Preliminary Analysis of Guillain-Barré Syndrome (GBS) following RSV Vaccination among adults 65 years and older

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MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)
Respiratory Syncytial Virus (RSV) Vaccines, Adults
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Outline

- Study Methods
- Statistical Analysis
- Study Results
- Limitations
- Conclusion
- Appendix

Study Methods

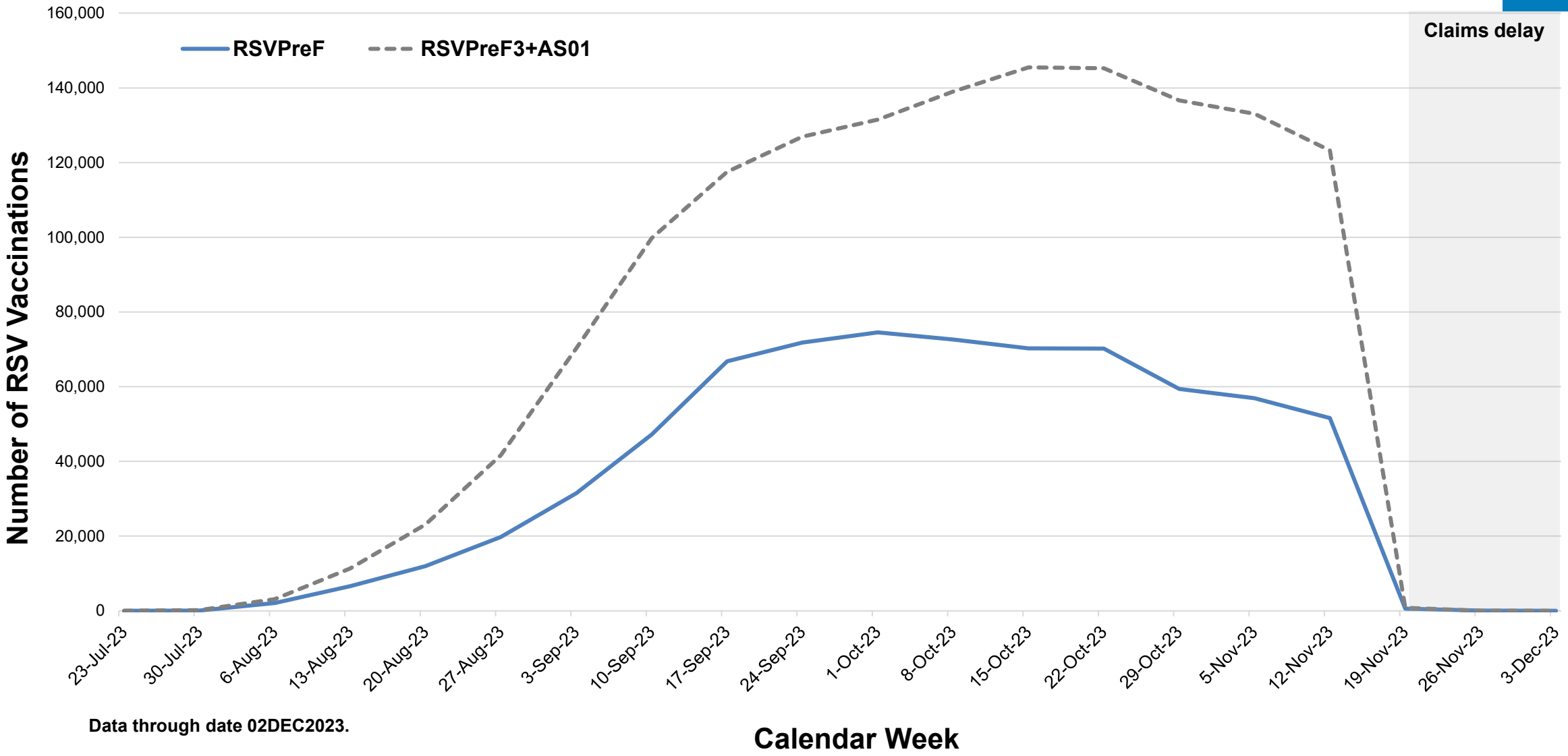
Study Objective	To evaluate preliminary rates of Guillain-Barré Syndrome (GBS) following one dose of either RSVPreF3+AS01 (AREXVY) or RSVPreF (ABRYSVO) vaccine and to compare the observed rates of GBS to the historical control (expected) rates
Study Design	Retrospective cohort analysis with a historical comparator group
Data Sources	Centers for Medicare & Medicaid Services (CMS) administrative claims and enrollment information derived from CMS Medicare Shared Systems Data (SSD) (Medicare Parts A, B, and D)
Study Population	CMS Medicare Beneficiaries ages 65 years and older, enrolled in Medicare Fee-for-Service (FFS) (Parts A and B) and Medicare Part D on the date of the first observed RSV vaccination
Study Period	• RSVPreF: May 31, 2023 – Dec 2, 2023 • RSVPreF3+AS01: May 3, 2023 – Dec 2, 2023
Exposures	One dose of either RSVPreF or RSVPreF3+AS01 that occurred after RSV vaccine authorization and prior to the data through date, i.e., Dec 2, 2023
Health Outcome	GBS (Risk Window: 1-42 days; Care Setting: Inpatient – primary position only)

Statistical Analyses

- The expected number of outcomes are standardized by age and sex
- The analyses are adjusted for observational delay based on estimates from historical data
- Incidence Rate Ratios (IRRs) are calculated by dividing observed rates by expected rates; corresponding 95% confidence intervals (CIs) are provided
- Estimation of GBS positive-predictive value (PPV)-adjusted rates is based on multiple imputed datasets
  - Chart review, PPV for GBS: 71% (95% CI: 63%, 79%)*

**Arya,D.P., et al. Surveillance for Guillain-Barré syndrome after 2015-2016 and 2016-2017 influenza vaccination of Medicare beneficiaries. Vaccine, 2019. 37(43): p. 6543-6549.*

RSV Vaccinations by Calendar Week and Vaccine Brand



Data through date 02DEC2023.

Results

Incidence Rate Ratio (IRR) and 95% Confidence Interval (CI) of GBS Following an RSV vaccination, stratified by age group and sex

RSV Vaccine Exposure	Age Group (years)	Sex	Eligible Vaccines	Observed Events	Incidence Rate Ratio (IRR)	IRR 95% Confidence Interval (CI)
RSVPreF	**Overall**	**Overall**	**682,267**	**13**	**6.9**	**(3.7, 11.9)**
RSVPreF	**65-74**	**Male**	**141,269**	**<11**	**5.8**	**(1.2, 17.0)**
RSVPreF	**75-84**	**Male**	**121,913**	**<11**	**8.5**	**(2.3, 21.8)**
RSVPreF	85+	Male	28,091	<11	13.3	(0.3, 74.2)
RSVPreF	65-74	Female	191,409	<11	4.9	(0.6, 17.8)
RSVPreF	**75-84**	**Female**	**154,152**	**<11**	**8.5**	**(1.8, 24.7)**
RSVPreF	85+	Female	45,433	<11	-	--
RSVPreF3+AS01	**Overall**	**Overall**	**1,379,335**	**<11**	**2.8**	**(1.3, 5.1)**
RSVPreF3+AS01	65-74	Male	287,780	<11	2.0	(0.2, 7.2)
RSVPreF3+AS01	75-84	Male	246,852	<11	3.3	(0.7, 9.6)
RSVPreF3+AS01	85+	Male	55,292	<11	-	--
RSVPreF3+AS01	65-74	Female	394,413	<11	3.8	(0.8, 11.0)
RSVPreF3+AS01	75-84	Female	310,546	<11	2.9	(0.4, 10.6)
RSVPreF3+AS01	85+	Female	84,452	<11	-	--

Red font indicates statistically significant elevation in GBS risk.

Summary

- A total of **2,061,602** RSV vaccine doses were observed
  - RSVPreF: 682,267 doses
  - RSVPreF3+AS01: 1,379,335 doses
- GBS was observed for both vaccines post-RSV vaccination
  - RSVPreF: 13 cases
  - RSVPreF3+AS01: <11 cases
- An elevated IRR was observed for GBS following RSV vaccination
  - RSVPreF: 6.9 (95% CI: 3.7, 11.9)
  - RSVPreF3+AS01: 2.8 (95% CI: 1.3, 5.1)
- Also observed was elevated risk by age groups and sex, but the number of cases were small by subgroups (<5)

Results – PPV-adjusted Analyses

Adjusted IRR and 95% CI of GBS Following an RSV vaccination

RSV Vaccine Exposure	Eligible Vaccines	IRR	IRR* 95% Confidence Interval (CI)	GBS Rate** per 1 million doses	95% CI**
RSVPreF	**682,267**	**6.9**	**(1.9, 12.0)**	**25.1**	**(6.7, 43.4)**
RSVPreF3+AS01	1,379,335	2.8	(0.5, 5.0)	10.0	(1.7, 18.3)

Summary

- An elevated IRR was observed for GBS following RSVPreF vaccination
  - 6.9 (95% CI: 1.9, 12.0)
- A non-statistically significant elevated IRR was observed for GBS following RSVPreF3+AS01 vaccination
  - 2.8 (95% CI: 0.5, 5.0)
- Adjusted GBS rates per 1 million doses:
  - RSVPreF: 25.1 (95% CI: 6.7, 43.4)
  - RSVPreF3+AS01: 10.0 (95% CI: 1.7, 18.3)
- Multiple imputation was not successful in estimating IRR for age and sex subgroups due to the small number of cases
- Medical charts for observed cases have been requested and will be reviewed

Red font indicates statistically significant elevation in GBS risk.
**Adjusted estimate based on multiple imputation.*
***Accounts for claims delay and 1-42 day risk window for GBS. The GBS rate per 1 million doses assuming a 1-21 risk window: RSVPreF 12.5 (95% CI 3.4, 21.7); RSVPreF3+AS01, 5.0 (95% CI 0.8, 9.2).*

Limitations

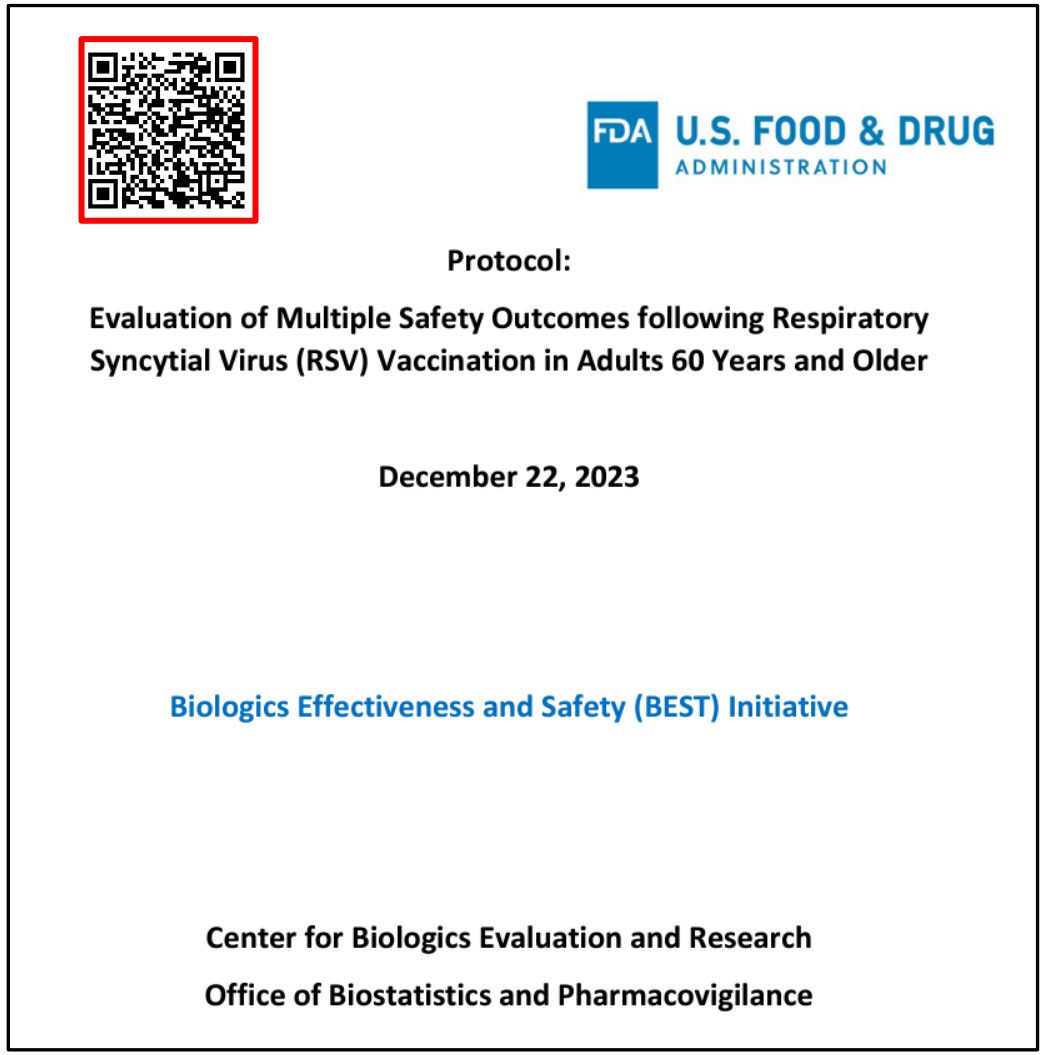
- The observed vs. expected analysis utilizes aggregate historical rates rather than individual historical persons as comparators, increasing the potential for confounding and bias

- Health outcomes are identified by International Classification of Disease – 10th Revision – Clinical Modification (ICD-10-CM) diagnosis codes in administrative claims databases, hence are subject to outcome misclassification

- GBS is a rare outcome, the number of cases are small, the uncertainty is high, therefore it poses a challenge for verification of a potential signal

Conclusions

- An elevated risk of GBS was observed following both RSV vaccines
  - RSVPreF (n=13 cases) and RSVPreF3+AS01 (n<11 cases)
- Results did not remain statistically significant for RSVPreF3+AS01 when adjusting for the PPV
- Safety monitoring following RSV vaccination using a self-controlled case series design is planned and will provide more conclusive evidence of the potential risks following RSV vaccination



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Protocol:

Evaluation of Multiple Safety Outcomes following Respiratory Syncytial Virus (RSV) Vaccination in Adults 60 Years and Older

December 22, 2023

Biologics Effectiveness and Safety (BEST) Initiative

Center for Biologics Evaluation and Research

Office of Biostatistics and Pharmacovigilance

https://bestinitiative.org/wp-content/uploads/2023/12/BEST_RSV_Safety_Older_Adults_2023-2024.pdf

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www.bestinitiative.org

Questions?