Bio Biotechnology Innovation Organization

New Vaccines in Development

May 10, 2023

Dr. Melinda Wharton

Phyllis Arthur

Session Agenda

- Welcome – Dr. Melinda Wharton
- Focus on RSV
  - Impact of RSV Disease in Adults
    - Dr. Katherine Fleming-Dutra, Medical Officer, CDC
  - Preventive Vaccines in late-stage development – Intro – Phyllis Arthur
    - Dr. Leonard Friedland, VP, Scientific Affairs and Public Health, Vaccines, GSK
    - Dr. Annaliesa Anderson, SVP, Head of Vaccine Research & Development, Pfizer
    - Dr. Christine Shaw, VP, Portfolio Head, Respiratory Vaccines, Moderna
  - Respiratory syncytial virus (RSV) illness prevention: Prevention products under ACIP consideration
    - Dr. Michael Melgar, Medical Officer, CDC
  - Q&A
- Vaccines & Immunizations in the Pipeline – Phyllis Arthur

Epidemiology of Respiratory Syncytial Virus (RSV)

May 10, 2023

Katherine Fleming-Dutra, MD

Co-Lead, ACIP Work Group for Maternal/Pediatric RSV
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

RSV is the leading cause of hospitalization in U.S. infants

- Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2[1]
- 79% of children hospitalized with RSV aged <2 years had no underlying medical conditions[2]
- 2-3% of all infants will be hospitalized for RSV[2,3]

Image: Goncalves et al. Critical Care Research and Practice 2012

[1]Glezen et al, Arch Dis Child, 1986; [2]Langley & Anderson, PIDJ, 2011; [3]Hall et al, Pediatrics, 2013

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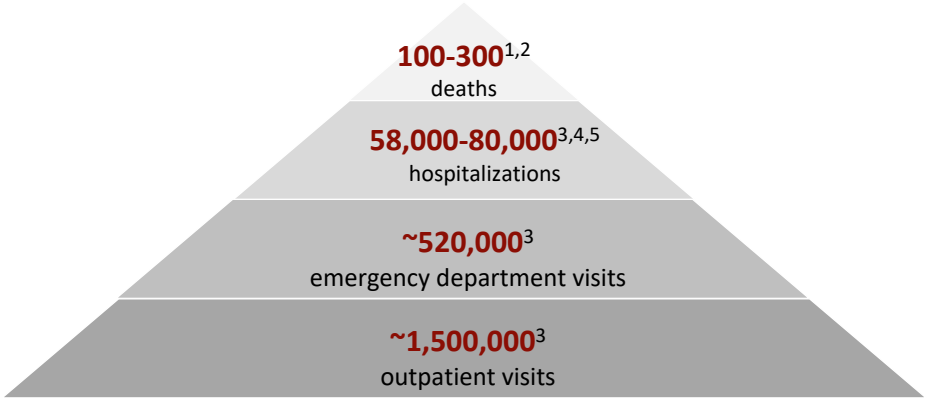
Each year among U.S. children aged less than 5 years, RSV is associated with…



[1]Thompson et al, JAMA, 2003; [2]Hansen et al, JAMA Network Open, 2022; [3]Hall et al, NEJM, 2009; [4]Rha et al., Peds, 2020; [5]McLaughlin et al, J Infect Dis, 2022; (*estimate 80,000 hospitalizations in infants <1y)

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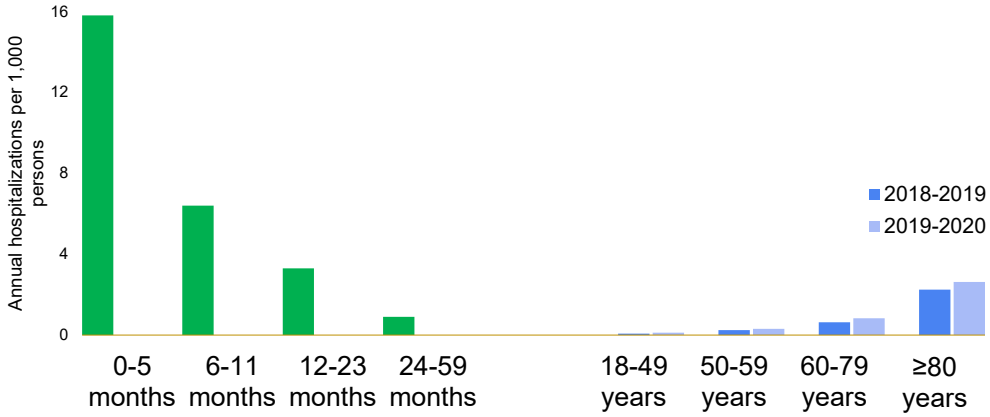
Estimated annual rate of RSV hospitalizations among children aged <5 and adults aged ≥18 years, United States



New Vaccine Surveillance Network, 2016–2020
Presented at ACIP meeting; McMorrow ML; 2022 Jun 22–23; Atlanta, GA.
https://www.cdc.gov/vaccines/acip/meetings/index.html

RSV-NET, 2018–2020
Presented at 12th International RSV Symposium; Havers FP; 2022 Sep 29 – Oct 2; Belfast, United Kingdom.

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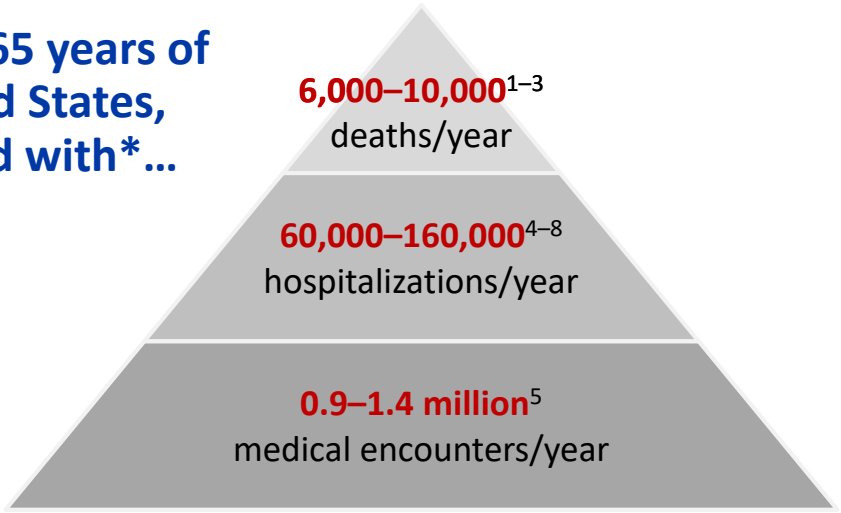
Among adults ≥65 years of age in the United States, RSV is associated with*…

*There is substantial uncertainty in burden of disease, reflected in wide ranges here.



1. Thompson et al, JAMA (2003): https://doi.org/10.1001/jama.289.2.179
2. Matias et al, Influenza Other Respi Viruses (2014): https://doi.org/10.1111/irv.12258
3. Hansen et al, JAMA Network Open (2022): https://doi.org/10.1001/jamanetworkopen.2022.0527
4. Widmer et al, JAMA Network Open (2012): https://doi.org/10.1093/infdis/jis309
5. McLaughlin et al, Open Forum Infect Dis (2022): https://doi.org/10.1093/ofid/ofac300
6. Zheng et al, Pneumonia (2022): https://doi.org/10.1186/s41479-022-00098-x
7. Branche et al, Clinical Infect Dis (2022): https://doi.org/10.1093/cid/ciab595
8. CDC RSV-NET data 2016–2020 (unpublished)

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Adults with certain underlying medical conditions are at higher risk of RSV hospitalization

- Immune compromise, especially hematopoietic stem cell transplant and solid organ transplant
- Cardiovascular disease (e.g., congestive heart failure)
- Diabetes mellitus
- Chronic obstructive pulmonary disease (COPD)
- Asthma

1. Anderson et al, Diagn Microbiol Infect Dis (2016): https://doi.org/10.1016/j.diagmicrobio.2016.02.025
2. Prasad et al, Clin Infect Dis (2020): https://doi.org/10.1093/cid/ciaa730
3. Kujawski et al, Plos One (2022): https://doi.org/10.1371/journal.pone.0264890
4. Branche et al, Clin Infect Dis (2022): https://doi.org/10.1093/cid/ciab595

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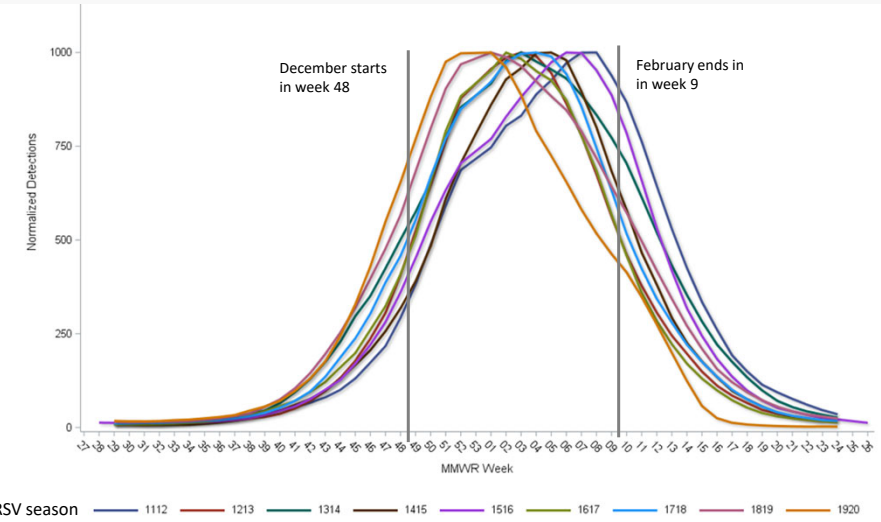
During 2011-2020, RSV circulation was highly seasonal in the U.S. with predictable peak activity during December – February annually



RSV Surveillance Data - NREVSS | CDC

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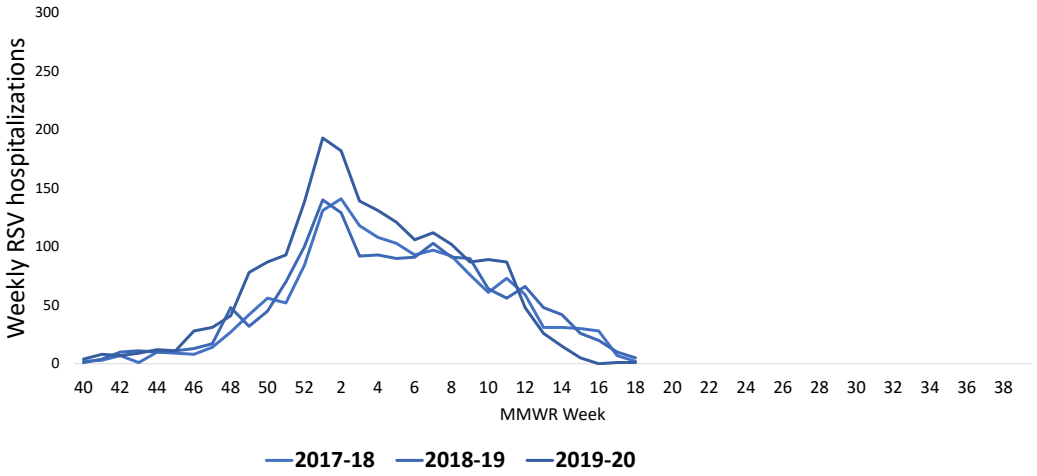
RSV Hospitalizations in adults ≥65 by season: RSV-NET 2017–2020



RSV-NET: unpublished data. Surveillance for 2015-16 through 2019-20 seasons were conducted from October – April; for 2020-21 and 2021-22 surveillance was conducted continuously from October – September. Data shown for 2022-23 season is from October – December 2022.

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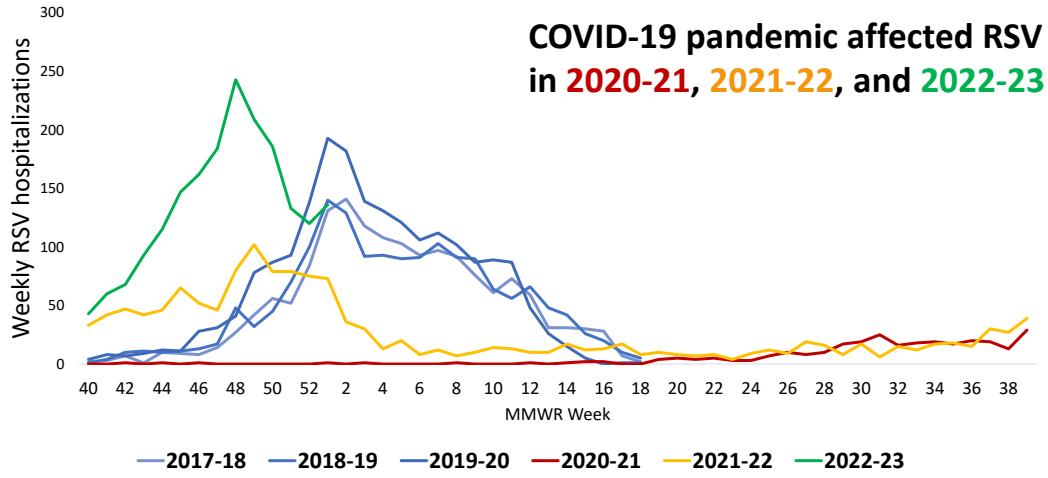
RSV Hospitalizations in adults ≥65 by season: RSV-NET 2017–2023



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Acknowledgements

- Michael Melgar
- Amadea Britton
- Fiona Havers
- Jefferson Jones
- Meredith McMorrow
- Mila Prill
- Lauren Roper
- Diya Surie

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Focus on RSV

RSV Vaccines in Late-Stage Development

- Dr. Leonard Friedland, VP, Scientific Affairs and Public Health, Vaccines, GSK
- Dr. Annaliesa Anderson, SVP, Head of Vaccine Research & Development, Pfizer
- Dr. Christine Shaw, VP, Portfolio Head, Respiratory Vaccines, Moderna
- Dr. Michael Melgar, Medical Officer, CDC

- Q&A

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GSK's RSV Adult Vaccine

Leonard Friedland, MD
Vice President, Director Scientific Affairs and Public Health, GSK

National Adult and Influenza Immunization Summit
Session on RSV Vaccines
May 10, 2023

GSK

This presentation is provided in response to the request from the organizers of NAIIS.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

Disclosure: Leonard Friedland is employed by GSK where he is a vaccine research scientist.

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AREXVY (Respiratory Syncytial Virus Vaccine, Adjuvanted)

FDA Approval received May 3, 2023

Indication	*AREXVY* is a vaccine indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in individuals 60 years of age and older.
Dosage & Administration	For intramuscular injection only. Administer a single dose (0.5 mL) as an intramuscular injection.

Prescribing Information for *AREXVY*.

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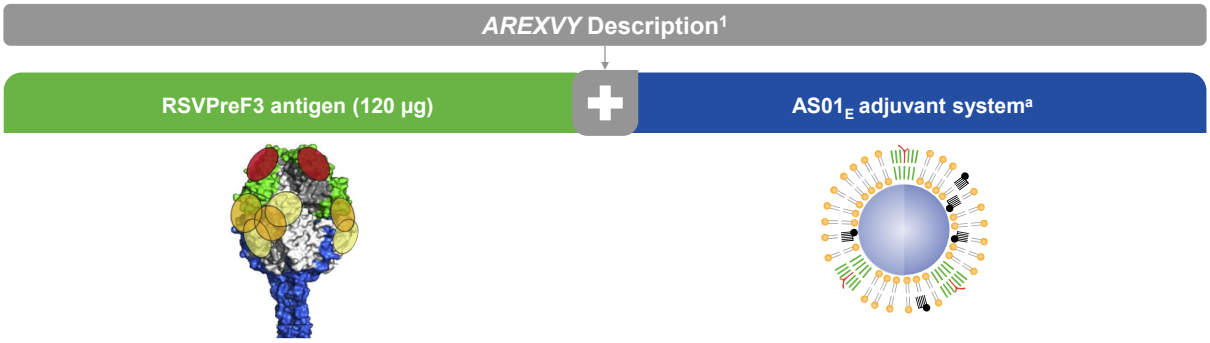
AREXVY (Respiratory Syncytial Virus Vaccine, Adjuvanted)

Mechanism of Action: AREXVY induces an immune response against RSVpreF3 that protects against LRTD caused by RSV.[1]



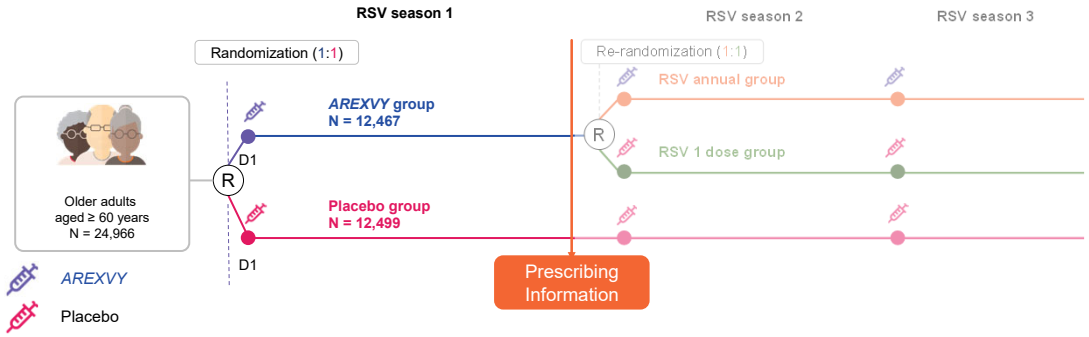
1. Prescribing Information for *AREXVY*.
Image of F protein reproduced from Graham BS, et al. *Curr Opin Immunol.* 2015;35:30–38, Copyright 2015, with permission from Elsevier.
[a]AS01$_E$ adjuvant system is composed of two immunostimulants (MPL [3-*O*-desacyl-4'-monophosphoryl lipid A] and QS-21 [a saponin purified from plant extract *Quillaja saponaria* Molina]).

GSK

LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus; RSVPreF3 = recombinant respiratory syncytial virus glycoprotein F stabilized in pre-fusion conformation

Ongoing Phase 3 clinical efficacy trial[1]

A randomized, placebo-controlled, observer-blind, multi-country efficacy study



The primary objective was to demonstrate the efficacy of *AREXVY* in the prevention of a first episode of confirmed RSV-A and/or B-associated LRTD during the first season.

1. Prescribing Information for *AREXVY*.
Confirmed RSV cases were determined by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) on a nasopharyngeal swab. [a]LRTD was defined based on the following criteria: the participant must have experienced at least 2 lower respiratory symptoms/signs, including at least 1 lower respiratory sign for at least 24 hours, or experienced at least 3 lower respiratory symptomsfor at least 24 hours. Lower respiratory symptoms included: new or increased sputum, new or increased cough, new or increased dyspnea (shortness of breath). Lower respiratory signs included: new or increased wheezing, crackles/rhonchi, respiratory rate ≥20 respirations/min, low or decreased oxygen saturation (O2 saturation <95% or ≤90% if baseline is <95%), need for oxygen supplementation.
LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus

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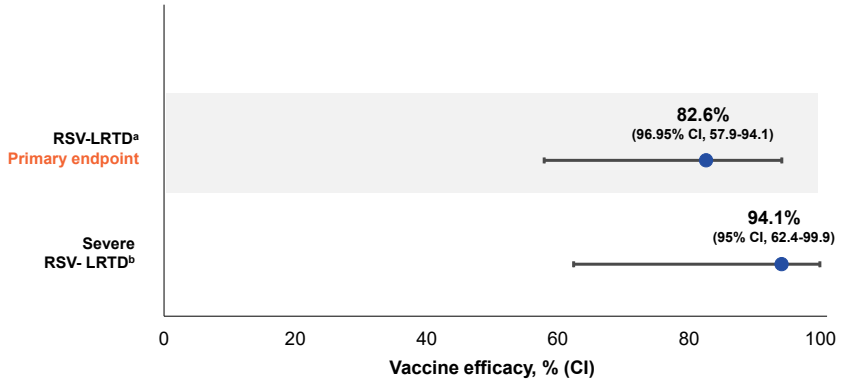
Vaccine efficacy in prevention of RSV-LRTD (primary endpoint) and severe RSV-LRTD[1]



	AREXVY N = 12,466	Placebo N = 12,494
RSV-LRTD[a] Primary endpoint	n=7	n=40
Severe RSV- LRTD[b]	n=1	n=17

N = Number of participants included in each group; n= Number of participants having first occurrence of RSV-confirmed LRTD occurring from Day 15 post-vaccination.

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[b]Severe LRTD was defined as an RT-PCR confirmed RSV-associated LRTD with at least 2 lower respiratory signs, or as an RT-PCR confirmed RSV-associated LRTD episode preventing normal, everyday activities.
CI = confidence interval; LRTD = lower respiratory tract disease; RT-PCR = reverse-transcriptase polymerase chain reaction; RSV = respiratory syncytial virus

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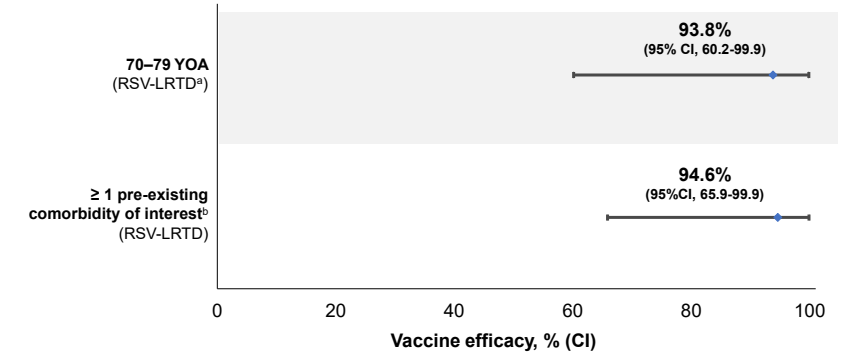
Vaccine efficacy in age subgroup 70-79 years and for participants with at least one comorbidity of interest[1]



	AREXVY	Placebo
70-70 YOA RSV-LRTD	N=4,487	N=4,487
	n=1	n=16
≥ 1 pre-existing comorbidity of interest[b] (RSV-LRTD)	N=4937	N=4861
	n=1	n=18

N = Number of participants included in each group; n= Number of participants having first occurrence of RSV-confirmed LRTD occurring from Day 15 post-vaccination.

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[b]COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, congestive heart failure, advanced liver or renal disease.
CI = confidence interval; LRTD = lower respiratory tract disease; RT-PCR = reverse-transcriptase polymerase chain reaction; RSV = respiratory syncytial virus; YOA = year of age

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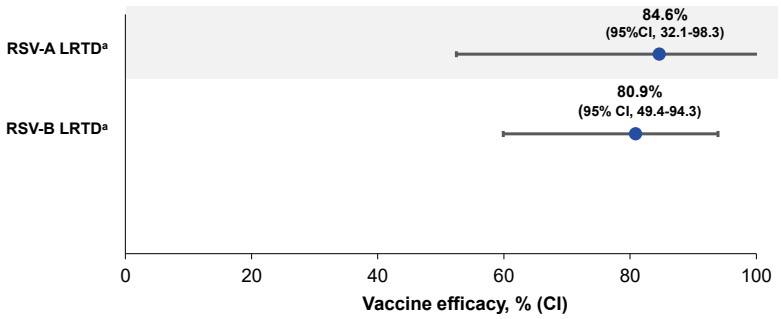
Vaccine efficacy against RSV A- and RSV B-associated LRTD disease[1]



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Confirmed RSV cases were determined by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR) on a nasopharyngeal swab. [a] LRTD was defined based on the following criteria: the participant must have experienced at least 2 lower respiratory symptoms/signs, including at least 1 lower respiratory sign for at least 24 hours, or experienced at least 3 lower respiratory symptomsfor at least 24 hours. Lower respiratory symptoms included: new or increased sputum, new or increased cough, new or increased dyspnea (shortness of breath). Lower respiratory signs included: new or increased wheezing, crackles/rhonchi, respiratory rate ≥20 respirations/min, low or decreased oxygen saturation (O2 saturation <95% or ≤90% if baseline is <95%), need for oxygen supplementation.
CI = confidence interval; LRTD = lower respiratory tract disease;RSV = respiratory syncytial virus

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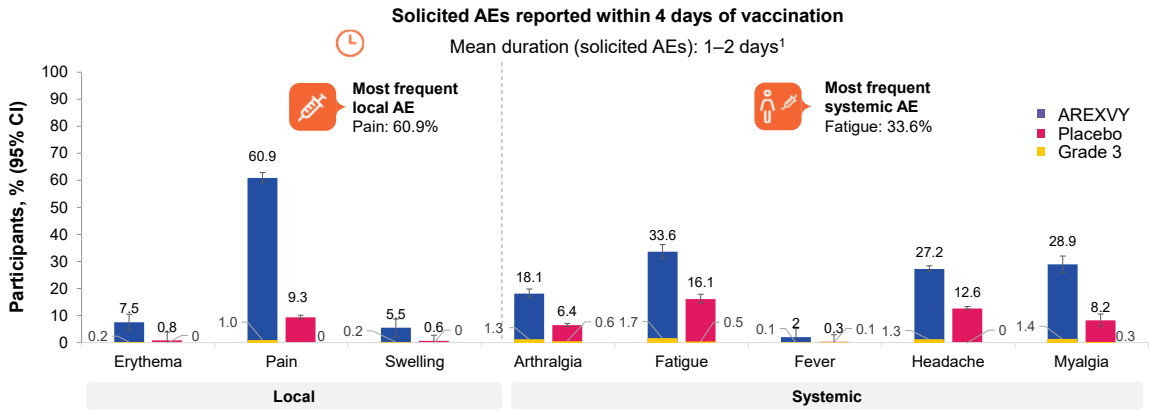
Safety and reactogenicity results[1]

Solicited AEs (Any & Grade 3) reported within 4 days of vaccination (Solicited Safety Set)



1. Prescribing Information for *AREXVY*.
A subset of study participants (solicited safety set) was monitored for solicited adverse reactions using standardized paper diary cards during the 4 days (i.e., day of vaccination and the next 3 days) following a dose of *AREXVY* or placebo; 879 participants received *AREXVY* and 874 participants received placebo. Error bars show 95% CIs for total AEs. Grade 3 Erythema and swelling is diameter > 100 mm; Grade 3 pain defined as significant pain at rest, preventing normal everyday activities; Grade 3 fever defined as temperature > 39°C/102.2°F; Grade 3 headache, fatigue, myalgia, arthralgia are defined as events preventing normal activity. In the solicited safety set, the local administration site adverse reactions reported with AREXVY had a median duration of 2 days, and the systemic adverse reactions reported with AREXVY had a median duration ranging between 1 and 2 days. AE = adverse event; CI = confidence interval.

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AREXVY (Respiratory Syncytial Virus Vaccine, Adjuvanted)

How Supplied	***AREXVY* is supplied as 2 components: A single-dose vial of lyophilized antigen component (powder) and a single-dose vial of adjuvant suspension component (liquid) (packaged without syringes or needles).**
Dosage and Administration	Administer a single dose (0.5 mL) as an intramuscular injection.
Storage	Storage before reconstitution: Store refrigerated between 2¶C and 8¶C (36¶F and 46¶F). Store in the original package in order to protect vials from light. Do not freeze. Discard if the adjuvant suspension component has been frozen. Storage after reconstitution: Administer immediately or store in the refrigerator between 2¶C and 8¶C (36¶F to 46¶F) or at room temperature [up to 25¶C (77¶F)] for up to 4 hours prior to use. Protect vials from light. Discard reconstituted vaccine if not used within 4 hours. Do not freeze. Discard if the vaccine has been frozen.
Presentation	See table below

Presentation	Carton NDC Number	Components	
		Adjuvant Suspension Component (liquid)	Lyophilized Antigen Component (powder)
Outer carton of 10 doses	58160-848-11	10 vials NDC 58160-744-03	10 vials NDC 58160-723-03

GSK

1. Prescribing Information for *AREXVY*.

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Respiratory syncytial virus (RSV) illness prevention: Prevention products under ACIP consideration

May 10, 2023
Michael Melgar, MD

Co-Lead, ACIP Work Group for RSV in Adults
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention

Disclosures

- Dr. Melgar has no financial relationship(s) with companies whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients
- The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention

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Maternal RSV vaccination

Maternal vaccination: Policy question being considered by ACIP

- Should the **Pfizer RSV bivalent prefusion F vaccine** be recommended for all pregnant people as a single dose given at 24–36 weeks gestation?
- This recommendation would be considered in the context of the current standard of care for prevention of RSV disease in infants at the time of ACIP vote.

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Key consideration for RSV bivalent prefusion F vaccine: Number of total lifetime doses

- All pregnant people in the trial received their first and only dose of RSV vaccine
- Currently there are no data available on
  - Efficacy of the first lifetime dose during subsequent pregnancies
  - Safety of additional doses given in subsequent pregnancies

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Next steps for Pfizer RSV bivalent prefusion F vaccine (tentative)

- June 2023
  - Summary of GRADE
  - Cost effectiveness analysis
  - EtR
- October 2023
  - ACIP vote (if product is licensed by this time)

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Older adult RSV vaccination

Older adult vaccination: Policy question being considered by ACIP

- Should vaccination with **GSK RSVpreF3 vaccine** (120 µg antigen + AS01E adjuvant, 1 dose IM) be recommended for all older adults*?
- Should vaccination with **Pfizer RSVpreF vaccine** (120 µg antigen, 1 dose IM) be recommended for all older adults*?

*Age ≥60 years? Age ≥65 years? Other?

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Phase 3 trial vaccine efficacy estimates, by age group

Age in years	**GSK:** RSV LRTD[a] VE (%) (96.95% CI)[b] *Case split: vaccine/placebo*	**Pfizer:** RSV LRTI[c], **≥2** symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*	**Pfizer:** RSV LRTI[c], **≥3** symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*
≥60	**82.6** (57.9, 94.1) *7/40*	**66.7** (28.8, 85.8) *11/33*	**85.7** (32.0, 98.7) *2/14*
60–69	81.0 (43.6, 95.3)[e] *4/21*	57.9 (–7.4, 85.3) *8/19*	77.8 (–18.7, 98.1) *2/9*
70–79	93.8 (60.2, 99.9)[e] *1/16*	77.8 (–18.7, 98.1) *2/9*	100.0 (–573.8, 100.0) *0/2*
≥80	33.8 (–477.7, 94.5)[e] *2/3*	80.0 (–104.3, 99.7) *1/5*	100.0 (–191.2, 100.0) *0/3*

[a]Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours. Events diagnosed on or after day 15 post-injection (vaccine or placebo). Median follow up 6.7 months.
[b]Efficacy estimated using the Poisson method, adjusted for age and geographic location. Age group-specific efficacy adjusted for geographic location only.
[c]Lower respiratory tract illness: ≥2 (or ≥3) lower respiratory symptoms/signs lasting more than 1 day. Events diagnosed on or after day 15 post-injection (vaccine or placebo). Mean duration of surveillance 7 months.
[d]Efficacy based on case count ratio. Confidence interval based on the conditional exact test based on the binomial distribution, adjusted by Pocock error spending.
[e]95% confidence interval. Not adjusted for multiplicity and cannot be used in place of a hypothesis test.

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Papi A, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. N Engl J Med. 2023 Feb 16;388(7):595-608. doi: 10.1056/NEJMoa2209604.
Walsh EE, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med. 2023 Apr 20;388(16):1465-1477. doi: 10.1056/NEJMoa2213836.

Phase 3 trial vaccine efficacy estimates, by age group

Age in years	GSK: RSV LRTD[a] VE (%) (96.95% CI)[b] *Case split: vaccine/placebo*	Pfizer: RSV LRTI[c], ≥2 symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*	Pfizer: RSV LRTI[c], ≥3 symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*
≥60	82.6 (57.9, 94.1) *7/40*	66.7 (28.8, 85.8) *11/33*	85.7 (32.0, 98.7) *2/14*
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70–79	93.8 (60.2, 99.9)[e] *1/16*	77.8 (–18.7, 98.1) *2/9*	100.0 (–573.8, 100.0) *0/2*
≥80	33.8 (–477.7, 94.5)[e] *2/3*	80.0 (–104.3, 99.7) *1/5*	100.0 (–191.2, 100.0) *0/3*

[a]Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours. Events diagnosed on or after day 15 post-injection (vaccine or placebo). Median follow up 6.7 months.
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Papi A, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. N Engl J Med. 2023 Feb 16;388(7):595-608. doi: 10.1056/NEJMoa2209604.
Walsh EE, et al. Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults. N Engl J Med. 2023 Apr 20;388(16):1465-1477. doi: 10.1056/NEJMoa2213836.

Phase 3 trial vaccine efficacy estimates, by risk group

Population	GSK: RSV LRTD[a] VE (%) (96.95% CI)[b] *Case split: vaccine/placebo*	Pfizer: RSV LRTI[c], ≥2 symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*	Pfizer: RSV LRTI[c], ≥3 symptoms VE (%) (96.66% CI)[d] *Case split: vaccine/placebo*
All participants	82.6 (57.9, 94.1) *7/40*	66.7 (28.8, 85.8) *11/33*	85.7 (32.0, 98.7) *2/14*
≥1 high-risk condition	94.6 (65.9, 99.9)[e] *1/18*	62.5 (–8.4, 89.1) *6/16*	75.0 (–39.1, 97.9) *2/8*
Pre-frail[f]	92.9 (53.4, 99.8)[e] *1/14*	Not evaluated	
Frail[f]	14.9 (–6638.7, 98.9)[e] *1/1*	Not evaluated	

[a]Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours. Events diagnosed on or after day 15 post-injection (vaccine or placebo). Median follow up 6.7 months.
[b]Efficacy estimated using the Poisson method, adjusted for age and geographic location.
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[d]Efficacy based on case count ratio. Confidence interval based on the conditional exact test based on the binomial distribution, adjusted by Pocock error spending.
[e]95% confidence interval. Not adjusted for multiplicity and cannot be used in place of a hypothesis test.
[f]Baseline frailty status was assessed with use of a gait speed test. Walking speed <0.4 m/s or inability to complete test indicated frail status. Walking speed 0.4–0.99 m/s indicated prefrail status.

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Vaccine efficacy may be higher against more severe outcomes

Increasing severity ↓

GSK RSVpreF3		Pfizer RSVpreF	
Outcome	**Efficacy point estimate**	**Outcome**	**Efficacy point estimate**
RSV acute respiratory illness[a]	71.7%	RSV acute respiratory illness[b]	62.1%
RSV lower respiratory tract disease[c]	82.6%	RSV lower respiratory tract illness ≥2 symptoms[d]	66.7%
		RSV lower respiratory tract illness ≥3 symptoms[d]	85.7%
RSV lower respiratory tract disease with ≥2 lower respiratory **signs** or assessed as '**severe**' by investigator	94.1%		

[a] Acute respiratory illness: ≥2 respiratory symptoms/signs for ≥24 hours OR ≥1 respiratory symptom/sign +1 systemic sign for ≥24 hours
[b] Acute respiratory illness: ≥1 respiratory symptom lasting more than 1 day
[c] Lower respiratory tract disease: ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours
[d] Lower respiratory tract illness: ARI with ≥2 or ≥3 lower respiratory signs/symptoms

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Cases of Guillain Barré syndrome (GBS) were reported after vaccination with both investigational vaccines

GSK	Pfizer
No cases of GBS observed in main phase 3 trial (N=24,966 participants, 12,467 received investigational vaccine) 1 case of GBS was reported in a randomized open-label study evaluating safety & long-term immunogenicity of different revaccination intervals (N=1,633 vaccinees) • Onset 9 days after receipt of investigational vaccine	2 cases of GBS (1 case Miller-Fisher syndrome) observed in main phase 3 trial (N=34,283 participants, 17,214 received investigational vaccine) • Onset 8 and 9 days after receipt of investigational vaccine
Total: 1 case of GBS / ~15,000 older adults who received the investigational vaccine	**Total: 2 cases of GBS / ~20,000 older adults who received the investigational vaccine**

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GSK: Acute Disseminated Encephalomyelitis (ADEM)

71-year-old male (Co-Ad group):

- Found lying on the floor shaking and shivering requiring hospitalization with a blood glucose reading of 1.4mmol/L seven days post co-administration of the study vaccines.
- Reported as ADEM based on CT scan, Brighton Collaboration Level 3
- The participant died 22 days after co-administration of the study vaccines.

71-year-old female (Co-Ad group):

Medical history of hyperlipidemia and hypertension

- Tiredness and headaches with intermittent double vision, forgetfulness, confusion, hand shaking, gait ataxia and clumsiness 22 days after the co-administration of the study vaccines
- Reported as ADEM based on symptomatology, Brighton Collaboration Level 3
- The participant demonstrated improvement, but the outcome was reported as not resolved by the time of receipt of the study report.

2 cases of ADEM in Study 007 (N= 890 vaccinees)

No cases of ADEM observed in Study 006 (N=24,966; n=12,467 vaccine) or other studies (N=2,370 vaccinees)

Total: 2 cases/~15,000 vaccinees

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https://www.fda.gov/media/165731/download

ACIP interpretation: Efficacy and safety

- GSK's adjuvanted RSVpreF3 and Pfizer's bivalent RSVpreF vaccines both have demonstrated significant efficacy against lower respiratory tract illness caused by RSV among older adults
  - Trials underpowered to show efficacy against RSV hospitalization
  - Trials underpowered to show efficacy among adults at highest risk of severe RSV disease
- Cases of inflammatory neurologic events have been observed among recipients of each investigational vaccine
- If licensed, post licensure surveillance for both safety and vaccine effectiveness will be critical

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ACIP interpretation: Duration of protection from RSV vaccination among older adults is unknown

- Trials are ongoing, with multiple years of follow up planned
- There is no established immunologic correlate of protection for RSV
- Need for revaccination, and the time interval, are yet to be determined

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ACIP interpretation: If approved, uptake of a novel RSV vaccine among older adults will depend on patient and clinician education

- Adult immunization schedule is becoming more complex
  - Primary series only: pneumococcal vaccines, recombinant zoster vaccine
  - Revaccination: influenza vaccine, COVID-19 vaccine, Td/Tdap, RSV?
- RSV is less well known as a pathogen in adults, compared with influenza* and SARS-CoV-2
- Safety and efficacy of coadministration of influenza, COVID-19, and RSV vaccines should be established

*Hurley LP, et. al. Vaccine 2019; https://doi.org/10.1016/j.vaccine.2018.12.031

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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Questions

Vaccines and Immunizations Pipeline Review

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Vaccines

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Vaccines in Late-Stage Development – Filed with FDA (BLA)

Disease	Number of Products	Under FDA Review
Respiratory Syncytial Virus (RSV)	2	Maternal and older adult indications – slides follow
Men ABCWY	2	Adding conjugated Meningitis B vaccine to the ACWY vaccine for adolescents
Chikungunya	2	Live-attenuated vaccine; Travel and possible use for outbreak control in areas of the U.S.
Dengue	1	Live-attenuated vaccine; Travel and possible pediatric use in endemic areas in the U.S.

Vaccines in Late-Stage Development – COVID Updated Vaccines

COVID / SARS CoV-2	**3**	• **This summer we anticipate that the FDA will conduct a meeting of their Advisory Committee to determine the best variants to include in the current Covid vaccines in the fall.** • **These potentially updated vaccines would be used for both primary and booster vaccination.** • **The current vaccine makers (Pfizer, Moderna and Novavax) would then produce and submit for FDA review these updated vaccines in time for the fall influenza season** • **Once approved, the CDC Advisory Committee on Immunization Practices (ACIP) would issue a set of recommendations advising clinicians and the public on the best use and appropriate populations who should get vaccinated / boosted.**

Vaccines in Late-Stage (Phase III) Development

Disease	Number of Products	Phase III or FDA Review
SARS CoV-2	4	Multiple vaccines using other platform technologies; partnership between US and Indian company
RSV	4	Multiple types of vaccines in development for adults and pregnant women, including mRNA and other novel platforms
Seasonal Influenza	2	New mRNA and protein-based vaccines for seasonal flu prevention; potentially available for this upcoming flu season
Chikungunya	1	Live-attenuated vaccine for travelers
Pneumococcal	1	21-valent pneumonia conjugate vaccine for older adults
Cytomegalovirus (CMV)	1	mRNA based vaccine for healthy young adult women 16-40 to prevent disease in the mother and newborn
Ebola / Marburg	1	Outbreak response in Africa and protection from known bio-threat for the military
Lyme Disease	1	Partnership between two companies; multivalent, recombinant; potentially children and adults

Vaccines in Phase II Development – Part 1

Disease	Number of Products	Phase III or FDA Review
SARS CoV-2	3	Updates to existing vaccines; Multiple vaccines using other platform technologies, including next generation mRNA and tablet form
RSV	2	Various platforms deployed targeting infant RSV vaccination
Seasonal Influenza	5	Includes mRNA flu vaccines, a live universal flu vaccine, a tablet platform and another universal flu approach
Pneumococcal	3	New mechanisms for developing higher valency pneumococcal vaccines
Pertussis	1	Live, attenuated nasal vaccine
Varicella	1	Updated strains
Zoster	1	New mRNA vaccine for older adults
Chikungunya	1	Recombinant vaccine
Norovirus	2	Bi-valent vaccine VLP protein vaccine for infants

Vaccines in Phase II Development – Part 2

Disease	Number of Products	Phase III or FDA Review
HIV	2	Includes vaccines based on adeno and modified vaccinia platforms
Malaria	3	New approaches leveraging mosquitos for malaria vaccines; adjuvanted version of existing vaccine
Group B Streptococcus (GBS)	1	Vaccine focused or pregnant persons for maternal immunization
Cytomegalovirus (CMV)	1	Vaccine focused on healthy young women

Trends is Earlier Stage R&D

- Over the next few years we will see new strategies for COVID-19 vaccines as well as possible seasonal respiratory combination vaccines – SARS CoV2 + Influenza + RSV.
- Several companies are working on vaccines for:
  - HPV, Herpes Simplex, pediatric combination vaccines
  - Hospital-acquired bacterial infections
  - Group B Strep
  - STI vaccines like Gonorrhea
  - New approaches to universal influenza vaccination

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Monoclonal Antibodies

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Monoclonal Antibodies in Development – Trends

- Increasing research of this new preventive / treatment modality is leading to a deep pipeline of possible products
- Many may be indicated for both prevention of severe disease in specific populations as well as treatment of early-stage disease
- The following therapeutic areas have mAbs on interest in development:
  - RSV
  - COVID
  - Influenza
  - HIV (Prep and prevention of severe disease)
  - Hospital-acquired infections for those at risk
  - Treatment and prevention of Sepsis

Questions