary care physician.[21,22] These demographic differences highlight the need for continued counseling of both elderly on the importance of RSV vaccination.

Neurologic adverse events, including headache, dizziness, and paresthesia, were the most reported symptoms. This is consistent with a Phase II trial of adults aged 18-40 years, where headache was the most frequently reported systemic adverse event (42-52%).[19] Similar findings were reported in a Phase III trial of adults aged ≥60 years, in which 27% of participants reported a systemic adverse event, most commonly headache (13%).[20]

In our study, 26.3% of patients reported injection-site symptoms. By comparison, the Phase II trial reported local reactions in 39-71% of participants,[19] and the Phase III trial reported local reactions in 12%.[20] Differences in symptom grouping and sample size may account for variability between this study's findings and those of the clinical trials.

Recipients of Arexvy™ reported injection-site symptoms more frequently than those who received Abrysvo™. This difference may reflect the presence of an adjuvant in Arexvy™, which is absent in Abrysvo™.[23,24] Adjuvants enhance immunogenicity by stimulating a stronger inflammatory response,[24] but they also are associated with increased reactogenicity, the physical manifestations of that response.[25]

In our study, vaccine administration problems accounted for 8.9% of reports, including administration errors, expired vaccines, or improper reconstitution. These events are not captured in controlled clinical trials but may arise in routine practice, underscoring the need for quality-control measures as RSV vaccines become more widely used. Serious adverse events were uncommon, representing 2.3% of all reports in our study. Neuroinflammatory conditions such as Guillain-Barré syndrome were reported by 0.9%, with no observed differences between vaccines. Mortality also is rare in our finding. Continued monitoring is warranted as vaccine uptake expands.

Overall, RSVpreF vaccines demonstrated a safety profile consistent with Phase II/III trials and offer important primary prevention for elderly populations who previously had no vaccine option.[19,20] Future research should aim to better characterize vaccination rates across demographic groups, identify barriers to uptake, and, ideally, benefit from a centralized database that includes all vaccine recipients, not only those who submit VAERS reports.

Limitations. This study differed from earlier clinical trials in that VAERS includes a much wider range of adverse events, necessitating grouped symptom categories. While this improved data usability, it limited the ability to assess the frequency of individual specific adverse events. As a cross-sectional study, causal relationships between the vaccines and reported adverse events cannot be established. Only individuals who submitted VAERS reports were included; therefore, the overall incidence of adverse events in the vaccinated population cannot be determined. VAERS reports may be incomplete, especially when submitted by individuals without medical training, and severe symptoms may overshadow mild ones, further contributing to incomplete reporting.

CONCLUSIONS

The most frequently reported adverse events among RSVpreF vaccine recipients were neurologic symptoms, musculoskeletal symptoms, and constitutional complaints. Recipients of Abrysvo™ were not more likely to report any specific adverse event compared with Arexvy™ recipients, whereas Arexvy™ recipients more commonly reported injection-site symptoms, likely related to the adjuvant. These findings are consistent with Phase II/III clinical trials and indicate that both vaccines provide safe and important protection for elderly adults, a group that previously had no primary prevention option for RSV. Given RSV's long-standing role as a major cause of lower respiratory infections in the United States, the availability of safe vaccines represents an important advancement in protecting older adults.

ARTICLE INFORMATION

Received May 16, 2025; Accepted for publication December 5, 2025; Published online Dec. 16, 2025, Kans J Med 2025 Nov-Dec; 18:129-133. https://doi.org/10.17161/kjm.vol18.23980.

Corresponding Author: Tyler McLaughlin,The University of Kansas School of Medicine-Wichita, Wichita, Kansas, 1010 N Kansas St., Wichita, KS, 67214, Tyler.jay25@gmail.com.

Author Affiliations: The University of Kansas School of Medicine-Wichita, Wichita, Kansas (McLaughlin); Department of Family Medicine, The University of Kan-sas School of Medicine-Wichita, Wichita, Kansas (Rakestraw); Department of Population Health, The University of Kansas School of Medicine-Wichita, Wichita, Kansas (Okut, Ablah).

Acknowledgments: The authors thank Rosey Zackula for her support with data management and commitment to this research. They also thank Melinda Chenault for her assistance with the data organization.

REFERENCES

1. Falsey AR, Hennessey PA, Formica MA, Cox C, Walsh EE. Respiratory syncytial virus infec-tion in elderly and high-risk adults. N Engl J Med 2005; 352(17):1749-1759. PMID: 15858184
2. Baraldi E, Checcucci Lisi G, Costantino C, et al. RSV disease in infants and young children: Can we see a brighter future? Hum Vaccin Immunother 2022; 18(4):2079322. PMID: 35724340.
3. Li Y, Wang X, Blau DM, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2019: A sys-tematic analysis. Lancet 2022; 399(10340):2047-2064. PMID: 35598608.
4. Respiratory syncytial virus (RSV), Mayo Clinic. 2023. https://www.mayoclinic.org/diseases-conditions/respiratory-syncytial-virus/symptoms-causes/syc-20353098. Accessed July 8, 2024
5. McLaughlin JM, Khan F, Begier E, Swerdlow DL, Jodar L, Falsey AR. Rates of medically at-tended RSV among US adults: A systematic review and meta-analysis. Open Forum Infect Dis 2022; 9(7):ofac300. PMID: 35873302.
6. Lively JY, Curns AT, Weinberg GA, et al. Respiratory syncytial virus–associated outpatient vis-its among children younger than 24 months. J Pediatric Infect Dis Soc 2019; 8(3):284-286. PMID: 30840770.
7. Gatt D, Martin I, AlFouzan R, Moraes TJ. Prevention and treatment strategies for respiratory syncytial virus (RSV). Pathogens 2023; 12(2):154. PMID 36839426.
8. Safrin S. Basic & Clinical Pharmacology. 15th edition. McGraw-Hill, 2021.
9. CDC updates RSV vaccination recommendation for adults, Centers for Disease Control and Prevention. 2024. https://www.cdc.gov/media/releases/2024/s-0626-vaccination-adults.html. Accessed July 17, 2024.
10. Abrysvo™ ™ , U.S. Food and Drug Administration. 2023. https://www.fda.gov/vaccines-blood-biologics/Abrysvo™ ™ . Accessed June 6, 2024.
11. Venkatesan P. First RSV vaccine approvals. Lancet Microbe 2023; 4(8):e577. PMID: 37390835.
12. Mastrangelo P, Chin AA, Tan S, et al. Identification of RSV fusion protein interaction domains on the virus receptor, nucleolin. Viruses 2021; 13(2):261. PMID 33567674.
13. Kampmann B, Madhi SA, Munjal I, et al. Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants. N Engl J Med 2023; 388(16):1451-1464. PMID: 37018474.
14. Respiratory syncytial virus (RSV) vaccine safety, Centers for Disease Control and Prevention. https://www.cdc.gov/vaccine-safety/vaccines/rsv.html. Accessed Febuary 10, 2025.
15. Vaers Home. VAERS. Accessed June 6, 2024. https://vaers.hhs.gov/data.html.
16. Sarah C. The strobe guidelines. Saudi J Anaesth 2019; 13(Suppl 1):S31-S34. PMID: 30930717.
17. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data cap-ture (REDCap) – A metadata-driven methodology and workflow process for providing transla-tional research informatics support. J Biomed Inform 2009; 42(2):377-381. PMID: 18929686.

18. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international com-munity of software partners. J Biomed Inform 2019; 95:103208. PMID: 31078660.
19. Walsh EE, Falsey AR, Scott DA, et al. A randomized phase 1/2 study of a respiratory syncytial virus prefusion F vaccine. J Infect Dis 2021; 225(8):1357-1366. PMID: 34932102.
20. Walsh EE, Pérez Marc G, Zareba AM, et al. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. N Engl J Med 2023; 388(16):1465-1477. PMID: 37018468.
21. Banks I, Baker P. Men and primary care: Improving access and outcomes. Trend Urol Mens Heal 2013; 4(5):39-41. doi:10.1002/tre.357.
22. Höhn A, Gampe J, Lindahl-Jacobsen R, Christensen K, Oksuyzan A. Do men avoid seeking medical advice? A register-based analysis of gender-specific changes in primary healthcare use after first hospitalisation at ages 60+ in Denmark. J Epidemiol Community Health 2020; 74(7):573-579. PMID: 32303595.
23. Leroux-Roels I, Davis MG, Steenackers K, et al. Safety and immunogenicity of a respiratory syncytial virus prefusion F (RSVPREF3) candidate vaccine in older adults: Phase 1/2 random-ized clinical trial. J Infect Dis 2022; 227(6):761-772. PMID: 35904987.
24. Arexvy™ (respiratory syncytial virus vaccine, adjuvanted) [package insert]. Rixensart, Bel-gium: GlaxoSmithKline Biologicals; 2025.
25. Hervé C, Laupèze B, Del Giudice G, Didierlaurent AM, Tavares Da Silva F. The how's and what's of vaccine reactogenicity. NPJ Vaccines 2019; 4:39. PMID: 31583123.

Keywords: *respiratory syncytial viruses, vaccines, adverse effects*