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7th EMIRATES FAMILY MEDICINE SOCIETY CONGRESS 2024

DUBAI | UAE | 22 to 24 APRIL

DUBAI WORLD TRADE CENTRE

Organized by

WiredIN

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RSV is a highly contagious seasonal virus that co-circulates with other respiratory viruses

Transmission

RSV is transmitted by inhalation of or contact with infected people's respiratory secretions[1]

RSV can spread within households[2]

RSV spreads easily

Mean basic reproduction number (R_0)*,[3]

R_0 ~ 3

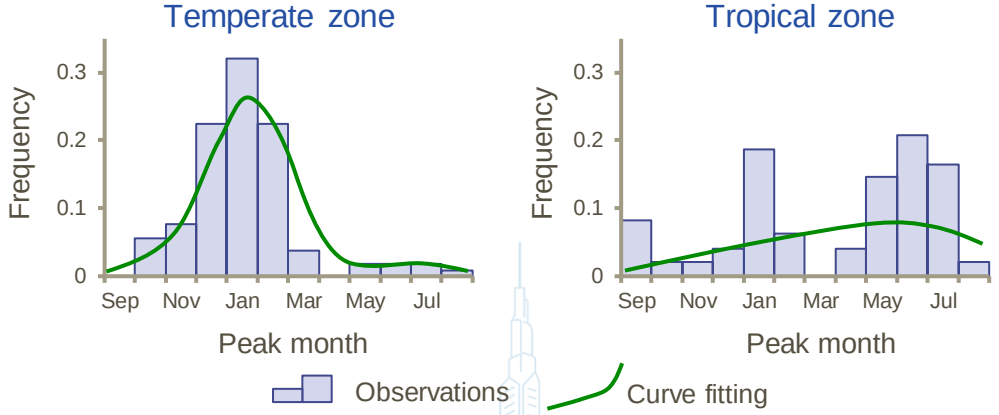
R_0 estimate = 2.82 (at peak timing)[4]
R_0 estimate = 3.02 (on last week)[4]

Infected people are typically contagious for 3−8 days,[1] although older adults may shed virus for longer periods of time[5]

Seasonality

- Seasonal RSV epidemics lasting up to 5 months occur concurrently with epidemic seasons of other respiratory viruses[6,7]

Northern Hemisphere[6]



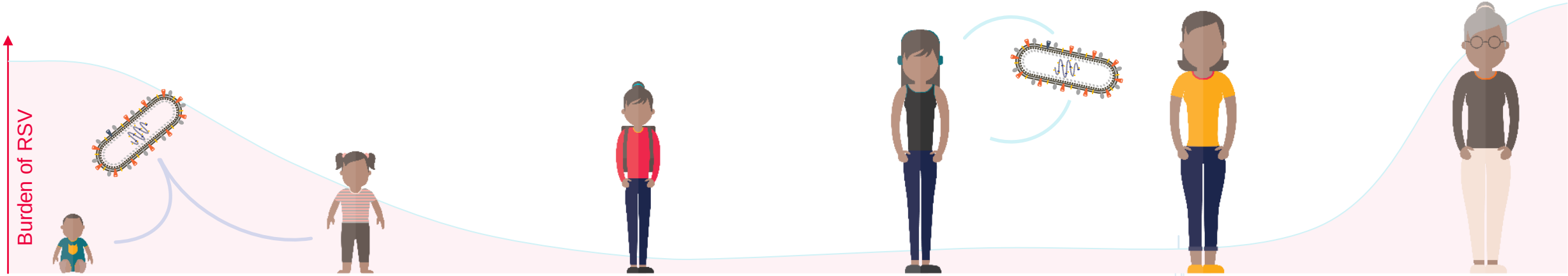
The graphs are reproduced from Bloom-Feshbach K *et al.* 2013[6] where they were published, free of copyright, under Creative Commons CCO public domain dedication

- Normal RSV seasonality was disrupted by COVID-19 mitigation measures, increasing the possibility of out-of-season outbreaks post-pandemic[8–11]
- During the 2022–23 season, a rise in viral respiratory diseases was observed due to increased circulation of RSV and influenza early in the season, co-circulating with other respiratory viruses e.g. SARS-CoV-2.[12,13]

*Meaning that, in a fully susceptible population, on average each infected person infects three other people.
COVID-19, coronavirus disease 2019
For references, please see notes page

RSV is a disease of all ages

Natural immunity is short-lived, and RSV may cause repeated infections throughout life, not only in childhood



Virtually all children will have been infected with RSV by age 2 years[1]

Immune response after natural infection is incomplete and is short-lived[2,3]
RSV reinfections may occur throughout life[3]

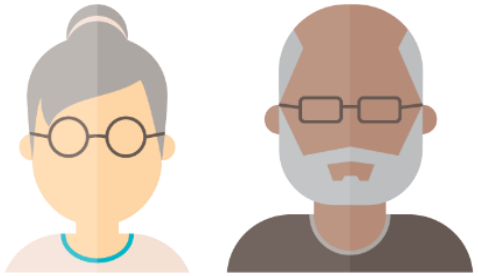
Older adults are at high risk of severe RSV infection. Those with certain comorbidities are at even greater risk[4,5]

The figure is for illustrative purposes only

1. Centers for Disease Control and Prevention (CDC), 2023. Symptoms and Care. http://www.cdc.gov/rsv/about/symptoms.html(accessed October 2023);
2. Openshaw PJM *et al. Annu Rev Immunol* 2017;35:501–532; 3. Walsh E *et al. Clin Chest Med* 2017;38(1):29–36; 4. Branche AR *et al. Clin Infect Dis* 2022;74(6):1004–1011; 5. Centers for Disease Control and Prevention (CDC), 2023. RSV in Older Adults and Adults with Chronic Medical Conditions. https://www.cdc.gov/rsv/high-risk/older-adults.html (accessed October 2023)

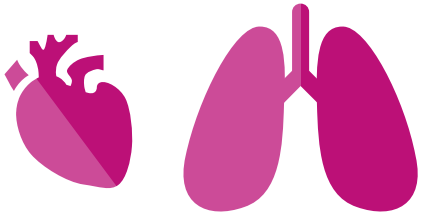
Risk factors for severe RSV-associated disease in adults

Risk of severe RSV-associated disease increases with age and certain comorbidities



Older age[1,2]

Especially for those **aged ≥60 years**



Comorbidities[1,3,4]

Adults at **increased risk** include those with certain **comorbidities**

(e.g., asthma, COPD, CHF, CAD, diabetes, CKD)

Weak immune status[1]

Adults with **weakened immune systems** are also at increased risk of severe RSV disease

CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

1. Centers for Disease Control and Prevention (CDC), 2022. RSV in Older Adults and Adults with Chronic Medical Conditions. https://www.cdc.gov/rsv/high-risk/older-adults.html (accessed September 2023); 2. Belongia EA *et al. Open Forum Infect Dis* 2018;27;5:ofy316; 3. Branche AR *et al. Clin Infect Dis* 2022;74:1004–1011; 4. Wyffels V *et al. Adv Ther* 2020;37(3):1203–1217

Annual burden of RSV in the USA

RSV infection is often thought of as a pediatric illness, but is associated with substantial burden in adults

RSV is the **leading cause of hospitalization** in infants

In children aged <5 years:

58,000–80,000
hospitalizations

~2.1 million outpatient visits

100–300 deaths

RSV is a **major cause of hospitalization and mortality** in older adults

In older adults aged ≥65 years:

60,000–160,000
hospitalizations

Outpatient and ED visits in adults underestimated due to lack of surveillance and underreporting

6000–10,000 deaths

The incidence of hospitalizations and mortality due to RSV is substantially higher in older adults than children

ED, emergency department

National Foundation for Infectious Diseases (NFID), 2023. Respiratory Syncytial Virus (RSV) https://www.nfid.org/infectious-disease/rsv/ (accessed October 2023)

Burden of RSV estimates in older adults in industrialized countries

RSV is prevalent but under-recognized in older adults

Systematic literature review and meta-analysis estimated the annual burden of RSV-ARI among those aged ≥60 years

Incidence

1.62% (95% CI: 0.84, 3.08)

or **~5.2 million** cases of RSV-ARI*

Hospitalization

0.15% (95% CI: 0.09, 0.22)

or **~470,000** hospitalizations*

In-hospital case fatality rate

7.13% (95% CI: 5.40, 9.36)

or **~33,000** deaths*

Global RSV burden may be under-estimated in older adults:

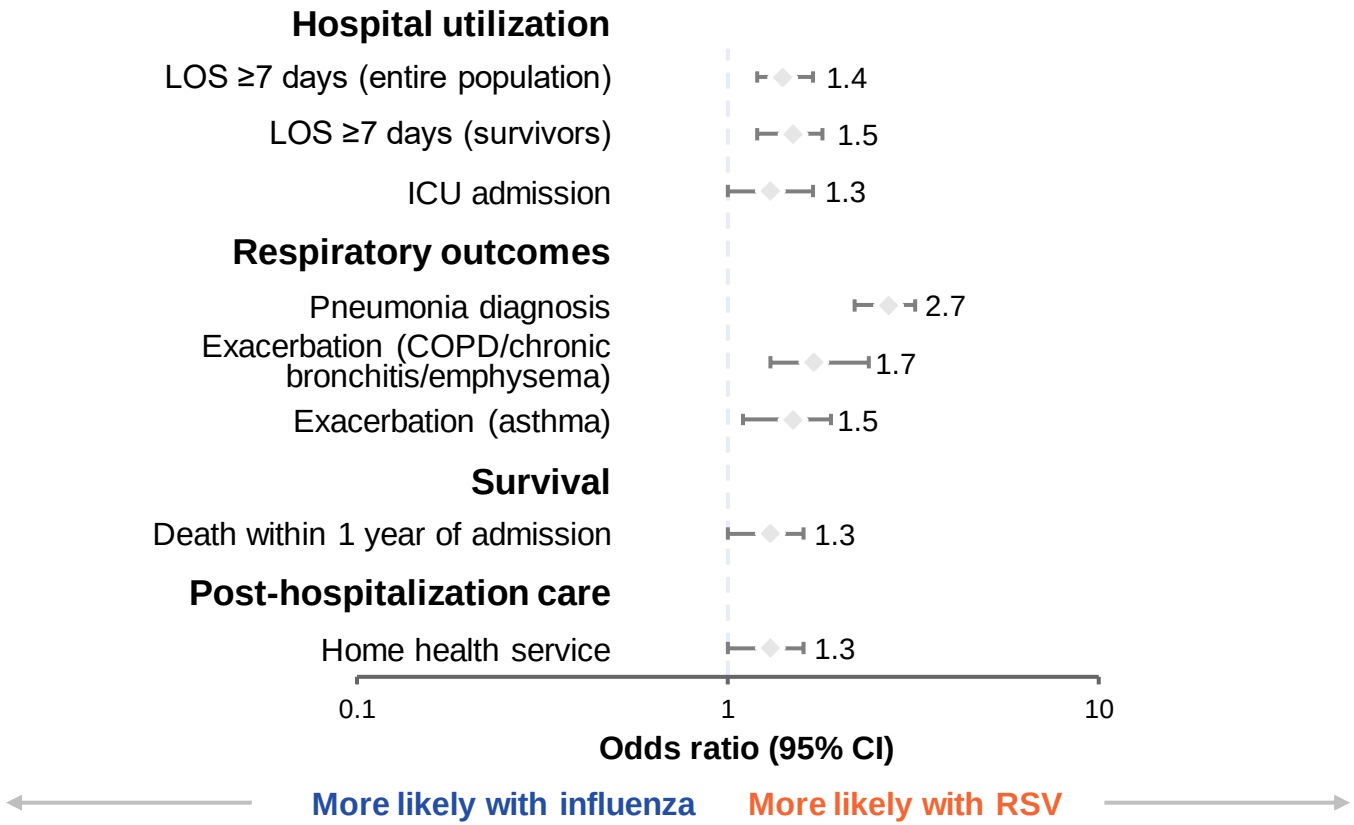
This study was carried out in high-income countries (North America, Europe, and Asia-Pacific regions)

Routine laboratory confirmation of RSV is not widely established in older adults

*Calculated using the European population aged ≥60 years old in 2019
ARI, acute respiratory infections; CI, confidence intervals
Savic M *et al. Influenza Other Respir Viruses* 2023;17(1):e13031

Rates of complications and severe outcomes are similar or worse in older adults with RSV than older adults with influenza1,2

Outcomes in older adults aged ≥60 years hospitalized in the US with influenza (N=1878) vs RSV (N=645)[2]*



The graph was independently created for GSK from the original data

*Between January 2011 and June 2015. A large proportion of patients in this study received an influenza vaccination in 1 year prior to admission. The odds ratio and 95% CI calculations included adjustments, including for history of influenza and pneumococcal vaccination

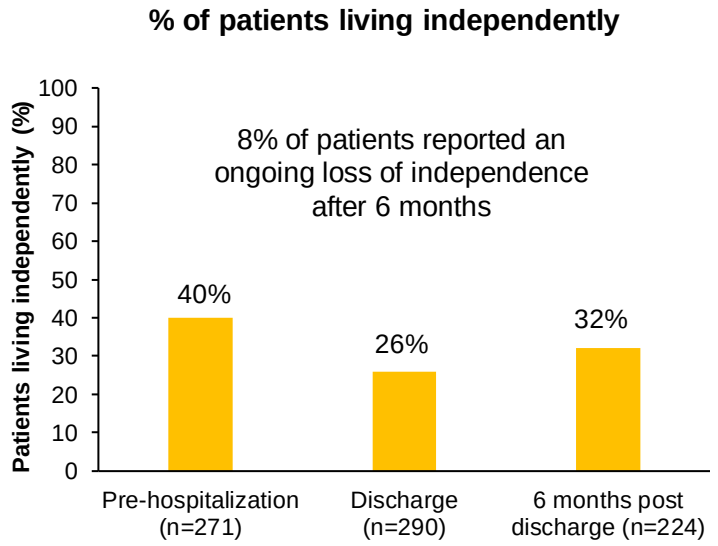
CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; LOS, length of stay

1. Maggi S *et al. Vaccines* 2022; 10(12);2092; 2. Ackerson B *et al. Clin Infect Dis* 2019;69:197–203

Long-term impact of RSV infection

RSV can have a considerable long-term impact on the functional status and quality of life of older adults

Functional status was evaluated for adults aged ≥60 years, hospitalized with confirmed RSV, New York State, USA, 2017–2020[1] (median age, 74 years)



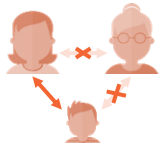
Older adults hospitalized with RSV showed acute functional decline, with approximately one-third demonstrating a persistent decline at 6 months post-discharge

Adult patients hospitalized with RSV-ARI

- Up to 24.5% required professional home care*,[2]
- Up to 26.6% required readmission within 3 months post discharge*,[2]

- Almost 33% mortality rate within a year of admission†,[3]

RSV is associated with adverse effects on:‡,[4]



- productivity
- social or leisure activities
- relationships
- emotional, physical or cognitive functioning
- sleep

The graph was independently created for GSK from the original data
*≥18 years old hospitalized with RSV-ARI, mean age 67.3 years (n=238); †Adults aged ≥75 years hospitalized with RSV (n=284 at risk); ‡Adults aged ≥50 years with an RSV diagnosis in the preceding 6 months
ARI, acute respiratory infection;
1. Branche A *et al. Influenza Other Respi Viruses* 2022;16:1151–1160; 2. Falsey AR *et al. Open Forum Infect Dis* 2021;8:11, ofab491; 3. Tseng HF *et al. J Infect Dis* 2020;222:1298–1310;
4. Curran D *et al. Influenza Other Respir Viruses* 2022;16:462–473

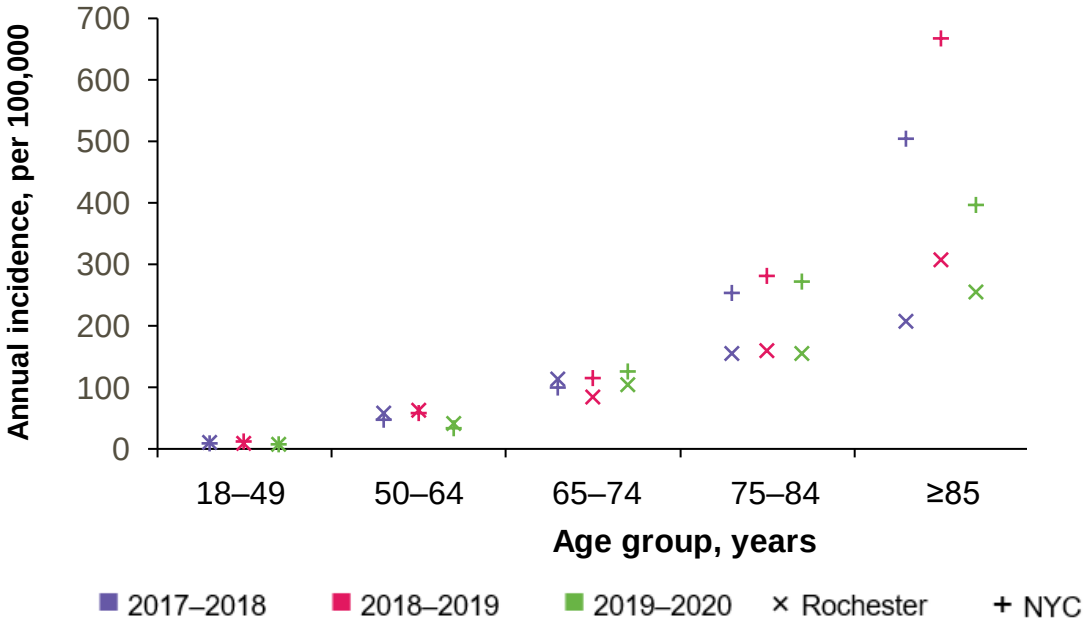
RSV and cardiorespiratory conditions

(Imperial College London)

Risk of RSV-associated hospitalization increases with age and certain comorbidities

A large prospective study estimated incidence of RSV-associated hospitalization in two regions of New York State, USA, 2017–2020. N=1099 cases

Incidence of RSV-associated hospitalization by age group and season



Hospitalization rates for RSV were higher in adults aged ≥50 years with comorbidities

Comorbidity	Incidence rate ratio*
Asthma	2.3–3.6
COPD	3.5–13.4
CAD	3.7–6.5
CHF†	4.0–7.6
Diabetes	2.4–6.4

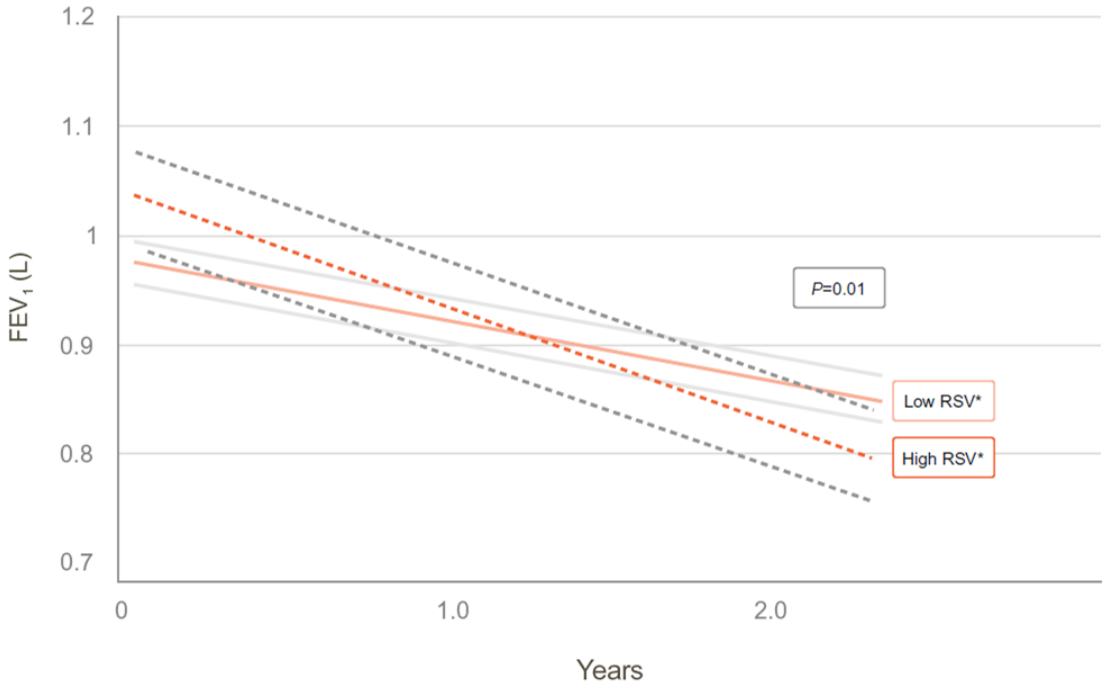
Figure and table independently created for GSK using the original data from Branche AR et al. Clin Infect Dis 2022;74(6):1004–1011
*Ratio of rate among people with each comorbidity vs those without it, in the surveillance area population; †Adults aged ≥60 years (incidence rate ratio for adults aged ≥40 years: 4.0–18.8)
CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; NYC, New York City
Branche AR *et al. Clin Infect Dis* 2022:74:1004–1011

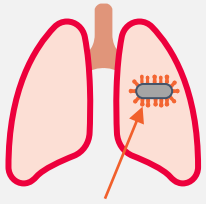
Persistent RSV infection in patients with COPD may be associated with accelerated decline in lung function

Further studies with a larger number of participants are required to confirm this finding

A prospective study evaluated the consequences of RSV persistence in adults with COPD over 2 years (N=74)

Relationship between RSV detection pattern and FEV_1 decline over study period*





Repeated positive tests for RSV (chronic infection) were associated with faster FEV_1 decline and higher inflammatory parameters in patients with stable COPD

Reproduced from Wilkinson *et al. Am J Resp Crit Care Med* 2006;173(8):871−876 under the terms of the GSK-American Thoracic Society Publication Rights agreement

*Orange lines represent decline in FEV_1 with standard errors (gray lines) for low RSV (solid lines; ≤50% of sputum samples were RSV PCR positive) and high RSV (dashed lines; >50% of sputum samples RSV PCR positive).

CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; PCR, polymerase chain reaction

Wilkinson TMA *et al. Am J Resp Crit Care Med* 2006;173(8):871−876

Global Initiative for Chronic Obstructive Lung Disease

2024 REPORT

Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease

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Vaccination for people with COPD*

01 Influenza vaccination is recommended **(Evidence B)**

02 The WHO and CDC recommends SARS-CoV-2 (COVID-19) vaccination **(Evidence B)**

03 The CDC recommends one dose of 20-valent PCV; or one dose of 15-valent PCV followed by 23-valent PPSV **(Evidence B)**

- Pneumococcal vaccination has been shown to reduce the incidence of community-acquired pneumonia and exacerbations in people with COPD **(Evidence B)**

04 The CDC recommends the new RSV vaccine for patients over 60 years old and/or with chronic heart or lung disease **(Evidence A)****

05 The CDC recommends Tdap (dTap/dTPa) vaccination to protect against pertussis (whooping cough) for people with COPD who were not vaccinated in adolescence **(Evidence B)**, and Zoster vaccine to protect against shingles for people with COPD over 50 years **(Evidence B)**

CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Tdap, Tetanus, diphtheria, and pertussis; WHO, World Health Organization.

*People with COPD should receive all recommended vaccinations in line with the relevant local guidelines. **CDC recommends that adults 60 years of age and older may receive a single dose of RSV vaccine using shared clinical decision-making (SCDM)

1. GOLD: Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease, 2024 Report. Available from https://goldcopd.org/2024-gold-report/ [accessed November 2023]

Summary for respiratory conditions

Older adults with COPD and asthma are at increased risk of severe RSV disease[1,2]

High proportions of older adults hospitalized with RSV experienced COPD and asthma exacerbations[3]

Persistent RSV infection is associated with decline in lung function and higher airway inflammation in patients with COPD[4]

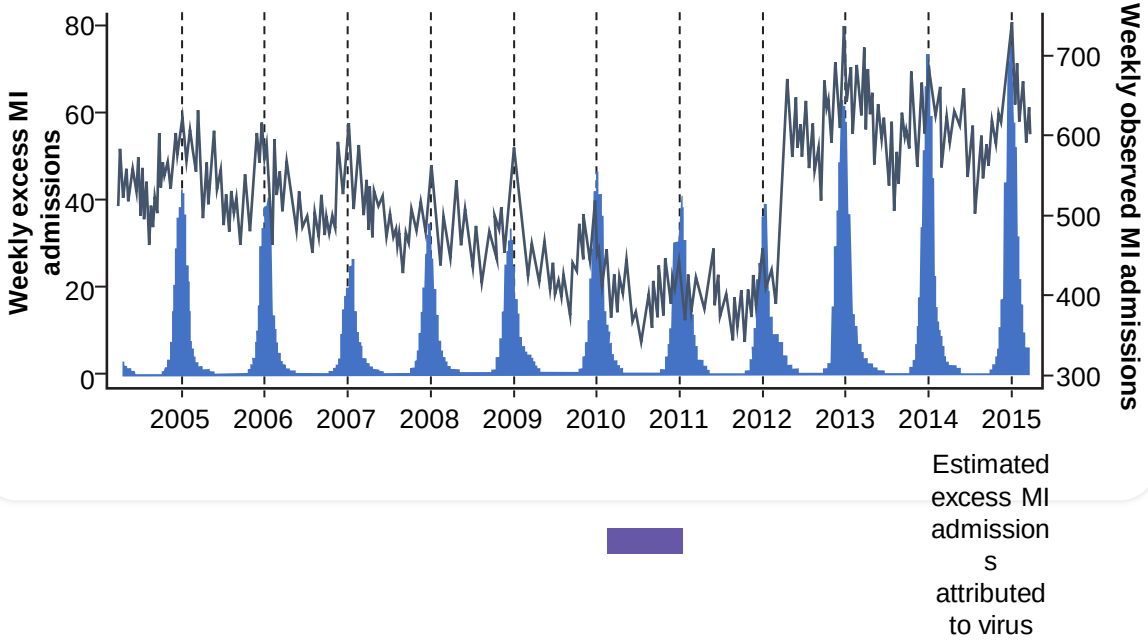
COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second

1. Branche AR *et al. Clin Infect Dis* 2022:74:1004–1011; 2. Centers for Disease Control and Prevention (CDC), 2023. RSV in older adults and adults with chronic medical conditions. https://www.cdc.gov/rsv/high-risk/older-adults.html (accessed September 2023); 3. Tseng HF *et al. J Infect Dis* 2020;222:1298–310; 4. Wilkinson TMA *et al. Am J Resp Crit Care Med* 2006;173(8):871–876

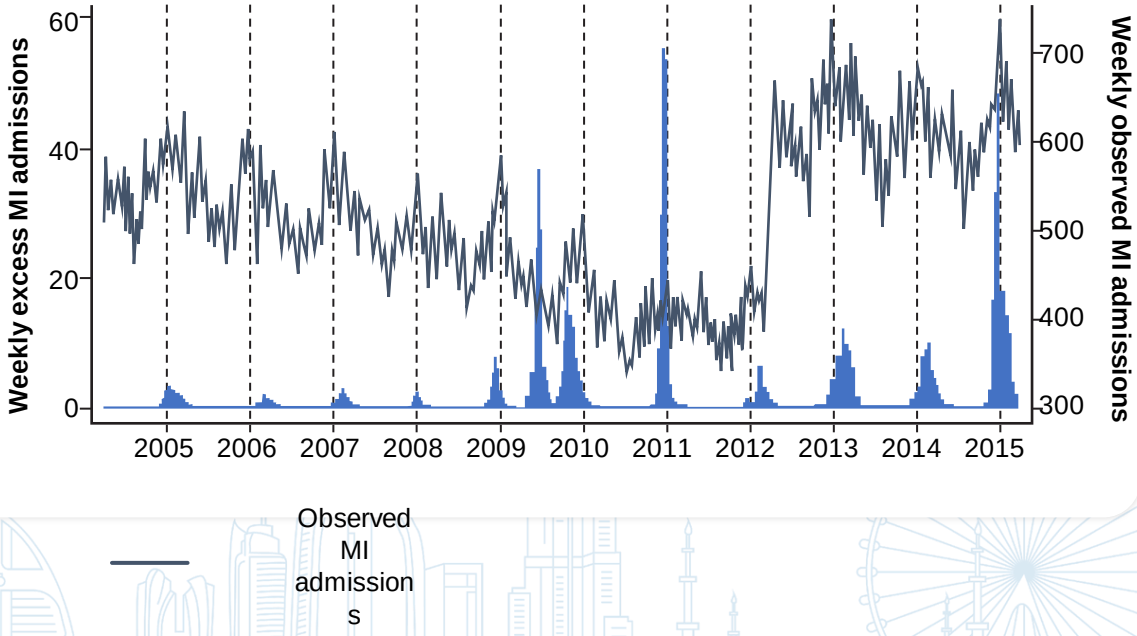
RSV is associated with an increased risk of myocardial infarction in older adults

Weekly observed admissions for MI in patients aged >75 years, and the estimated excess admissions attributable to RSV and influenza (England)

RSV



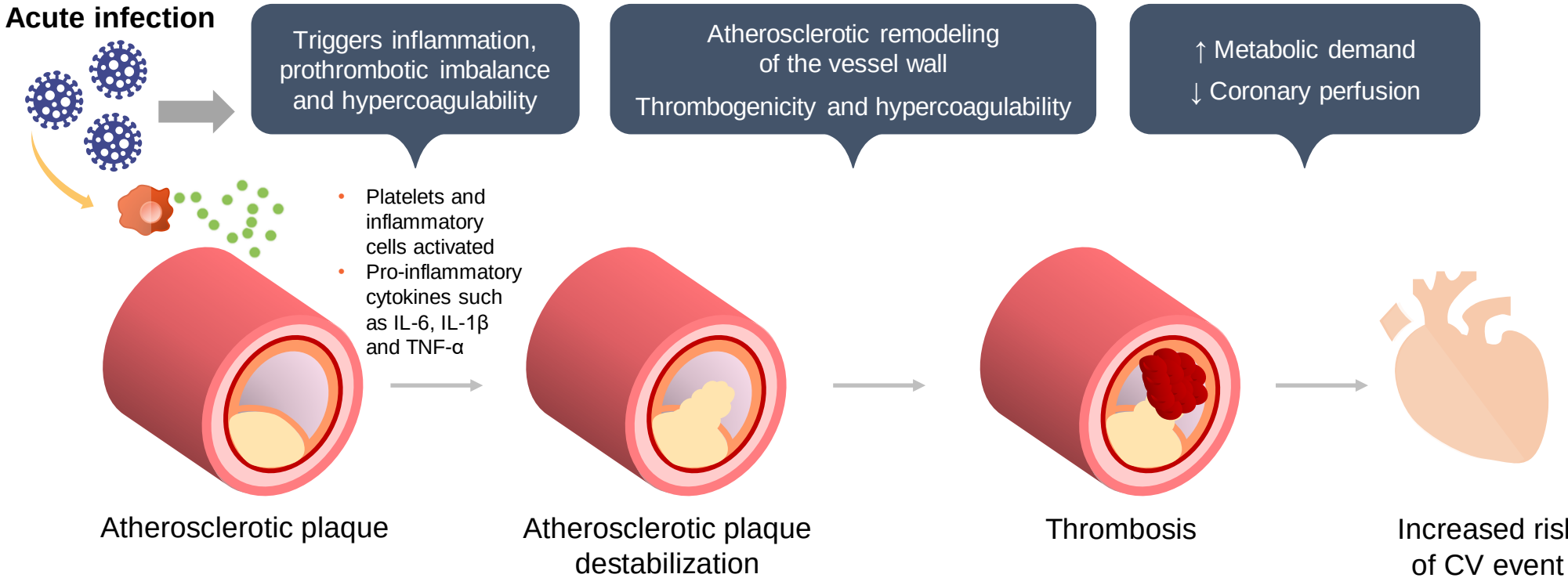
Influenza



Figures adapted from Blackburn R, et al. *Clin Infect Dis*. 2018;67(1):8–17 under the terms of the Creative Commons CC BY 4.0 license [https://creativecommons.org/licenses/by/4.0/])
MI, myocardial infarction
Blackburn R *et al. Clin Infect Dis*. 2018;67(1):8–17

Systemic inflammation due to respiratory viral infections such as RSV can may trigger or worsen cardiovascular events1,2

The inflammatory response may lead to disruption and rupture of arterial plaques and increased risk of acute coronary syndrome such as myocardial infarction[1]



There is evidence that RSV may share some of the mechanisms by which other viral infections contribute to cardiovascular injury[1]

The figure is for illustrative purposes only
CV, cardiovascular; IL, interleukin; TNF, tumor necrosis factor
1. Ivey KS *et al*. *J Am Coll Cardiol* 2018;71:1574–1583; 2. Franczuk P *et al*. *Biomedicines* 2023;11(1):71

Summary for cardiovascular conditions

RSV may cause cardiovascular complications in older adults including CHF, atrial fibrillation and myocardial infarction[1]

Older adults with CHF* or CAD are at increased risk of RSV-associated hospitalization than those without[2]

One-year survival rates following hospitalization with RSV are poorer among adults with CHF or with CHF exacerbations[3]

CAD, coronary artery disease; CHF, congestive heart failure.

1. Ivey KS *et al. J Am Coll Cardiol* 2018;71(14):1574–1583; 2. Branche AR, et al. Clin Infect Dis 2022;74:1004–1011; 3. Tseng HF *et al. J Infect Dis* 2020;222:1298–1310

Local (GCC) RSV Data

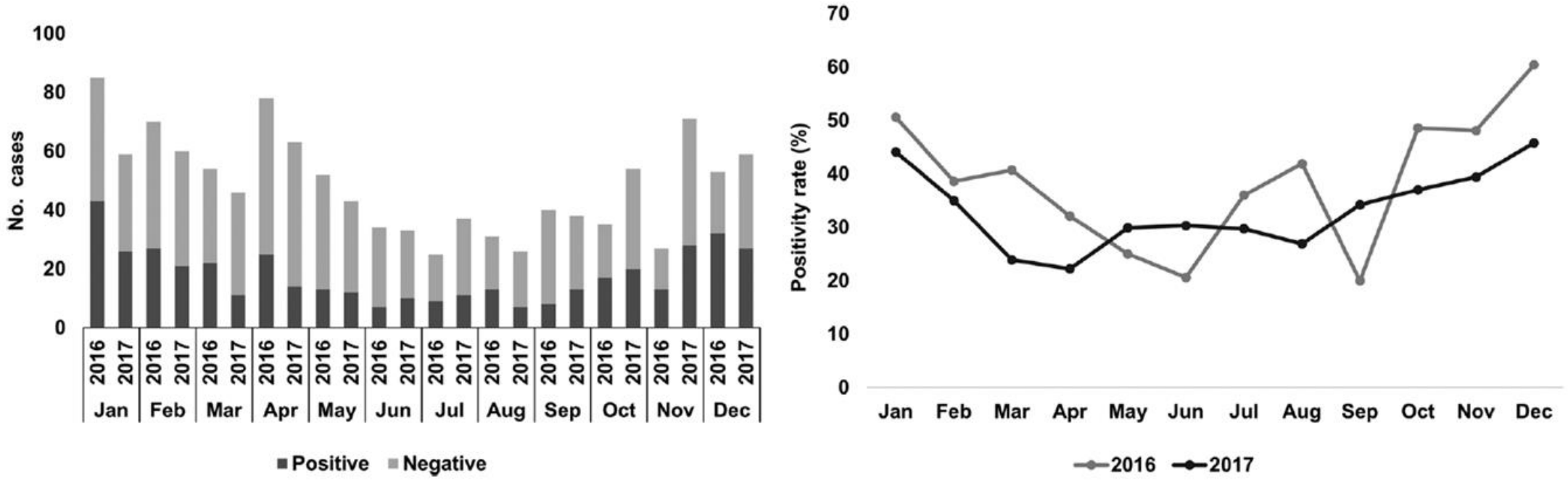


FIGURE 1 Monthly number and positivity rate of all respiratory viruses in 2016 and 2017, in patients with acute respiratory illness who visited the Sheikh Khalifa Specialty Hospital. Isolation rate and positivity rate of all respiratory viruses showed seasonal variation

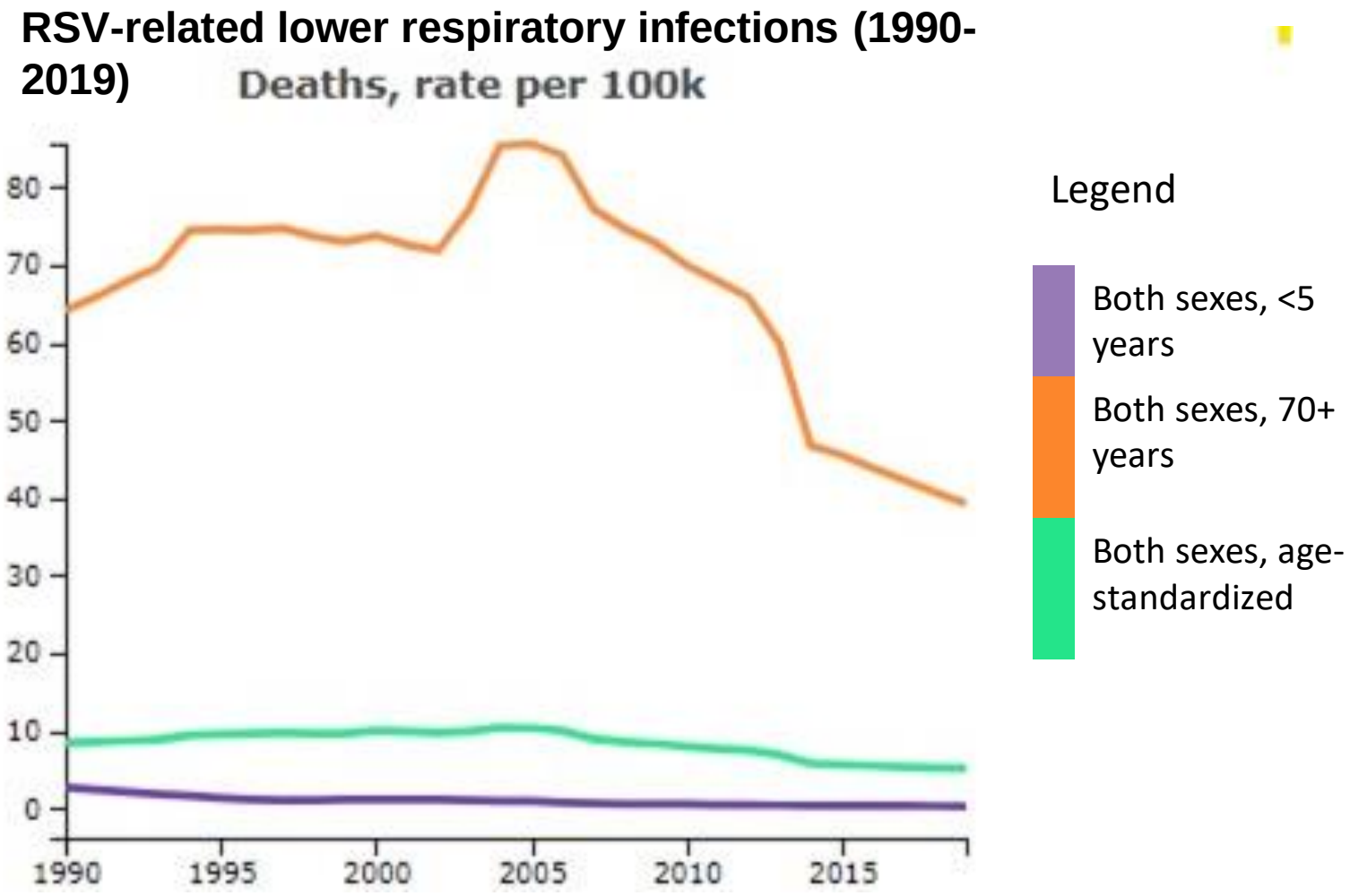
Jeon et al. J Med Virol. 2019;91:1378-1384.; 5

RSV in the GCC: The United Arab Emirates (UAE)

Data from GBD 2019 study

- Persistent burden of RSV in 3 decades.

- In the UAE in 2019, RSV was attributed to:
  - age-standardized rate of 5.08 deaths per 100,000 (10.2%)
  - 0.25 deaths per 100,000 in children younger than 5 (17.25%)
  - 39.21 deaths per 100,000 in elderly 70+ years (9.54%)



Global Burden of Disease Collaborative Network.
Global Burden of Disease Study 2019 (GBD 2019) Results.
Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2020.
Available from https://vizhub.healthdata.org/gbd-results/.
RSV: Respiratory Syncytial Virus; GBD: Global Burden of Disease study

Respiratory Syncytial Virus (RSV) and GSK’s RSVPreF3 OA vaccine

November 2023 | NX-AE-RSA-PPT-230004
GlaxoSmithKline Biologicals SA, Rixensart, Belgium
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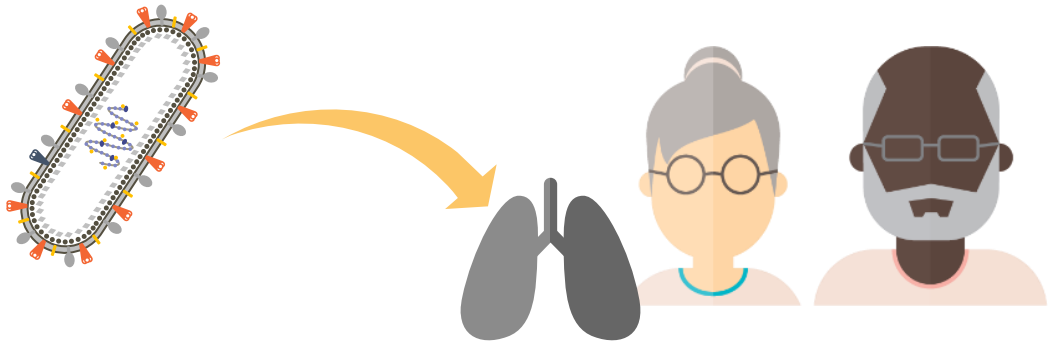
Immune responses to protect against RSV

Humoral and cellular immune responses are thought to be essential in preventing severe RSV disease in adults



Humoral immune response

Neutralizing antibodies are thought to prevent RSV infection by **inhibiting viral entry into host cells**[1]

- Lower serum neutralizing antibodies have been associated with **increased RSV-associated disease severity** among older adults[2]

Cellular immune response

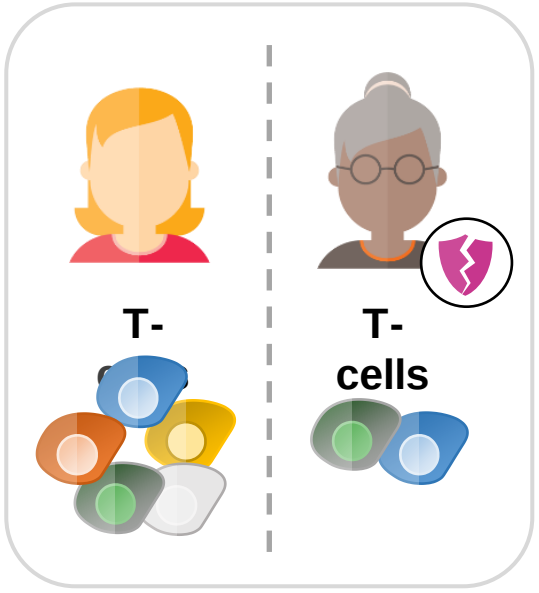
RSV-specific **T-cell responses** are thought to **promote viral clearance** and to be **critical for reducing disease severity**[1]

- **CD4⁺ T-cells** may play a key role in preventing the spread of viral infection by **supporting an efficient and balanced antibody response**[1]
- **CD8⁺ T-cells** may be involved in the resolution of symptoms by **promoting viral clearance**[3]

CD, cluster of differentiation

1. Openshaw PJM, *et al. Annu Rev Immunol* 2017;35:501–532; 2. Walsh EE *et al. J Infect Dis* 2004;189(2):233–238; 3. Jozwik A *et al. Nat Commun* 2015;6:10224

Age-related decline in immunity and challenges in protecting older adults against severe RSV-associated disease



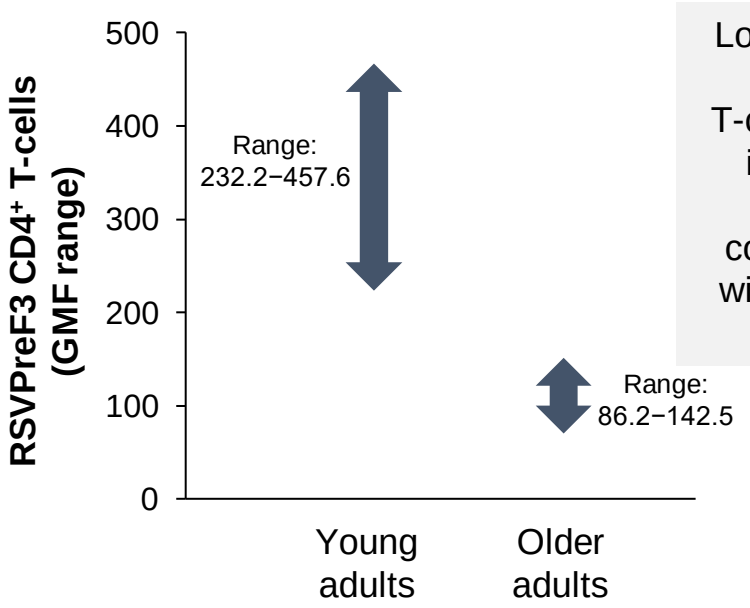
The quality and quantity of immune cells diminishes with older age[1]

RSV F protein-specific T-cell responses were shown to be deficient in older adults compared to younger individuals[2,3]

T-cell response declines with age, making it challenging for older adults to not only mount immunity to RSV infection, but also to achieve high levels of protection following vaccination[1,2]

Baseline RSV-specific cellular immune response assessed in young adults aged 18–40 years (N=48) and older adults aged 60–80 years (N=1005)[3]

RSV F protein-specific CD4⁺ T-cell levels



Lower RSV CD4⁺ T-cell levels in older adults compared with young adults

Graph was independently created for GSK from the original data
CD, cluster of differentiation; GMF, geometric mean frequency

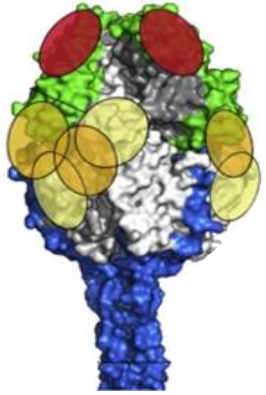
1. Stephens LM and Varga SM. *Vaccines (Basel)* 2021;9(6):624; 2. Cherukuri A *et al*. *Clin Vaccine Immunol* 2013;20:239–247; 3. Leroux-Roels I *et al. J Infect Dis* 2022; Epub ahead of print (doi: 10.1093/infdis/jiac327)

GSK's RSV older adult vaccine

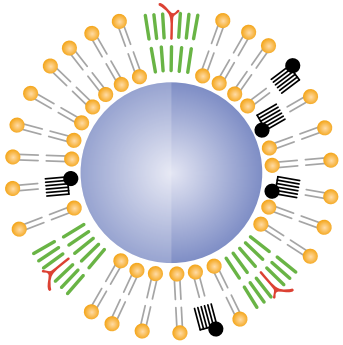
The combination of RSVPreF3 (120 µg) and $AS01_E$ is designed to induce a robust humoral and cellular immune response, to help protect older adults and those with comorbidities

RSVPreF3 OA vaccine

RSVPreF3 antigen (120 µg) + **$AS01_E$ adjuvant system**



Antigen* engineered to preferentially maintain the prefusion conformation and display potent neutralizing epitopes to boost humoral immune response in older adults[1,2]



Boosts cellular immune response and restores the RSVPreF3 $CD4^+$ T-cell level in older adults[2]

***RSV fusion (F) glycoprotein is highly conserved between RSV-A and RSV-B subtypes[1]**

Image of F protein reproduced from Graham BS *et al. Curr Opin Immunol* 2015;35:30–38, Copyright 2015, with permission from Elsevier

$AS01_E$, Adjuvant System 01_E (25 µg *Quillaja saponaria* Molina, fraction 21, 25 µg 3-O-desacyl-4'**- monophosphoryl lipid A, combined in a liposomal formulation**); CD, cluster of differentiation

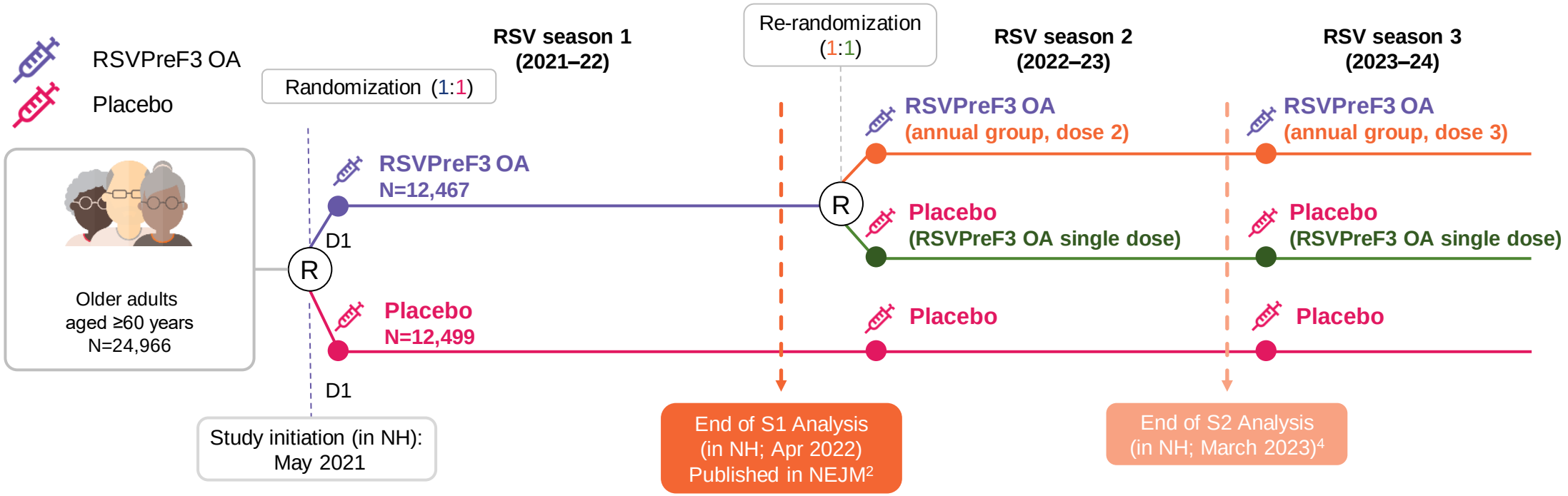
1. Graham BS *et al. Curr Opin Immunol* 2015;35:30–38; 2. Leroux-Roels I *et al. J Infect Dis* 2022; Epub ahead of print (doi: 10.1093/infdis/jiac327)

AReSVi-006

Pivotal efficacy study: Phase 3, randomized, placebo-controlled, multi-country study to demonstrate efficacy and safety of single and annual revaccination doses in adults aged 60 years and older

Ongoing AReSVi-006 Phase 3 trial design[1–4]

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



<u>Primary endpoint:</u> To demonstrate the efficacy of RSVPreF3 OA in the prevention of RSV* LRTD† in adults ≥60 years of age during the first season[2,3]

<u>Confirmatory secondary endpoint:</u> To demonstrate the efficacy of RSVPreF3 OA in the prevention of RSV* LRTD† in adults ≥60 years of age over 2 seasons, following a single dose of RSVPreF3 OA and following annual revaccination dose[4]

All RSV-LRTD† cases were adjudicated by an independent external adjudication committee

Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA

*RT-PCR confirmed; †LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours

D, day; LRTD, lower respiratory tract disease; NH, Northern Hemisphere; RT-PCR, reverse-transcriptase polymerase chain reaction; S, season

1. ClinicalTrials.gov, 2022. NCT04886596. https://clinicaltrials.gov/ct2/show/NCT04886596; 2. Papi A *et al*. *N Engl J Med* 2023;388(7):595–608; 3. Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA; 4. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf URLs accessed July 2023

Demographic characteristics[1,2]

Demographic characteristics were balanced between study groups (exposed set)

RSVPreF3 OA (N=12,467)		Characteristics	Placebo (N=12,499)	
69.5 years		Mean age	69.6 years	
n	%	Age category	%	n
12,467	100.0%	≥60 years	100.0%	12,499
6,963	55.9%	60–69 years	55.8%	6,980
4,487	36.0%	70–79 years	35.9%	4,491
1,017	8.2%	≥80 years	8.2%	1,028
n	%	Sex	%	n
6,488	52.0%	Female	51.4%	6,427
5,979	48.0%	Male	48.6%	6,072
n	%	Race	%	n
9,887	79.3%	White	79.5%	9,932
1,064	8.5%	Black or African American	8.8%	1,101
953	7.6%	Asian	7.6%	956
563	4.5%	Other*	4.1%	510
n	%	Frailty status†	%	n
189	1.5%	Frail	1.4%	177
4,793	38.4%	Pre-frail	38.3%	4,781
n	%	Comorbidity of interest‡	%	n
4,937	39.6%	≥1 pre-existing comorbidity of interest	38.9%	4,864
2,504	20.1%	≥2 pre-existing comorbidity of interest	19.5%	2,434
805	6.5%	≥3 pre-existing comorbidity of interest	6.6%	827

Around 39% of participants in each group had ≥1 pre-existing comorbidity of interest associated with an increased risk of severe RSV disease‡

Figure was independently created for GSK from the original data.

*Includes Native American, Alaska Native, Native Hawaiian and other Pacific Islanders; †assessed by a gait speed test; **‡COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, chronic heart failure, advanced liver or renal disease. COPD, chronic obstructive pulmonary disease**

1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 2. Feldman RG *et al. Clin Infect Dis* 2023:ciad471. doi: 10.1093/cid/ciad471. Epub ahead of print.

AReSVi-006 case definitions[1,2]

ARI
≥2 respiratory symptoms or signs
OR
≥1 respiratory and 1 systemic symptom or sign for at least 24 hours

Systemic symptoms or signs

- Fever/feverishness
- Fatigue
- Body aches
- Headache
- Decreased appetite

Respiratory symptoms or signs

Upper respiratory symptoms or signs

- Nasal congestion
- Sore throat

Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O_2 supplement

LRTD*
≥2 lower respiratory symptoms or signs (≥1 sign)
OR
≥3 lower respiratory symptoms for at least 24 hours

Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O_2 supplement

Severe LRTD*
≥2 lower respiratory signs
OR
episode preventing normal, everyday activities

Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O_2 supplement

Figure reproduced from GSK, 2023. Presentation at ACIP Meeting, June 21, 2023
*USPI case definitions
ARI, acute respiratory infection; LRTD, lower respiratory tract disease; USPI, US prescribing information
1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Accessed July 2023; 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608.

The primary endpoint met: a single dose of RSVPreF3 OA vaccine is highly efficacious in the prevention of RSV-LRTD during the first RSV season[1,2]

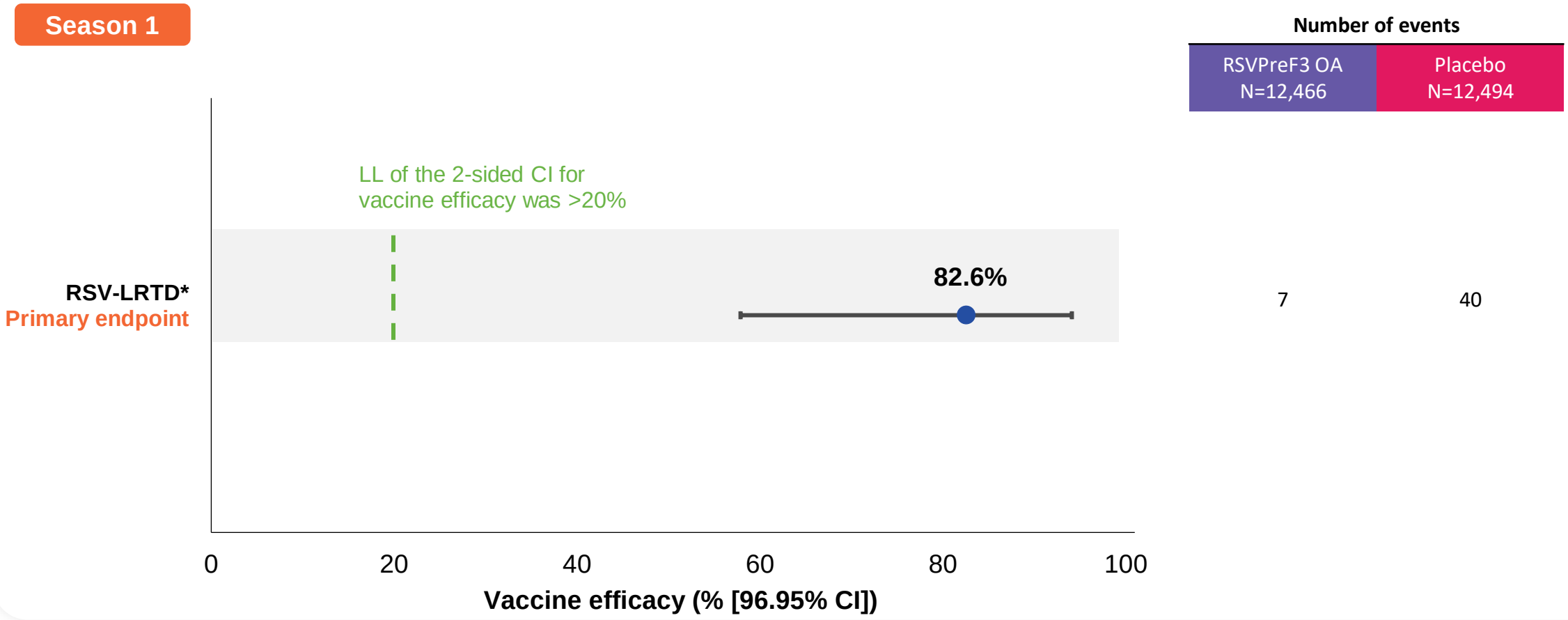


Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19–23, 2022, Washington, DC, USA

*LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours; All RSV cases confirmed by RT-PCR

CI, confidence interval; LL, lower limit; LRTD, lower respiratory tract disease; RT-PCR, reverse-transcriptase polymerase chain reaction

1. Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA;
2. Papi A *et al. N Engl J Med* 2023;388(7):595–608

Consistently high vaccine efficacy across a broad spectrum of RSV-associated disease during the first RSV season[1,2]

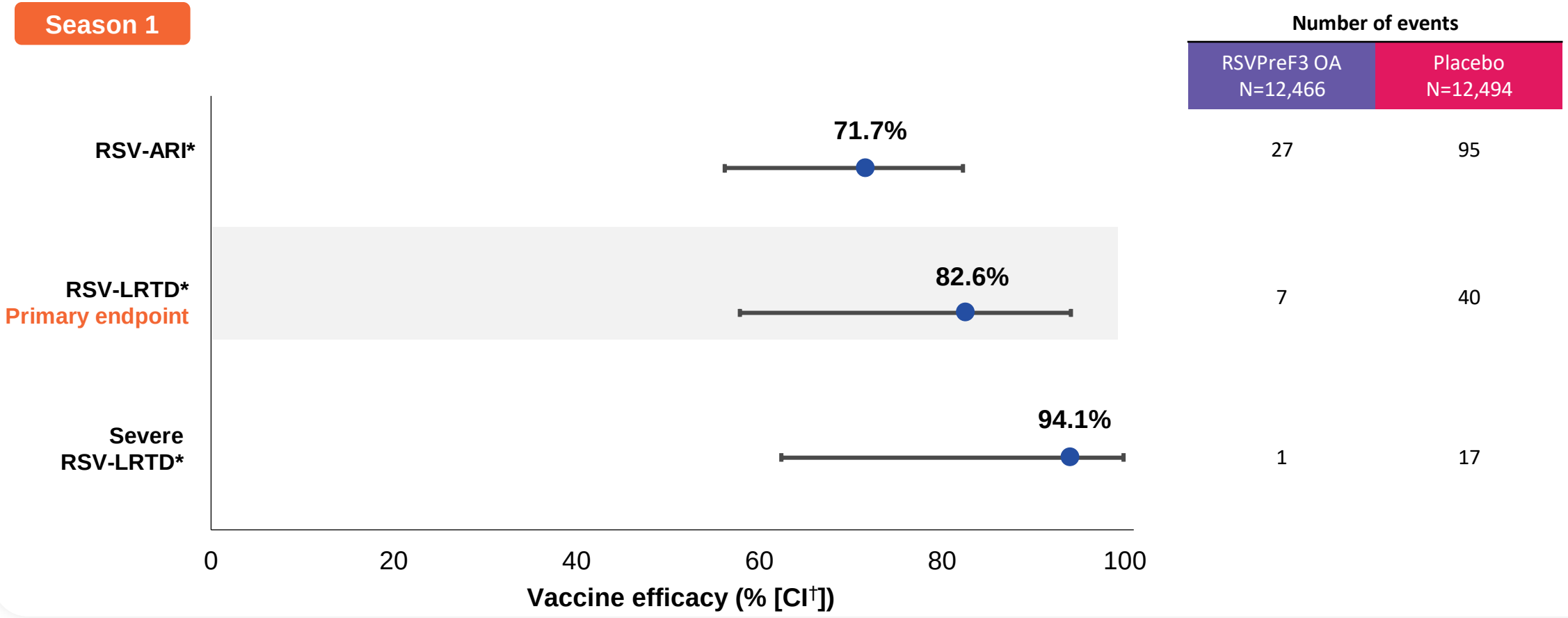


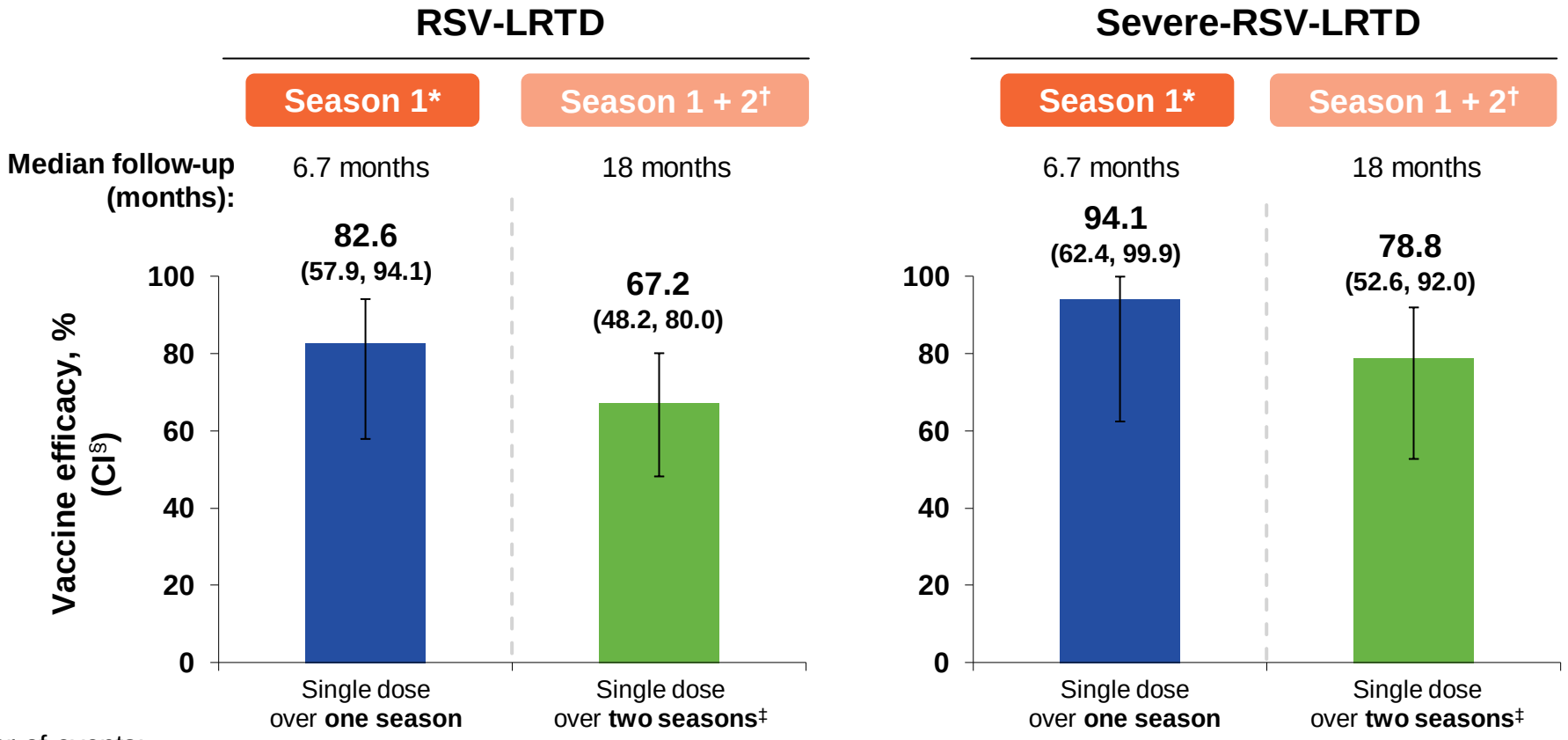
Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA

*ARI defined as ≥2 respiratory symptoms/signs for ≥24 hours, or ≥1 respiratory symptom/sign + 1 systemic symptom/sign for ≥24 hours. LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign, or ≥3 lower respiratory symptoms for ≥24 hours. Severe LRTD defined as LRTD with ≥2 lower respiratory signs, or an LRTD episode assessed as severe by the investigator. All RSV cases confirmed by RT-PCR; †96.95% CI for primary endpoint, 95% for all secondary endpoints

ARI, acute respiratory infection; CI, confidence interval; LRTD, lower respiratory tract disease; RT-PCR, reverse-transcriptase polymerase chain reaction

1. Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA;
2. Papi A *et al. N Engl J Med* 2023;388(7):595–608

One dose of RSVPreF3 OA produces durable vaccine efficacy against RSV-LRTD and severe RSV-LRTD over 2 full seasons[1]



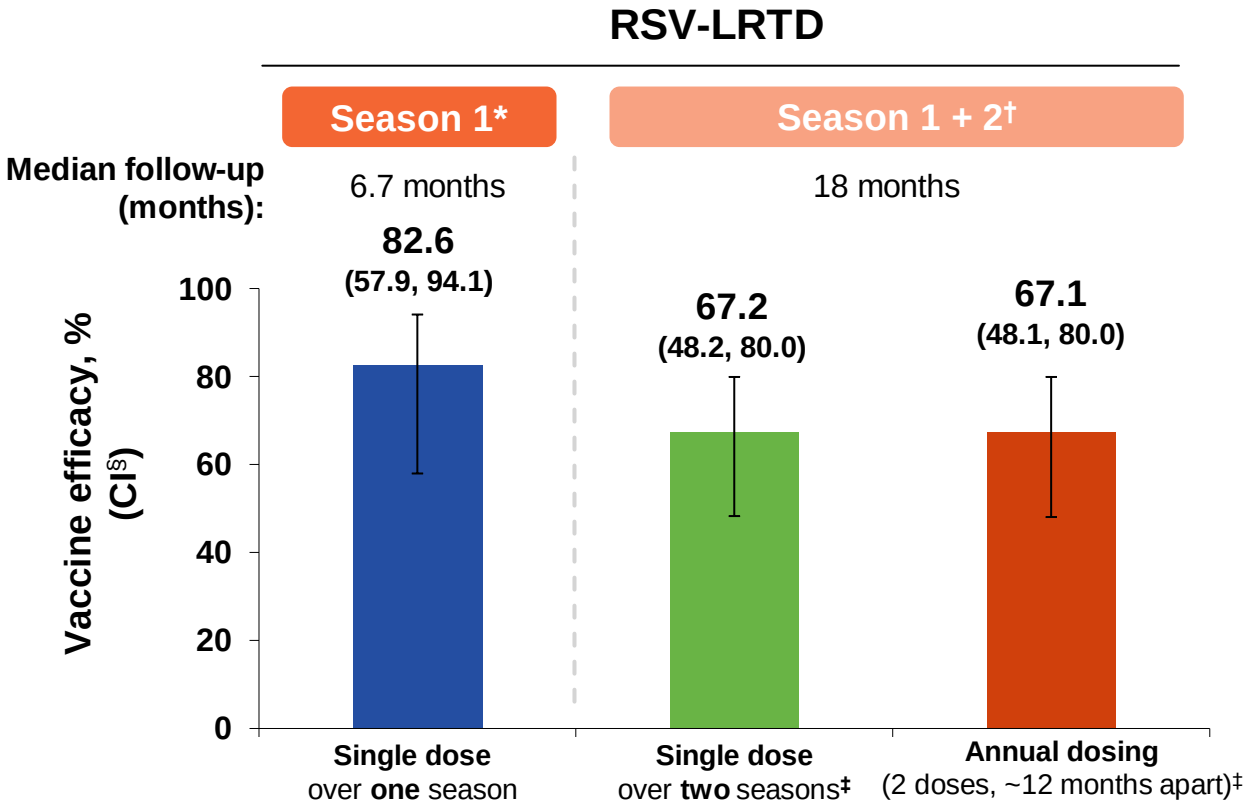
Number of events:

	RSV-LRTD		Severe-RSV-LRTD	
	Season 1*	Season 1 + 2†	Season 1*	Season 1 + 2†
RSVPreF3 OA	**7** / 12,466	**30** / 12,469	**1** / 12,466	**7** / 12,469
Placebo	**40** / 12,494	**139** / 12,498	**17** / 12,494	**48** / 12,498

Figures were independently created for GSK from the original data.
Modified exposed set. *Up to end of Season 1 in the Northern Hemisphere (April 2022 analysis). †From 15 days post-Dose 1 up to end of Season 2 in the Northern Hemisphere (March 2023 analysis). ‡The VE is estimated using a Poisson regression model adjusted using age, region and season[2]; §96.95% CI for VE Season 1, 97.5% CI for Season 1 + 2
CI, confidence interval; LRTD, lower respiratory tract disease; VE, vaccine efficacy

1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf; 2. GSK Press release, https://www.gsk.com/en-gb/media/press-releases/gsk-shares-positive-data-for-arexvy-its-respiratory-syncytial-virus-older-adult-vaccine-indicating-protection-over-two-rsv-seasons/#:~:text=Cumulative%20efficacy%20over%20two%20seasons,benefit%20for%20the%20overall%20population. URLs accessed July 2023

Revaccination after 12 months does not appear to confer additional efficacy benefit against RSV-LRTD for the overall population; future data will inform optimal timing of revaccination[1]



Number of events:			
RSVPreF3 OA	**7** / 12,466	**30** / 12,469	**30** / 12,469
Placebo	**40** / 12,494	**139** / 12,498	**139** / 12,498

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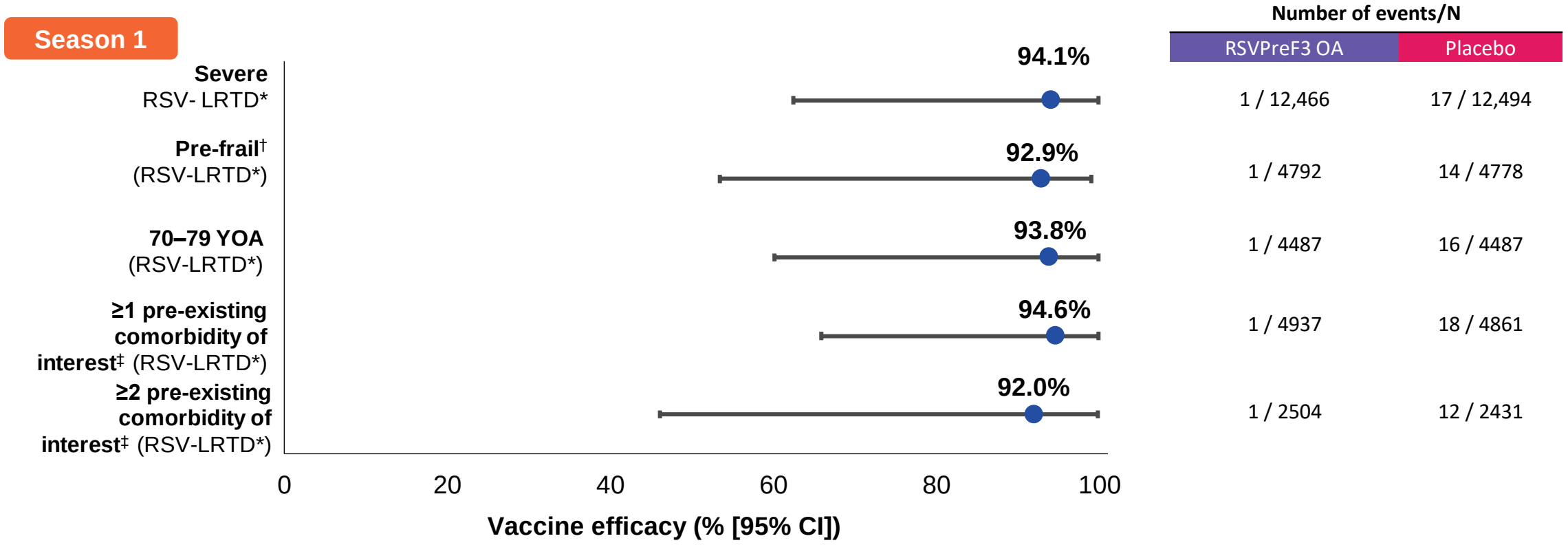
Modified exposed set. *Up to end of Season 1 in the Northern Hemisphere (April 2022 analysis). †From 15 days post-Dose 1 up to end of Season 2 in the Northern Hemisphere (March 2023 analysis). ‡The VE is estimated using a Poisson regression model adjusted using age, region and season[2]; §96.95% CI for VE Season 1, 97.5% CI for Season 1 + 2. CI, confidence interval; LRTD, lower respiratory tract disease; VE, vaccine efficacy

1. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf; 2. GSK Press release, https://www.gsk.com/en-gb/media/press-releases/gsk-shares-positive-data-for-arexvy-its-respiratory-syncytial-virus-older-adult-vaccine-indicating-protection-over-two-rsv-seasons/#:~:text=Cumulative%20efficacy%20over%20two%20seasons,benefit%20for%20the%20overall%20population. URLs accessed July 2023

Very high and consistent vaccine efficacy against severe RSV-associated disease and in older adults at increased risk[1–3]



Due to too few cases observed in adults aged 80 years and older and those considered frail, we cannot conclude on VE

- ≥80 YOA (number of events/N): **RSVPreF3 OA** (2/1016); **placebo** (3/1028)
- Frail (number of events/N): **RSVPreF3 OA** (1/189); **placebo** (1/177)

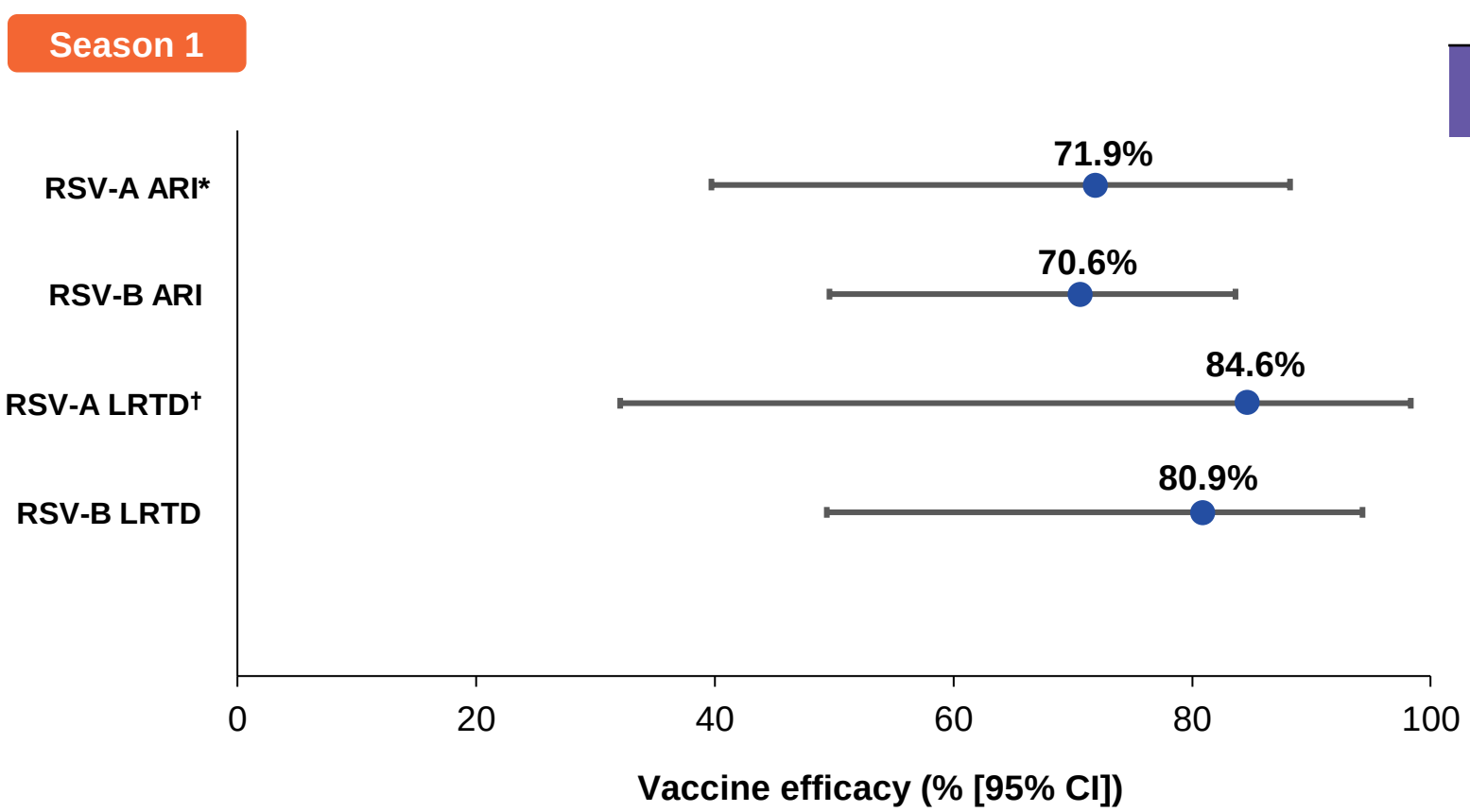
Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at ID Week, October 19−23, 2022, Washington, DC, USA. *LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign, or ≥3 lower respiratory symptoms for ≥24 hours. Severe LRTD defined as LRTD with ≥2 lower respiratory signs, or an LRTD episode assessed as severe by the investigator. All RSV cases confirmed by RT-PCR; †**Frailty was assessed by a gait speed test; ‡COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, chronic heart failure, advanced liver or renal disease.**

COPD, chronic obstructive pulmonary disease; CI, confidence interval; LRTD, lower respiratory tract disease; RT-PCR, reverse-transcriptase polymerase chain reaction; VE, vaccine efficacy; YOA, years of age

1. Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA; 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 3. Feldman RG *et al. Clin Infect Dis* 2023:ciad471. doi: 10.1093/cid/ciad471. Epub ahead of print.

Consistently high vaccine efficacy against RSV-A– and RSV-B–associated disease[1,2]

Season 1



	Number of events	
	RSVPreF3 OA N=12,466	Placebo N=12,494
RSV-A ARI*	9	32
RSV-B ARI	18	61
RSV-A LRTD†	2	13
RSV-B LRTD	5	26

2/3 of RSV-LRTD cases were associated with RSV-B

Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA

*ARI defined as ≥2 respiratory symptoms/signs for ≥24 hours or ≥1 respiratory symptom/sign + 1 systemic symptom/sign for ≥24 hours; †LRTD defined as ≥2 lower respiratory symptoms/signs for ≥24 hours including ≥1 lower respiratory sign OR ≥3 lower respiratory symptoms for ≥24 hours. All RSV cases confirmed by RT-PCR

ARI, acute respiratory infection; CI, confidence interval; LRTD, lower respiratory tract disease; RT-PCR, reverse transcriptase polymerase chain reaction

1. Ison MG, *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA;
2. Papi A *et al. N Engl J Med* 2023;388(7):595–608

RSVPreF3 OA was well tolerated: most events were transient and mild to moderate[1,2]

Solicited AEs (any and Grade 3) reported within 4 days of vaccination (solicited safety set, n=1757)

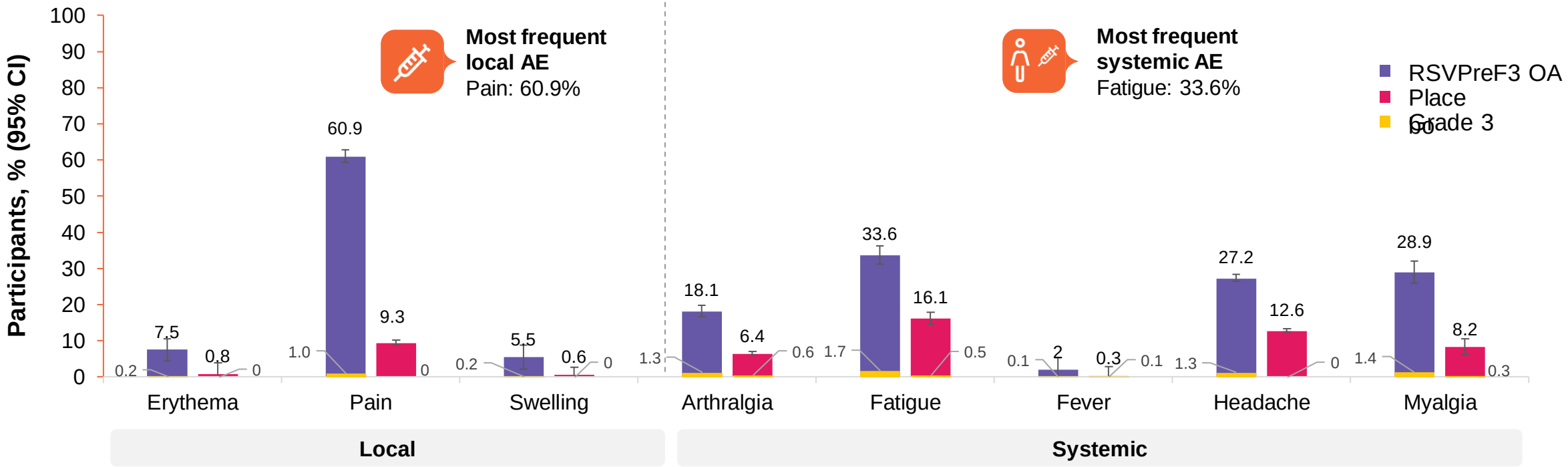
Season 1

Solicited AEs reported within 4 days of vaccination

Mean duration (all solicited AEs): 1–2 days

Most frequent local AE
Pain: 60.9%

Most frequent systemic AE
Fatigue: 33.6%



Reactogenicity profile of a second dose was in line with the first dose[3]

Figure adapted with permission from Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA

Error bars show 95% CIs for total AEs; AE, adverse event; CI, confidence interval

1. Ison MG *et al*. A respiratory syncytial virus (RSV) prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥60 years of age (YOA). Presented at IDWeek, October 19−23, 2022, Washington, DC, USA; 2. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 3. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Accessed July 2023

Summary: AReSVi-006 Study[1,2]

Efficacy

- The first season analysis demonstrated that RSVPreF3 OA provides high and consistent efficacy against the full spectrum of RSV disease regardless of RSV subtype in adults ≥60 years of age

Efficacy over an entire RSV season (based on Season 1 analysis):

82.6%	**94.1%**	**94.6%**	**93.8%**
RSV-LRTD (≥60 YOA)	Severe RSV-LRTD (≥60 YOA)	RSV-LRTD (≥1 with comorbidity of interest*)	RSV-LRTD (70−79 YOA)

- One dose of RSVPreF3 OA vaccine provides durable efficacy against RSV-associated LRTD for 2 full RSV seasons, including against severe RSV disease, in adults with underlying comorbidities, and across advancing ages
- Revaccination after 12 months does not appear to confer additional efficacy benefit for overall population; future data will inform optimal timing of revaccination

Safety

- RSVPreF3 OA vaccine candidate is well tolerated with an acceptable safety profile
- Most solicited reactions were of mild to moderate intensity and transient
- Reactogenicity and safety profiles of a second dose of RSVPreF3 OA were in line with the first dose

*Included chronic obstructive pulmonary disease, asthma, any chronic respiratory/pulmonary disease and chronic heart failure (cardiorespiratory), diabetes mellitus type 1 or type 2, and advanced liver or renal disease (endocrine or metabolic)
LRTD, lower respiratory tract disease; YOA, years of age
1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 2. GSK 2023. GSK's RSVPreF3 OA Vaccine (AREXVY). Presented at ACIP, 21 June 2023 https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf Accessed September 2023

RSVPreF3 OA licensures & recommendations

Dec. 23

Approvals & Supply across the Globe

41 Approvals

US	UK	France	Brazil	Estonia
Canada	Spain	Poland	Hong Kong	Croatia
Germany	Austria	Greece	UAE	Cyprus
Japan	Finland	Czech Rep	Philippines	Hungary
Sweden	Denmark	Norway	Saudi Arabia	Slovakia
Netherlands	Australia	Iceland	United Arab Emirates	Slovenia
Belgium	Portugal	Liechtenstein	Romania	Latvia
Italy	Ireland	Luxembourg	Bulgaria	Lithuania

22 Supplied

US	Belgium	Denmark	Norway
Canada	Italy	Portugal	Hong Kong
Germany	UK	Ireland	Saudi Arabia
Japan	Spain	France	
Sweden	Austria	Poland	
Netherlands	Finland	Czech Rep	

RSVPreF3 OA vaccine (Arexvy) licensures

Indications and contraindications

USA[1]

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.

Contraindication:

History of severe allergic reaction (eg, anaphylaxis) to any component of the vaccine.

European Union[2]

Indication:

Arexvy is indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 60 years of age and older.
The use of this vaccine should be in accordance with official recommendations.

Contraindication:

Hypersensitivity to the active substances or to any of the components.

UK[3]

Indication:

Arexvy is indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 60 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

Contraindication:

Hypersensitivity to the active substances or to any of the excipients.

Canada[4]

Indication:

Arexvy, an RSV vaccine, has been authorized for use in Canada for the prevention of lower respiratory tract disease caused by RSV in adults 60 years of age and older.

Contraindication:

Hypersensitivity to the active substances or to any of the excipients.

Japan[5]

Indication:

The Ministry of Health, Labour and Welfare has approved Arexvy for the prevention of RSV (respiratory syncytial virus) disease for adults aged 60 years and above.The use of this vaccine should be in accordance with official recommendations.

Contraindication:

TBC

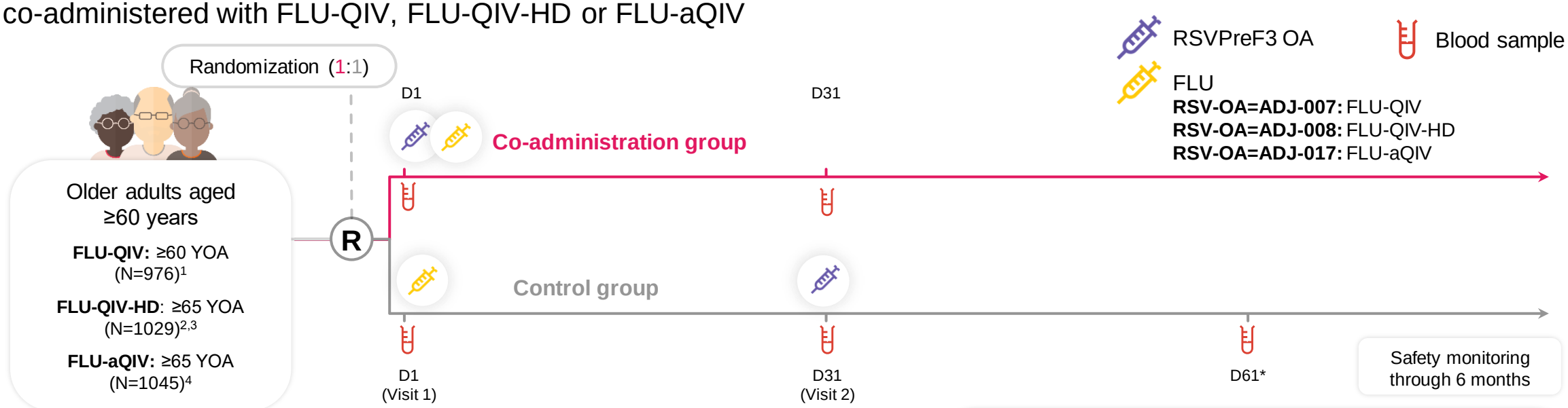
1. Food and Drug Administration (FDA), 2023. Arexvy Prescribing Information (PI). https://www.fda.gov/media/167805/download; 2. European Medicines Agency (EMA), 2023. Arexvy Summary of Product Characteristics (SmPC). https://www.ema.europa.eu/en/documents/product-information/arexvy-epar-product-information_en.pdf; 3. Medicines & Healthcare products Regulatory Agency (MHRA), 2023. Arexvy Summary of Product Characteristics. https://mhraproducts4853.blob.core.windows.net/docs/3f34cc46c0a49922e5014f7cfff730b205d353a0 4. Government of Canada. 2023. Respiratory syncytial virus (RSV): Canadian Immunization Guide. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/respiratory-syncytial-virus.html; 5. GSK press release 25 Sept 2023. https://www.gsk.com/en-gb/media/press-releases/japan-s-ministry-of-health-labour-and-welfare-approves-gsk-s-arexvy/; All URLs accessed September 2023

Influenza vaccine co-administration studies: Immunogenicity and safety

Open-label, randomized, controlled, multi-country studies to evaluate immune response, safety, and reactogenicity of RSVPreF3 OA when co-administered with an influenza vaccine in adults aged 60 years and above (RSV OA=ADJ-007; FLU-QIV) or 65 years and above (RSV OA=ADJ-008; FLU-QIV-HD, and RSV OA=ADJ-017; FLU-aQIV)

Phase 3 influenza vaccine co-administration studies: Design[1–5]

Open-label, randomized controlled study evaluating immunogenicity, safety, and reactogenicity of RSVPreF3 OA co-administered with FLU-QIV, FLU-QIV-HD or FLU-aQIV



Co-primary objectives:

- Non-inferiority* (1 month post-vaccination) of co-administration versus administration of each vaccine alone for:
  - RSVPreF3 OA in terms of:
    - RSV-A NAb GMT ratio
    - RSV-B NAb GMT ratio (for RSV-OA=ADJ-008 & 017 studies only†)
  - FLU in terms of HI Ab GMT ratio for each flu strain

Secondary objectives:

- Reactogenicity and safety
- Secondary humoral immunogenicity

Key safety and reactogenicity endpoints:

- Solicited events up to 4 days post-vaccination (7 days for RSV-OA=ADJ-017 study)
- Unsolicited AEs up to 30 days post-vaccination
- All SAEs and pIMDs up to study end

*To demonstrate non-inferiority: UL of the 95% CI of the group GMT ratio (control/co-administration) ≤1.5. †RSV-B NAb was a descriptive and secondary endpoint for RSV-OA=ADJ-007 study
Co-ad group: Participants receiving single dose of RSVPreF3 OA vaccine and single dose of FLU vaccine at Visit 1. Control group: Participants receiving a single dose of FLU vaccine at Visit 1 (Day 1), followed by a single dose of RSVPreF3 OA vaccine at Visit 2
Ab, antibody; AE, adverse event; CI, confidence interval; D, day; FLU-aQIV, adjuvanted quadrivalent influenza vaccine; FLU-QIV, quadrivalent influenza vaccine; FLU-QIV-HD: high-dose quadrivalent influenza vaccine; GMT, geometric mean titer; HI, hemagglutinin inhibition; NAb, neutralizing antibody; pIMD, potential immune-mediated disease; R, randomization; SAE, serious adverse event; UL, upper limit; YOA, years of age

See notes for references.

Summary: Co-administration of RSVPreF3 OA vaccine with influenza (FLU-QIV / FLU-QIV-HD / FLU-aQIV) vaccines

Immune response[1–3]	RSVPreF3 OA and influenza vaccines were co-administered without evidence of clinically meaningful immune interference with respect to available immunogenicity results
Safety[1–3]	Co-administration of RSVPreF3 OA with influenza vaccines is well-tolerated with acceptable safety profiles
Conclusion[1–4]	The totality of available evidence across three Phase 3 co-administration trials supports concurrent administration of RSVPreF3 OA with the FLU-QIV / FLU-QIV-HD / Flu-aQIV influenza vaccines*

FLU-aQIV, adjuvanted quadrivalent influenza vaccine; FLU-QIV, quadrivalent influenza vaccine; FLU-QIV-HD, high-dose quadrivalent influenza vaccine * FLU-aQIV results under final analysis

1. Chandler R *et al*. Immunogenicity, reactogenicity and safety of a respiratory syncytial virus prefusion F (RSVPreF3) candidate vaccine co-administered with the seasonal quadrivalent vaccine in older adults. Presented at IDWeek, October 19−23, 2022, Washington, DC, USA; 2. Valenciano S *et al*. Phase 3, open-label, randomised, controlled study to evaluate immune response, safety and reactogenicity of the RSVPreF3 OA vaccine when coadministered with FLU-QIV-HD vaccine in adults aged ≥65 years. Presented at 9th ESWI Influenza Conference, 17−20 September, 2023, Valencia, Spain; 3. Clark R *et al*. Safety and immunogenicity of the respiratory syncytial virus (RSV) prefusion F protein vaccine (RSVPreF3 OA) when co-administered with adjuvanted quadrivalent influenza vaccine (FLU-aQIV) in adults ≥65 years of age (YOA). Presented at 9th ESWI Influenza Conference, 17−20 September, 2023, Valencia, Spain; 4. Melgar M, Britton A, Roper LE, 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;72:793–801. DOI: http://dx.doi.org/10.15585/mmwr.mm7229a4. (accessed September 2023)

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