Virus respiratorio sinciziale

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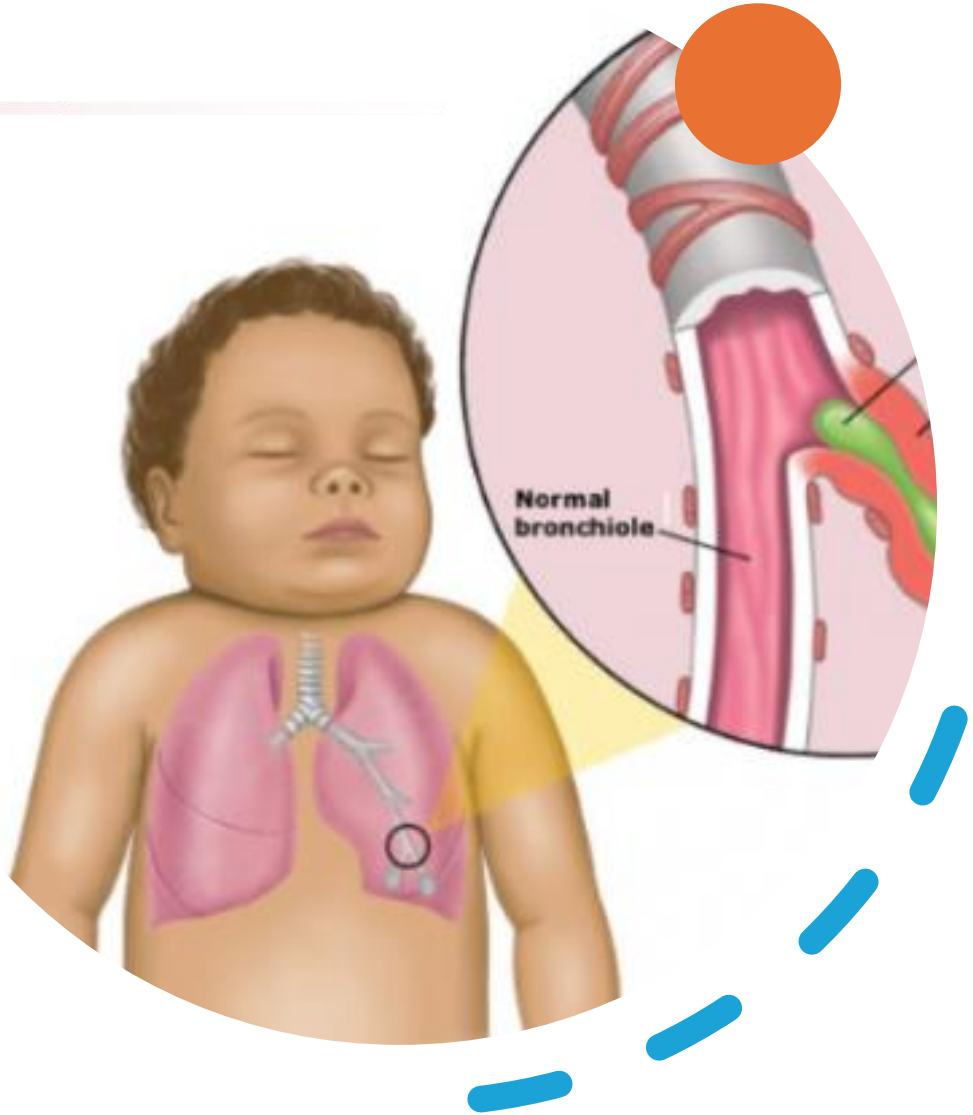
Conflicts of interest

- AG received speaker's honoraria and fees for attending advisory boards from ViiV Healthcare, Gilead, Janssen-Cilag, Merck Sharp & Dohme, Bristol-Myers Squibb, GSK, Pfizer and Novartis and received research grants from ViiV, Bristol-Myers Squibb, GSK, MSD, Angelini, Janssen-Cilag and Gilead

Why it's relevant: clinical vignette

- Previously healthy 4-month boy
- Born prematurely at 34wks
- Rhinorrhea and tachypnea for the past 4 days brought to the ED for fever
- Recently exposed to other sick children at daycare center
- Tachypnoeic, wheezing. Temperature 38.6°C, 156 bpm, RR 54/min, AP 74/46 mmHg; SpO2, 91% room air
- Need for oxygen (2L/min) → becomes lethargic with further desaturation
- Transferred to PICU after 24h from admission → need for CPAP and corticosteroids
- Weaning from supportive therapies
- PICU discharge on day 5, hospital discharge on hospital day 8



- **Could this be prevented?**

RSV burden of disease

- Approximately **33 million** lower respiratory tract infections requiring medical assistance in children under 5 years old
- **3.6 million hospitalizations** - over **100,000 deaths**
- Estimated cost of approximately **€4.82 billion**
- 60% of children contract RSV within the first year of life, nearly 100% by 2 years old
- **20% develop a severe RSV infection** requiring medical assistance
- **4%** will require **hospitalization**
- Among hospitalized children, approximately **20% need intensive care**
- Complications: recurrent bronchospasm,

Risk of severe infection increases with:

- Seasonality (October/November - March/April)
- Age under 1 year (especially <3 months)
- Premature birth
- Bronchopulmonary dysplasia
- Hemodynamically significant congenital heart diseases
- Diseases involving immune or neuromuscular deficits
- Immunocompromise
- Cystic fibrosis

RSV natural history

- Infants are protected against infection by the maternal-specific antibodies in the first months of life
- Individuals are exposed to multiple RSV infections during their life (seasonal RSV epidemics)
- The primary RSV infection is associated to a higher risk of severe disease
- Each acute episode provides temporary immunity against reinfection in the short term
- Primary infection also provides a partial reduction in susceptibility to reinfection

Borchers et al. Clin Rev Allergy Immunol 2013

Ohuma et al. Am J Epidemiol 2012

Poletti et al. BMC Med 2015

RSVpreF vaccine (*Abrysvo®*)

- Bivalent (RSV A and RSVB) prefusion form of the RSV fusion glycoprotein (preF), same formulation as for individuals >60yrs
- Licensed by EMA and FDA in **2023**
- Aim: prevention of LRTI in **infants < 6 months** with **maternal** vaccination
- One single im in pregnant individuals
  - Between weeks 24 and 36 of gestation (EMA)
  - Between weeks 32 and 36 of gestation (FDA)

RSVpreF: evidence from clinical trials

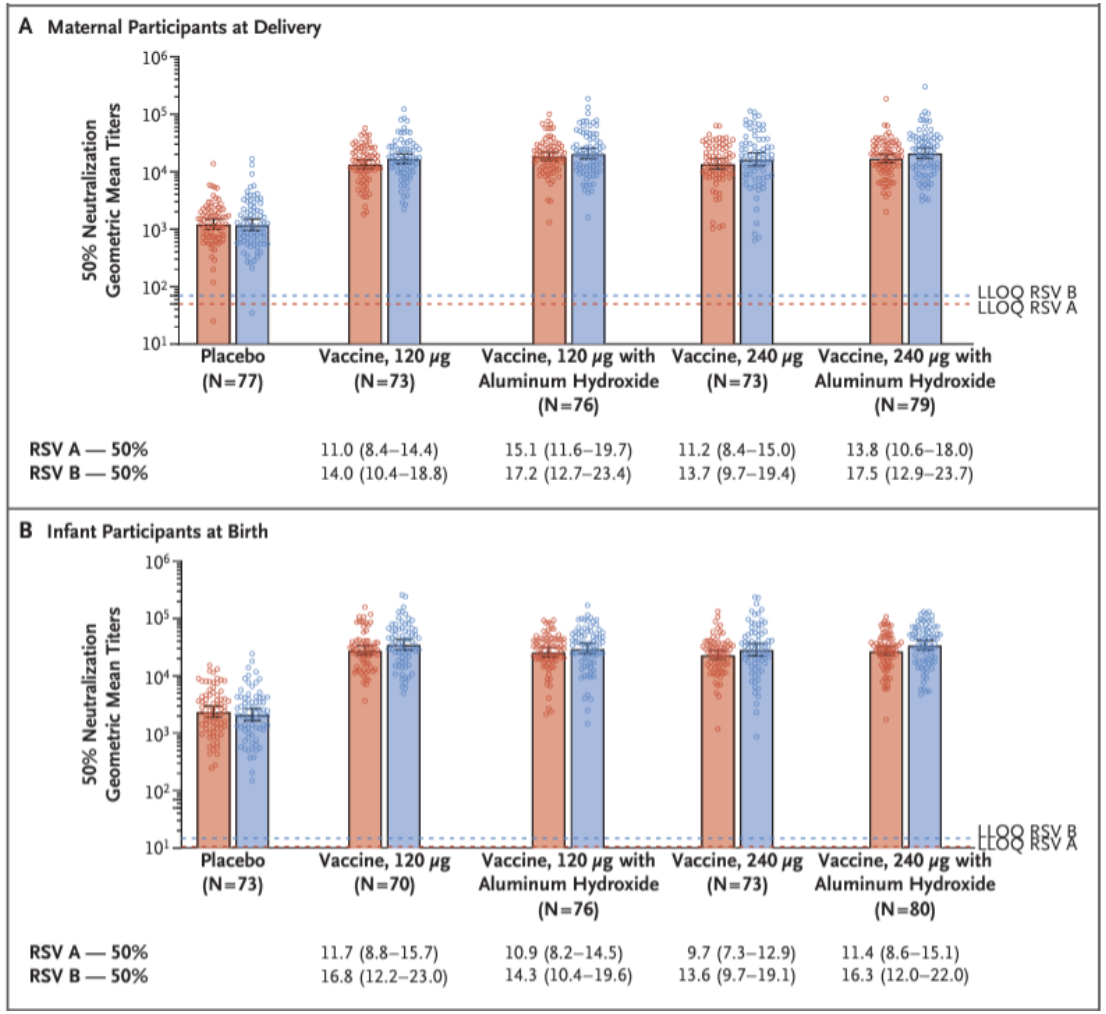
ORIGINAL ARTICLE

Prefusion F Protein–Based Respiratory Syncytial Virus Immunization in Pregnancy

Eric A.F. Simões, M.D., Kimberly J. Center, M.D., Alan T.N. Tita, M.D., Ph.D., Kena A. Swanson, Ph.D., David Radley, M.S., John Houghton, D.O., Stephanie B. McGrory, B.S.N., Emily Gomme, Ph.D., Marquita Anderson, M.D., John P. Roberts, M.D., Daniel A. Scott, M.D., Kathrin U. Jansen, Ph.D., William C. Gruber, M.D., Philip R. Dormitzer, M.D., Ph.D., and Aleiandra C. Gurtman. M.D.

N ENGL J MED 386;17 NEJM.ORG APRIL 28, 2022

- Phase 2b trial
- 406 pregnant women (24-36 wks gestation), and 403 infants
- Receive either 120 or 240 µg of RSVpreF vaccine or placebo
- 327 women (80.5%) received RSVpreF vaccine
- **Adverse events similar** vaccine and placebo
- **Neutralizing antibody responses**



RSVpreF: evidence from clinical trials

The NEW ENGLAND JOURNAL of MEDICINE

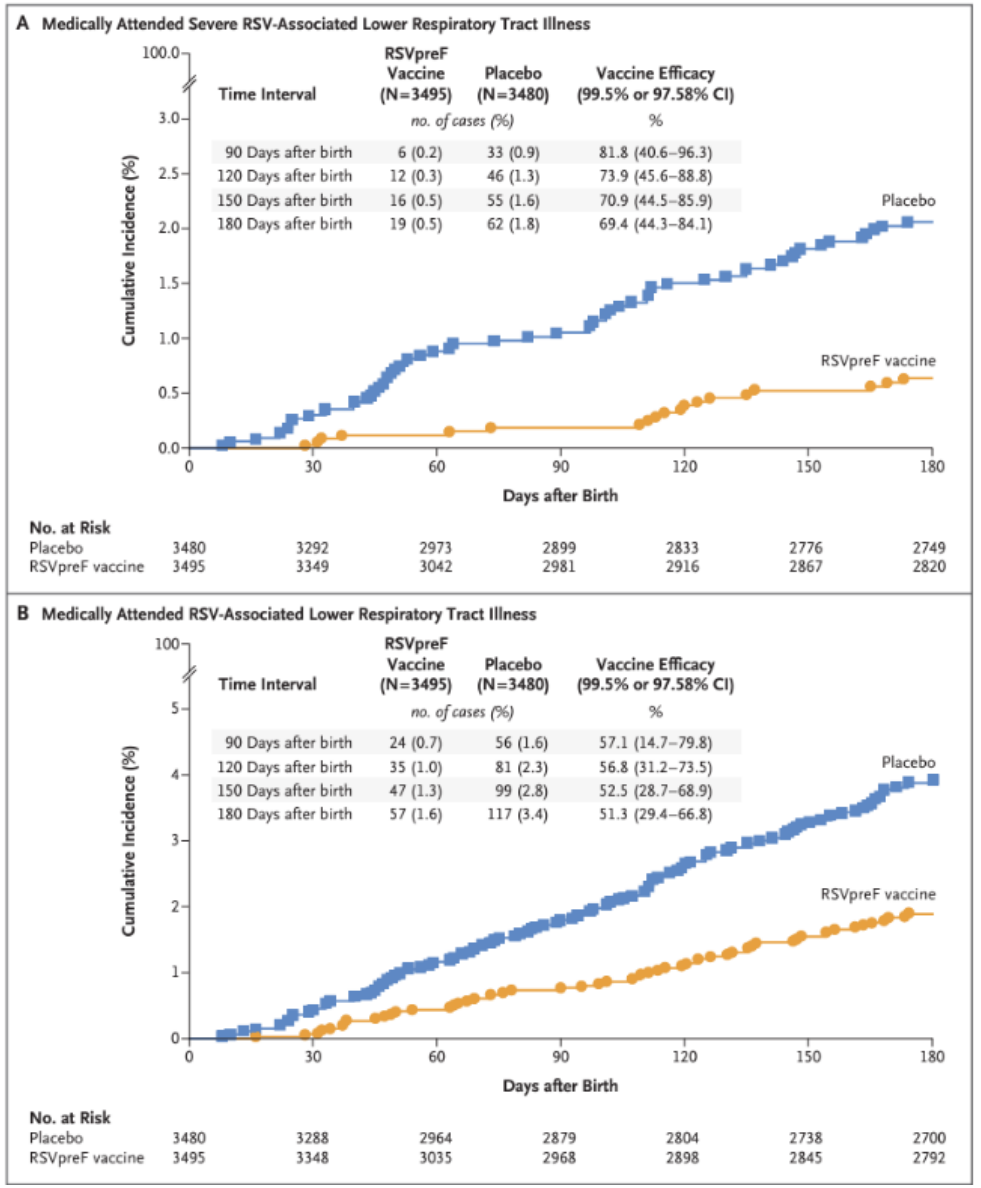
ESTABLISHED IN 1812 APRIL 20, 2023 VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

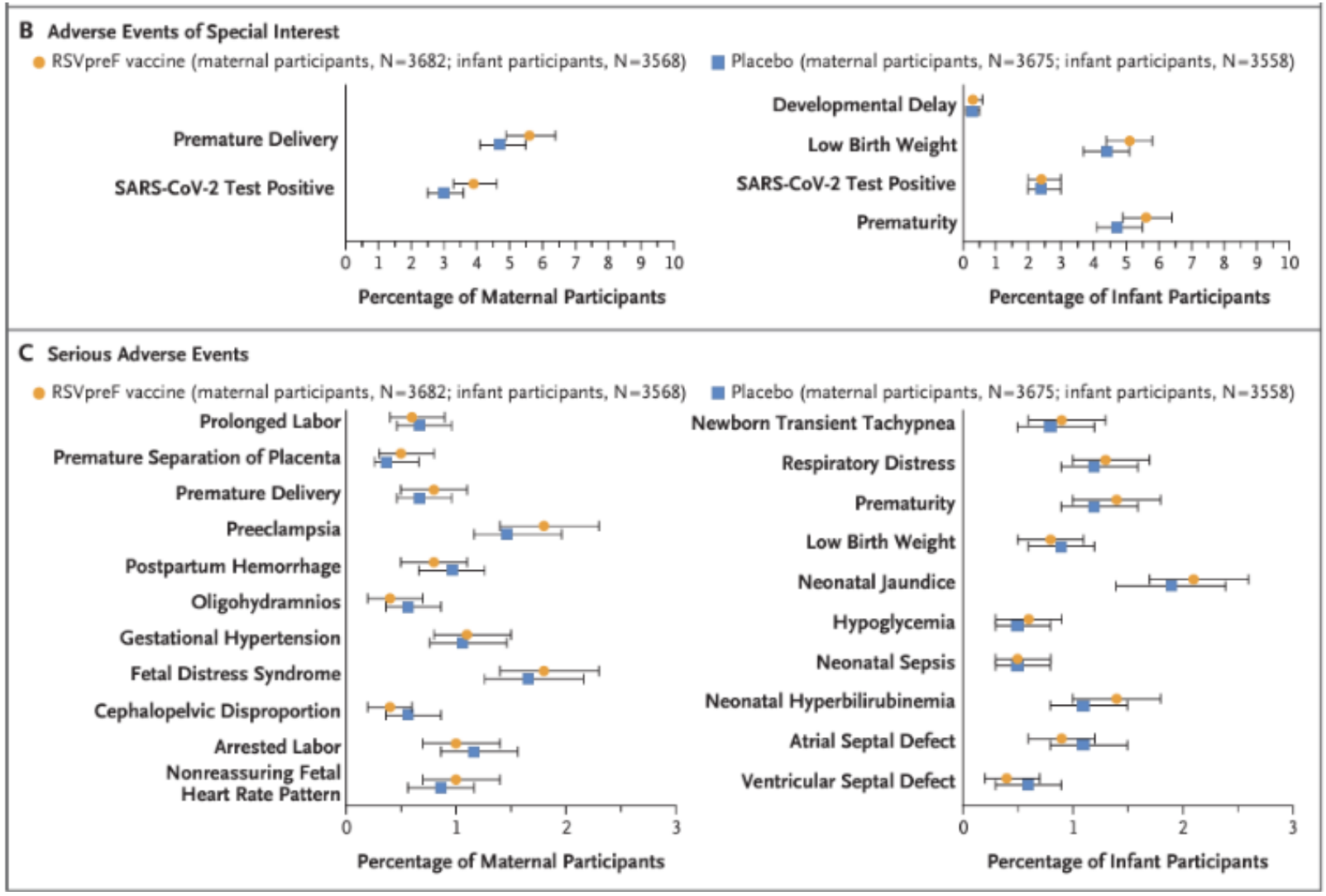
B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*

- Phase 3 trial
- 7358 pregnant women (24-36 wks gestation), and 7128 infants
- Receive either 120µg of RSVpreF vaccine or placebo
- 3682 women received RSVpreF vaccine

- RSV LRTI at 90 days: vaccine **efficacy, 57.1%**
- RSV LRTI at 180 days: vaccine **efficacy, 51.3%**
- Severe RSV at 90 days: vaccine **efficacy,**



RSVpreF: evidence from clinical trials



- More **premature delivery** in vaccine arm: 5.6% vs 4.7%
- Subset analysis 32-36 wks: premature delivery 4,2% vs. 3,7% →ACIP recommendations: 32-36wks (very low GRADE overall certainty of this evidence)

- More **low birth weight** in vaccine arm: 5.1% vs 4.4%
- More **neonatal jandice** in vaccine arm: 7.2% vs 6.7%

- No significant safety signals were detected in maternal participants or in infants and toddlers up to 24 mo

Kampmann et al. NEJM, 2023

Nirsevimab

- Extended half-life (5 months) monoclonal antibody specific for the prefusion conformation of the RSV F protein
- Licensed by EMA in **2022** and FDA in **2023**
- Single shot allows the development of an immune response to RSV → prevention of infection in **infants and children aged <24 mo**
- Suggested to be administered to infants entering their first RSV season
  - Newborns and babies under 1 year of age born during or entering their first RSV season
  - Children up to 24 months of age who remain at risk of severe RSV disease through

Nirsevimab: evidence from clinical trials

The NEW ENGLAND JOURNAL of MEDICINE

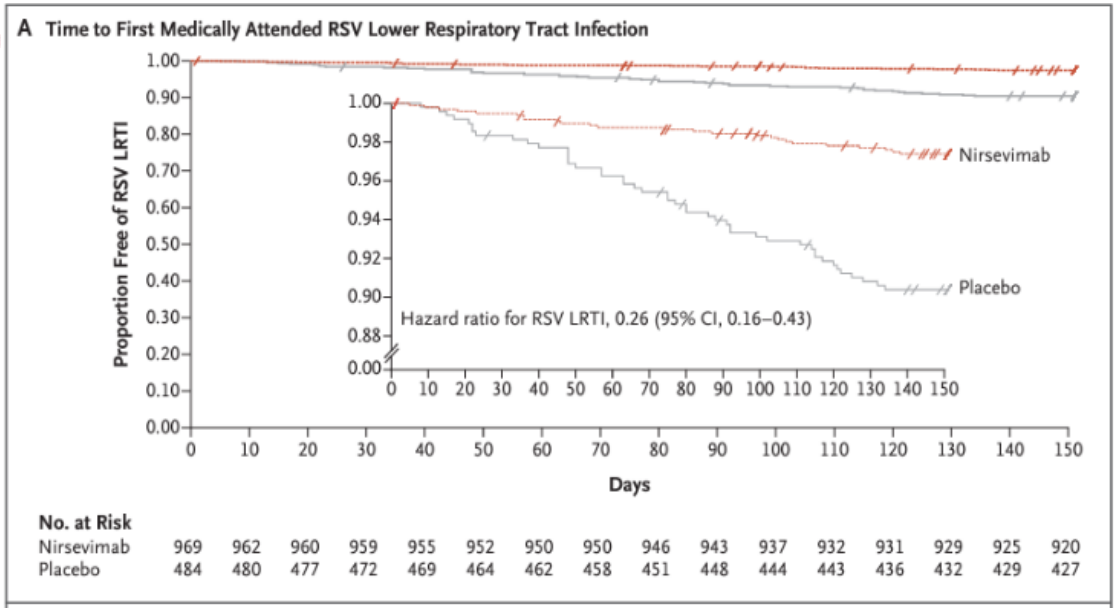
ESTABLISHED IN 1812 JULY 30, 2020 VOL. 383 NO. 5

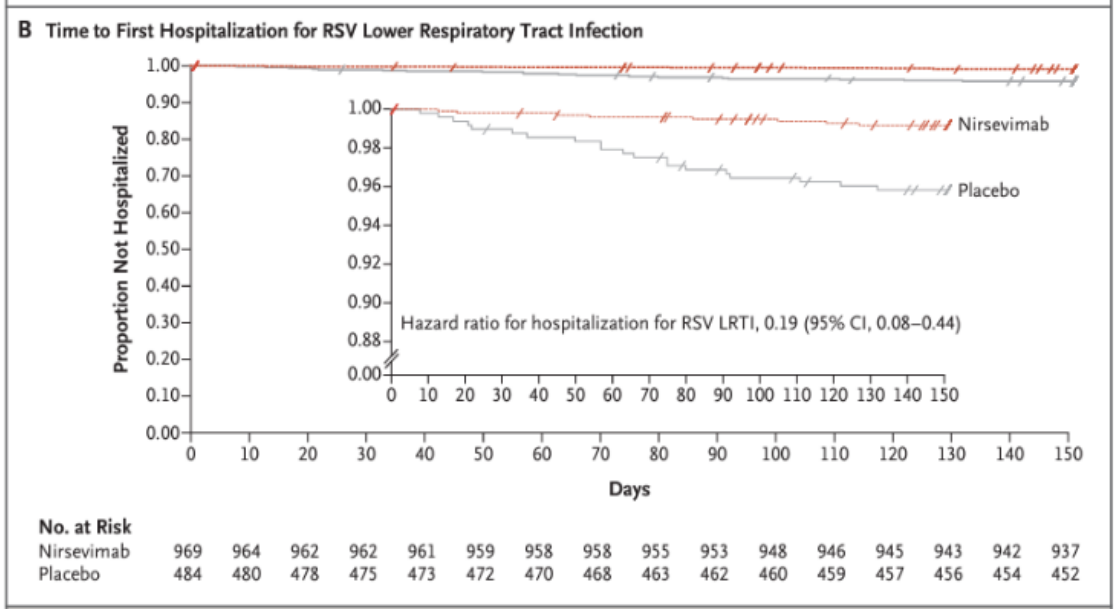
Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

M. Pamela Griffin, M.D., Yuan Yuan, Ph.D., Therese Takas, B.S., Joseph B. Domachowske, M.D., Shabir A. Madhi, M.B., B.Ch., Ph.D., Paolo Manzoni, M.D., Ph.D., Eric A.F. Simões, M.D., Mark T. Esser, Ph.D., Anis A. Khan, Ph.D., Filip Dubovsky, M.D., Tonya Villafana, Ph.D., and John P. DeVincenzo, M.D., for the Nirsevimab Study Group*

- 1453 infants born **preterm (29-34wks)**
- 969 nirsevimab vs 484 placebo

- RSV LRTI: **efficacy of 70.1%**
- RSV hospitalisation: **efficacy of 78.4%**
- Differences consistent throughout the **150-day period** after the dose was administered





Nirsevimab: evidence from clinical trials

ORIGINAL ARTICLE

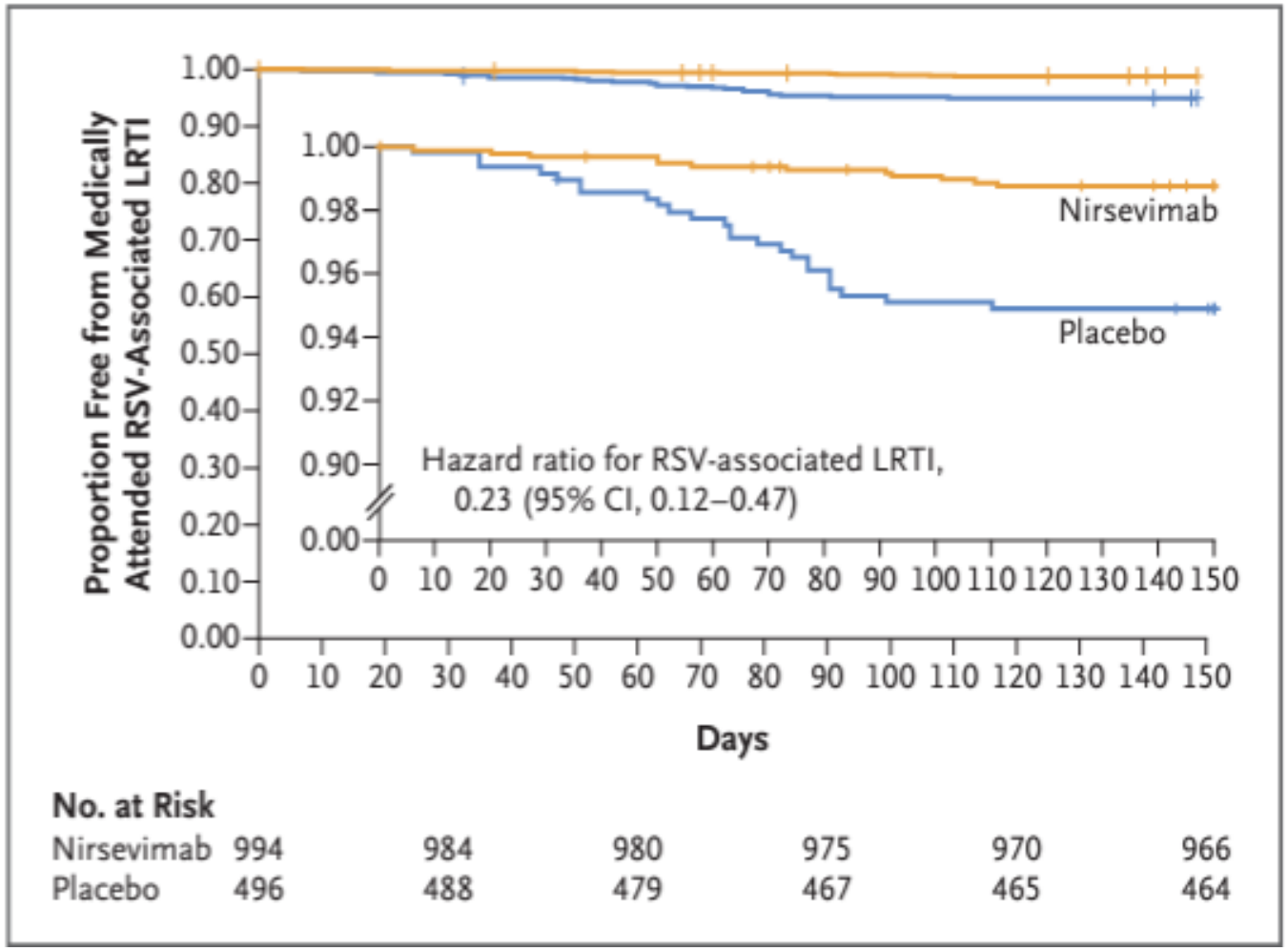
Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

Laura L. Hammitt, M.D., Ron Dagan, M.D., Yuan Yuan, Ph.D., Manuel Baca Cots, M.D., Miroslava Bosheva, M.D., Shabir A. Madhi, Ph.D., William J. Muller, Ph.D., Heather J. Zar, Ph.D., Dennis Brooks, M.D., Amy Grenham, M.Sc., Ulrika Wählby Hamrén, Ph.D., Vaishali S. Mankad, M.D., Pin Ren, Ph.D., Therese Takas, B.Sc., Michael E. Abram, Ph.D., Amanda Leach, M.R.C.P.C.H., M. Pamela Griffin, M.D., and Tonya Villafana, Ph.D., for the MELODY Study Group*

N ENGL J MED 386;9 NEJM.ORG MARCH 3, 2022

- 1490 infants born at a gestational age of **at least 35 weeks**
- 994 nirsevimab vs 496 placebo

- RSV LRTI: **efficacy of 74.5%**
- RSV hospitalisation: **efficacy of 62.1%**



Nirsevimab: pooled data from RCT

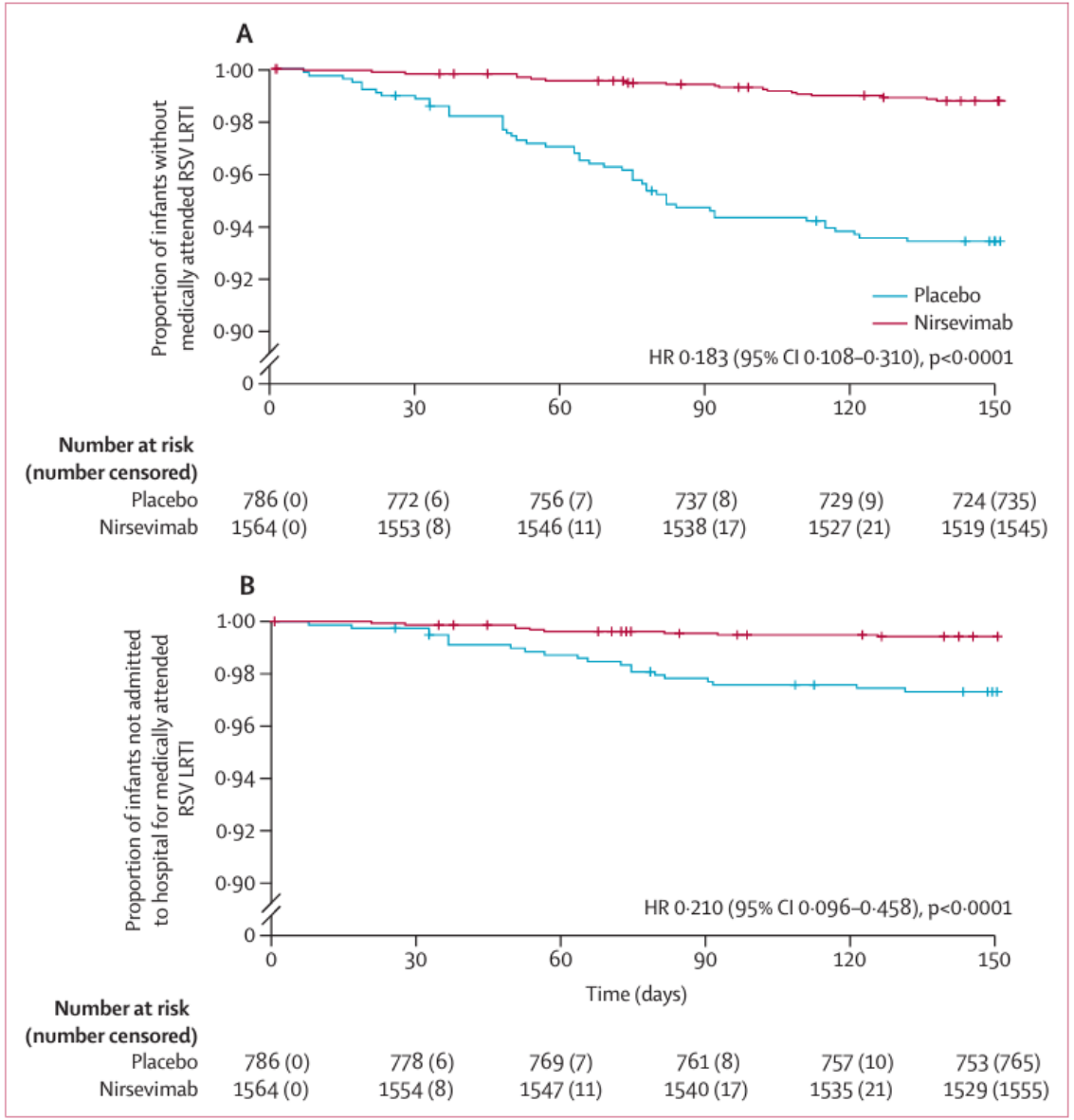
Efficacy of nirsevimab against respiratory syncytial virus lower respiratory tract infections in preterm and term infants, and pharmacokinetic extrapolation to infants with congenital heart disease and chronic lung disease: a pooled analysis of randomised controlled trials

Eric A F Simões, Shabir A Madhi, William J Muller, Victoria Atanasova, Miroslava Bosheva, Fernando Cabañas, Manuel Baca Cots, Joseph B Domachowske, Maria L Garcia-Garcia, Ineta Grantina, Kim A Nguyen, Heather J Zar, Anna Berglind, Celeste Cummings, M Pamela Griffin, Therese Takas, Yuan Yuan, Ulrika Wählby Hamrén, Amanda Leach, Tonya Villafana

Lancet Child Adolesc Health
2023; 7: 180–89

- Pooled efficacy analysis of previous trials
- 2,350 infants; 1564 nirsevimab vs 786 placebo

- RSV LRTI: **relative risk reduction (RRR) 79.5%**
- Maintained **over 150 days** after administration



Nirsevimab vs Palivizumab

CORRESPONDENCE

Safety of Nirsevimab for RSV in Infants with Heart or Lung Disease or Prematurity

N ENGL J MED 386;9 NEJM.ORG MARCH 3, 2022

- 925 infants eligible for palivizumab
- 615 preterm (<35wks) and 310 infants at risk of congenital heart disease or chronic lung disease
- 1-dose nirsevimab vs 5-dose palivizumab

- RSV LRTI: **1.0% palivizumab, nirsevimab 0.6%**

Data deducted from pharmacological analysis

Similar efficacy

Presumable lower costs (1 vs 5 administrations)

Vaccination vs monoclonal antibodies

No direct comparison available

RSVpreF

- Immediate protection after birth
- Greater resistance to mutations in the F protein

- Less protection if mother is immunocompromised or if there's reduced transfer from the pregnant woman to the baby (e.g., premature birth)
- Increased risk of premature birth

Nirsevimab

- Longer duration of protection
- Assured administration (rather than relying on transplacental transfer)
- No adverse events in pregnancy

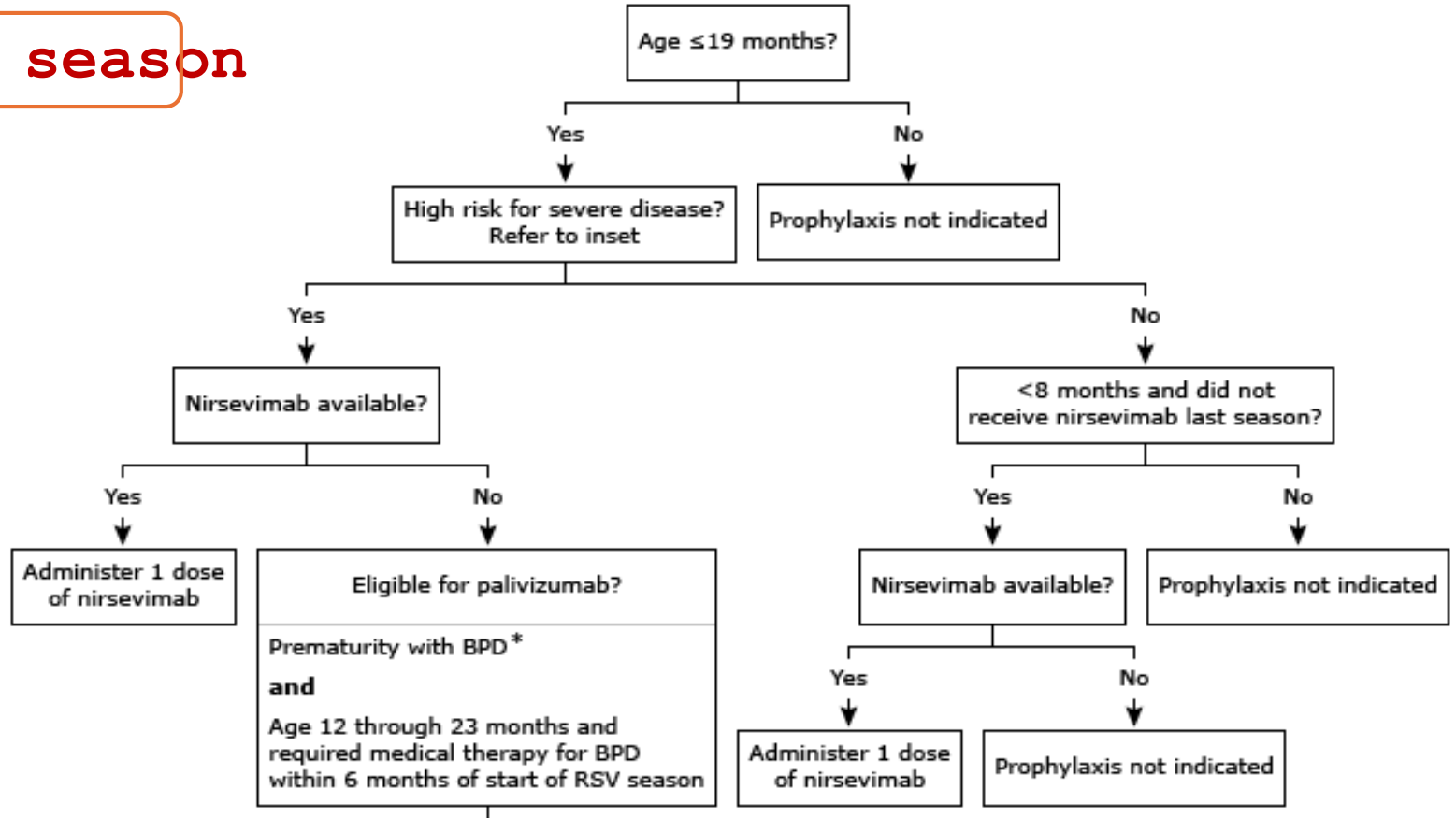
- Potentially limited availability of the drug
- Injection directly into the newborn

First RSV season

Inset 1: Palivizumab eligibility (use only when nirsevimab is unavailable)
Prematurity with BPD¶ ▪ Age <1 year at start of RSV season ▪ Age 12 through 23 months and required medical therapy for BPD within 6 months of start of RSV season
Prematurity without BPD **and** Born <29 weeks gestation and <12 months at start of RSV season
Congenital heart disease - decision should be made in consultation with infant's cardiologist

Inset 2: High risk for severe disease
Chronic lung disease of prematurity and receipt of medical support during the 6 months prior to start of RSV season
Severe immunocompromise
Cystic fibrosis with ▪ Manifestations of severe disease **or** ▪ Weight for length <10th percentile
American Indian and Alaska Native children

Second RSV season



High risk for severe disease
Chronic lung disease of prematurity and receipt of medical support during the 6 months prior to start of RSV season
Severe immunocompromise
Cystic fibrosis with ▪ Manifestations of severe disease **or** ▪ Weight for length <10th percentile
American Indian and Alaska Native children

Annual burden of RSV in older adults

RSV is prevalent but under-recognized in older adults

Estimated cases, hospitalizations, and in-hospital deaths due to RSV-associated acute respiratory infections among adults aged 60 years and older per region, 2019 population.

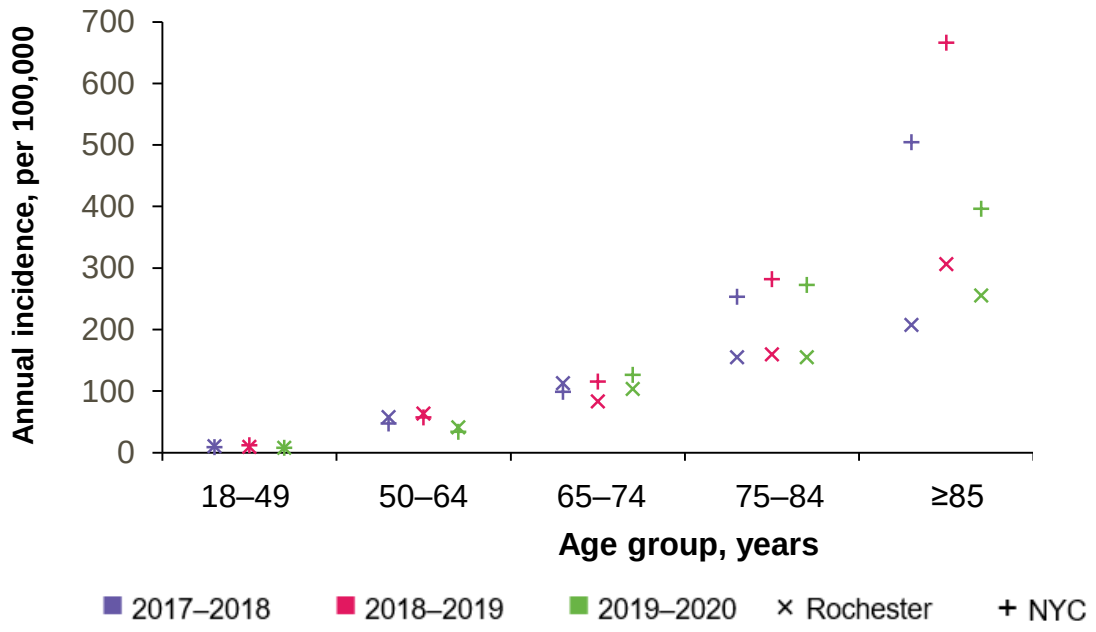
	RSV-ARI	RSV hospitalizations	RSV in-hospital deaths
Overall (point estimates, 95% CI)	Attack rate 1.62% (0.84–3.08)	Hospitalization rate 0.15% (0.09–0.22)	hCFR 7.13% (5.40–9.36)
Population ≥60 years of age in 2019	Number of cases (95% CI)	Number of hospitalizations (95% CI)	Number of in-hospital deaths (95% CI)
Germany 23,738,453	383,376 (199,403–731,382)	34,421 (22,314–53,174)	2,455 (1,206–4,978)
Italy 18,043,000	291,394 (151,561–555,905)	26,162 (16,960–40,416)	1,866 (917–3,783)
France 17,510,000	282,787 (147,084–539,483)	25,390 (16,459–39,222)	1,811 (889–3,672)
United Kingdom 16,569,000	267,589 (139,180–510,491)	24,025 (15,575–37,115)	1,714 (842–3,474)
Spain 12,278,000	198,290 (103,135–378,285)	17,803 (11,541–27,503)	1,270 (624–2,575)

Savic M *et al.* A systematic literature review and a meta-analysis of the respiratory syncytial virus (RSV) burden of disease in adults over 60 years of age. Influenza Other Respi Viruses. 2022;1-10;

Risk of RSV-associated hospitalization increases with age and chronic medical conditions

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* with underlying conditions

Comorbidity	Incidence rate ratio†
Asthma	2.0–3.6
CAD	3.7–7.0
Diabetes	2.4–11.4
COPD	3.2–13.4
CHF	4.0–33.2

*Adults aged ≥18 years. †Ratio of rate among people with each comorbidity vs those without it, in the surveillance area population

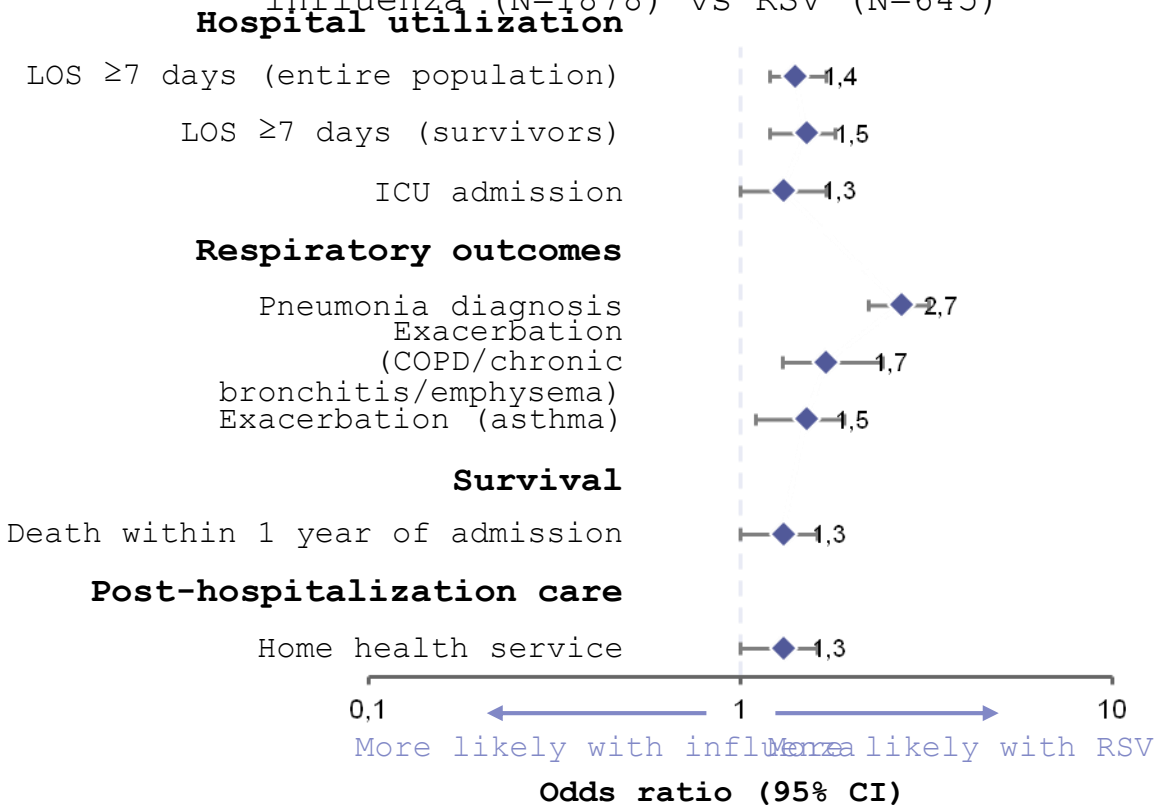
Graph and table were independently created for GSK from the original data

CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; NYC, New York City

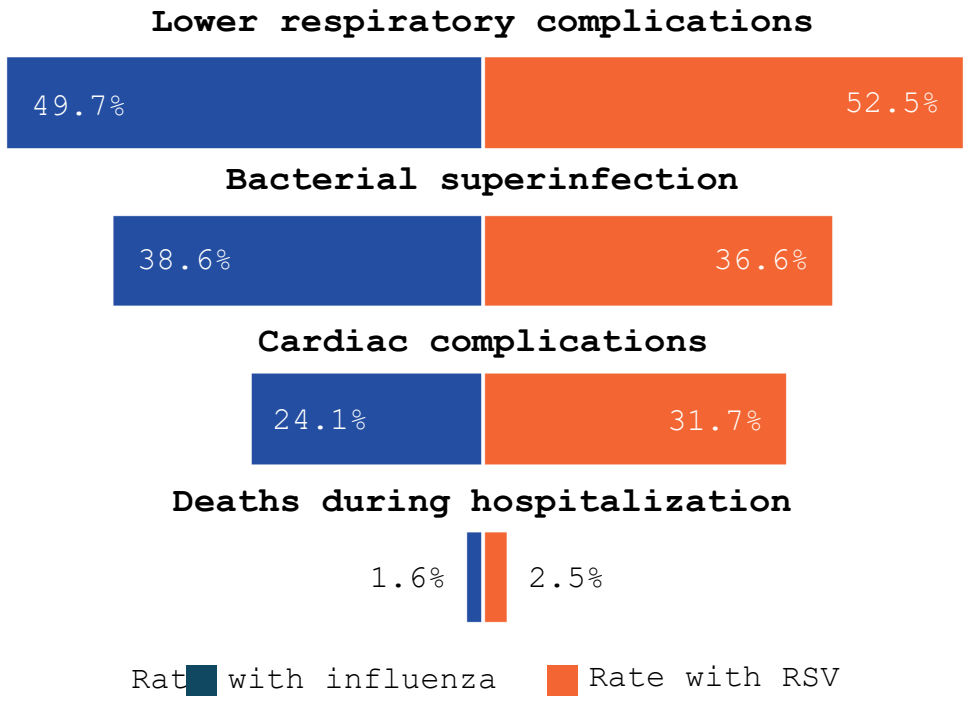
Branche AR *et al. Clin Infect Dis* 2022:74:1004–1011

Complications and severe outcomes are comparable between older adults with RSV and influenza

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



Rates of complications and mortality in adults* hospitalized with ARTI due to **influenza** (N=366, mean age = 64.4 years) and **RSV** disease (N=238, mean age = 67.3 years)[3]



*Adults aged ≥18 years
ARTI, acute respiratory tract infection; 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; 3. Falsey AR *et al. Open Forum Infect Dis* 2021;8(11):ofab491

Spotlight: vaccination in people aged ≥60yrs

- **Rationale:** individuals ≥60 years with comorbidities that put them at increased risk for severe disease
- **Single-shot**
- **Formulations:** subunit vaccines based on prefusion RSV F glycoproteins (including an adjuvant or non-adjuvanted)
  - For immunocompromised patients, theoretical benefit using the adjuvanted vaccine
  - Non-adjuvanted is approved for pregnant women

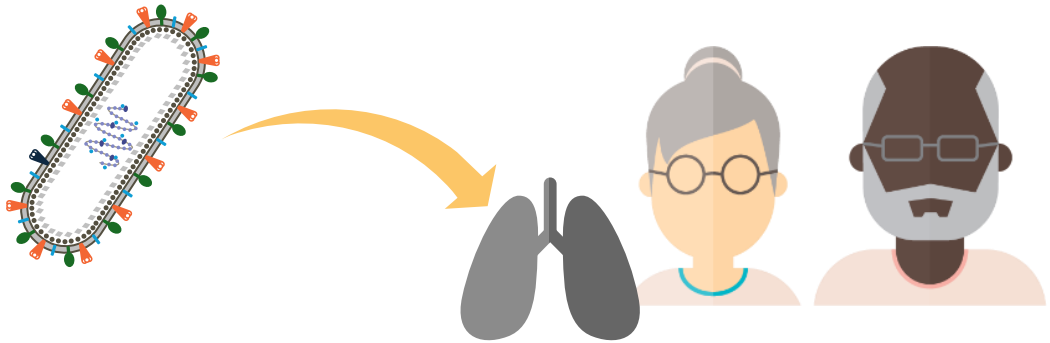
RSVPreF3 OA in Time's best inventions 2023

RSVPreF3+AS01 (*Arexvy*®)

Arexvy RSV Vaccine: The 200 Best Inventions of 2023 | TIMEArexvy RSV Vaccine: The 200 Best Inventions of 2023 | TIMEArexvy RSV Vaccine: The 200 Best Inventions of 2023 | TIME

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]

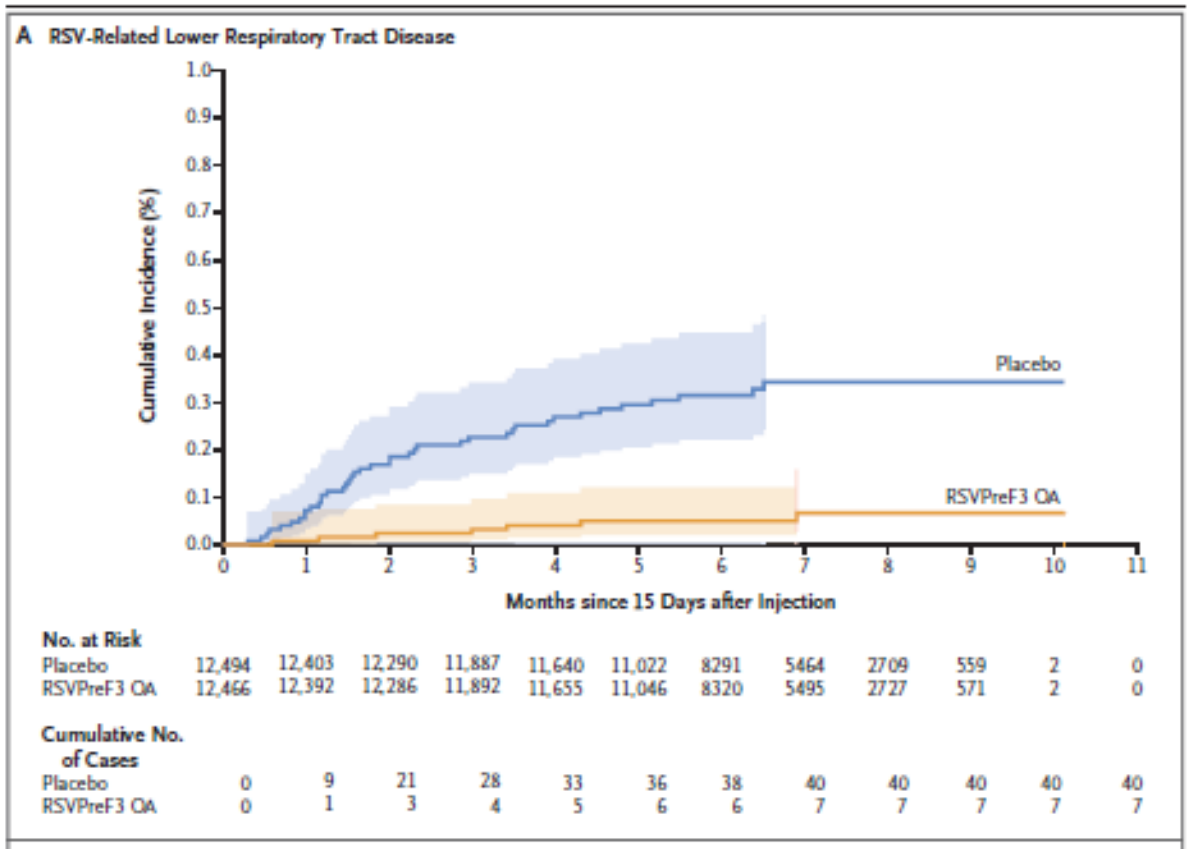
Cellular immune response

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



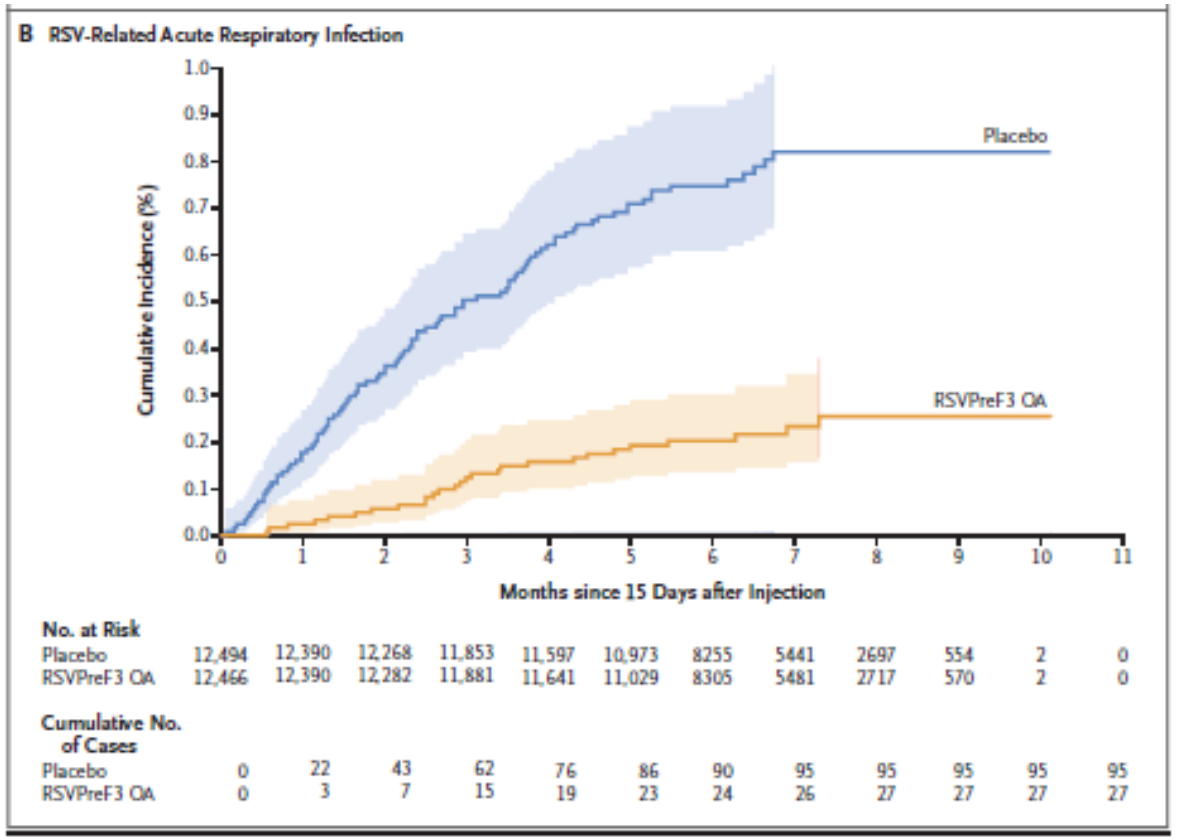


Figure 2 (facing page). Cumulative Incidence of RSV-Related Lower Respiratory Tract Disease and RSV-Related Acute Respiratory Infection (Modified Exposed Population).

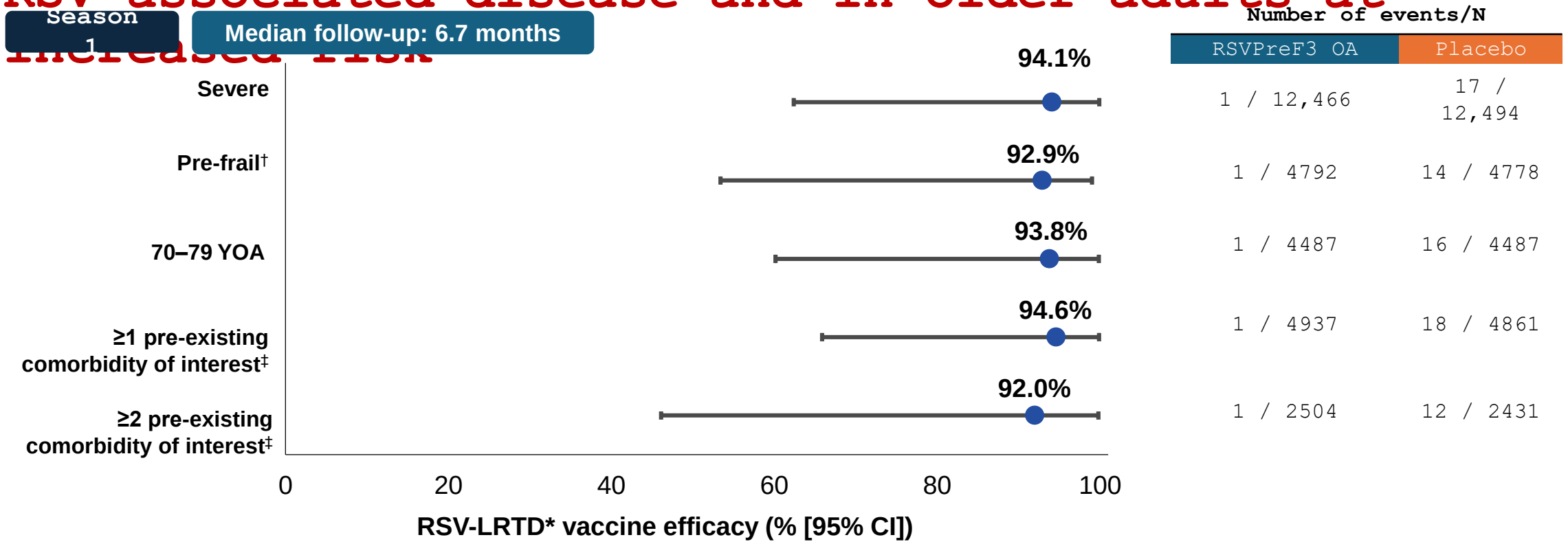
Cases were reported until the efficacy database-lock point of April 11, 2022. Cases of RSV-related lower respiratory tract disease were identified by the adjudication committee. Shaded areas indicate 96.95% confidence intervals for the incidence of RSV-related lower respiratory tract disease (Panel A) and 95% confidence intervals for the incidence of RSV-related acute respiratory infection (Panel B). Confidence intervals were computed at each case reported and end at the last reported case in each group.

N Engl J Med 2023;388:595-608.

Very high and consistent vaccine efficacy against severe RSV-associated disease and in older adults at increased risk

Season 1

Median follow-up: 6.7 months



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

Spotlight: vaccination in people aged ≥60yrs

ORIGINAL ARTICLE

Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

A. Papi, M.G. Ison, J.M. Langley, D.-G. Lee, I. Leroux-Roels, F. Martinon-Torres, T.F. Schwarz, R.N. van Zyl-Smit, L. Campora, N. Dezutter, N. de Schrevel, L. Fissette, M.-P. David, M. Van der Wielen, L. Kostanyan, and V. Hulstrøm, for the AReSVi-006 Study Group*

N ENGL J MED 388;7 NEJM.ORG FEBRUARY 16, 2023

- **Adjuvanted** RSV vaccine
- RSV LRTI efficacy over follow-up of 6.7mo: **82.6%**
- Severe RSV: efficacy **94.1%**
- Second season efficacy **decreased to 56.1%** [*MMWR Morb Mortal Wkly Rep. 2023*]

- Vaccine was more reactogenic than

ORIGINAL ARTICLE

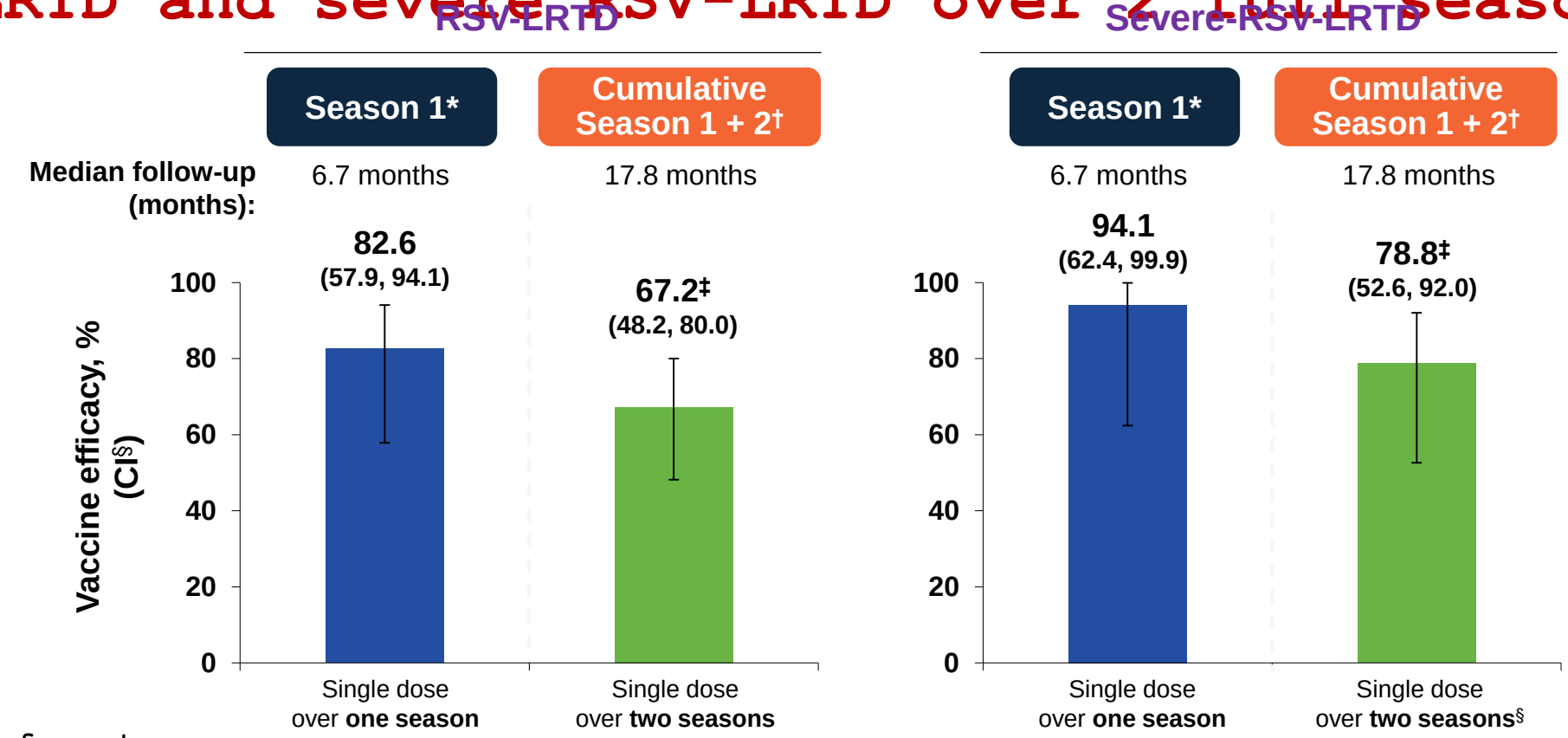
Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

E.E. Walsh, G. Pérez Marc, A.M. Zareba, A.R. Falsey, Q. Jiang, M. Patton, F.P. Polack, C. Llapur, P.A. Doreski, K. Ilangovan, M. Rämet, Y. Fukushima, N. Hussen, L.J. Bont, J. Cardona, E. DeHaan, G. Castillo Villa, M. Ingilizova, D. Eiras, T. Mikati, R.N. Shah, K. Schneider, D. Cooper, K. Koury, M.-M. Lino, A.S. Anderson, K.U. Jansen, K.A. Swanson, A. Gurtman, W.C. Gruber, and B. Schmoele-Thoma, for the RENOIR Clinical Trial Group*

N ENGL J MED 388;16 NEJM.ORG APRIL 20, 2023

- **Non-adjuvanted** RSV vaccine
- RSV LRTI with 2 or more symptoms: efficacy **66.7%**
- RSV LRTI with 3 or more symptoms: efficacy **85.7%**
- Second season efficacy **decreased to 48.9%** (≥2 symptoms) **and to 78.6%** (≥3 symptoms)

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

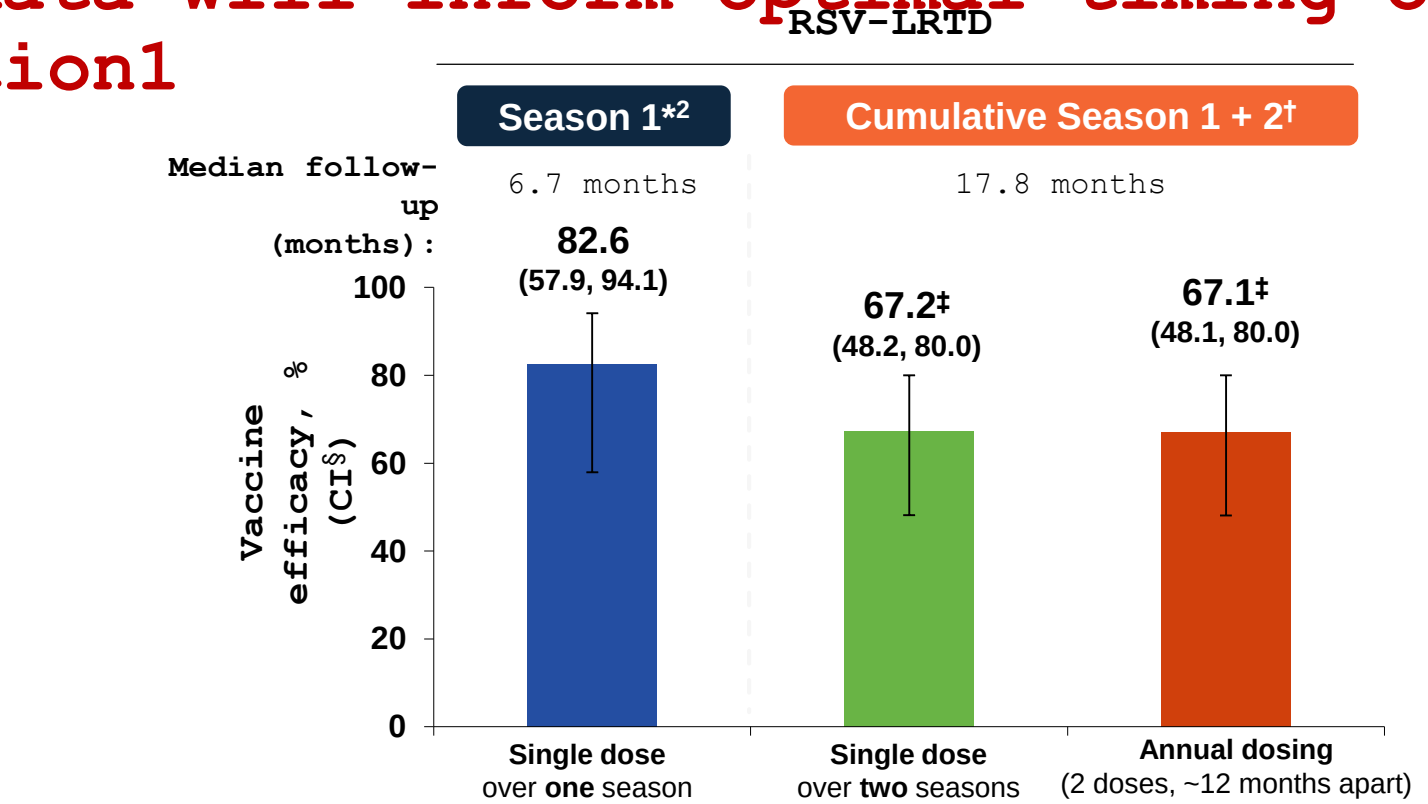


Number of events:

	RSV-LRTD		Severe RSV-LRTD	
	Season 1*	Cumulative Season 1 + 2†	Season 1*	Cumulative 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); ‡VE with season as a covariate. VE is estimated using a Poisson regression model adjusted using age, region and season; §96.95% CI for VE Season 1 (RSV-LRTD), 97.5% CI for cumulative Season 1 + 2 (RSV-LRTD), 95% CI for severe RSV-LRTD (Season 1 and cumulative Season 1 + 2).
CI, confidence interval; LRTD, lower respiratory tract disease; VE, vaccine efficacy
1. Papi A *et al. N Engl J Med* 2023;388(7):595–608; 2. Ison MG *et al. Clin Infect Dis.* 2024:ciae010. doi: 10.1093/cid/ciae010. Epub ahead of print

Re-vaccination after 12 months does not appear to confer additional efficacy benefit against RSV-LRTD; future data will inform optimal timing of re-vaccination1



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RSVPreF3 OA	**7** / 12,466	**30** / 12,469	**30** / 12,469
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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); ‡VE with season as a covariate. VE is estimated using a Poisson regression model adjusted using age, region and season; §96.95% CI for VE Season 1 (RSV-LRTD), 97.5% CI for Cumulative Season 1 + 2 (RSV-LRTD). CI, confidence interval
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Approved vaccines: Abrysvo and Arexvy target groups

Vaccine	Target Group	Details of Vaccine Administration	Regulatory Approval by the U.S. FDA	Regulatory Approval by the EMA
RSVpreF vaccine (Abrysvo™, Pfizer Inc.), a non-adjuvanted, bivalent recombinant stabilized prefusion F protein subunit vaccine	Infants (via maternal immunization at 32–36 weeks gestation for U.S. FDA, and at 24–36 weeks gestation for EMA)	Single intramuscular dose of 120 mcg (0.5 mL). Coadministration with Tdap, influenza, and COVID-19 vaccines is possible	21 August 2023 [10,59]	23 August 2023 [58]
RSVpreF vaccine (Abrysvo™, Pfizer Inc.), a non-adjuvanted, bivalent recombinant stabilized prefusion F protein subunit vaccine	Individuals aged ≥ 60 years	Single intramuscular dose of 120 mcg (0.5 mL). Coadministration with influenza vaccine is possible	31 May 2023 [11]	23 August 2023 [58]
RSVpreF3 vaccine (Arexvy™, GSK Inc.), an AS01E-adjuvanted, non-bivalent recombinant prefusion F protein subunit vaccine	Individuals aged ≥ 60 years	Single intramuscular dose of 120 mcg (0.5 mL). Coadministration with influenza vaccine is possible	3 May 2023 [11]	6 June 2023 [61]

COVID-19: Coronavirus disease 2019; EMA: European Medicines Agency; FDA: Food and Drug Administration; GSK GlaxoSmithKline; RSV: Respiratory syncytial virus; Tdap: Tetanus, diphtheria, and pertussis; U.S.: United States.

- The over all efficacy of both vaccines in preventing LRTI exceeded 80% in adults age 60years.
- Abrysvo had 81.8% efficacy in preventing severe RSV LRTI in infants within 90 days of birth and circa 69.4% efficacy within 180 days of birth.

Guideline recommendations

Guideline Agency	Target Group	Details
American College of Obstetricians and Gynecologists (ACOG)	Pregnant women at 32 through 36 weeks gestation	Seasonal administration of one dose of RSV vaccine (Abrysvo, Pfizer Inc.) to prevent RSV LRTD in infants
U.S. Centers for Disease Control and Prevention	Pregnant women at 32 through 36 weeks gestation	Seasonal administration of one dose of RSV vaccine (Abrysvo, Pfizer Inc.) to prevent RSV LRTD in infants
U.S. Centers for Disease Control and Prevention	Adults 60 years and older	Single dose of RSV vaccine with either Abrysvo™, (Pfizer Inc.) or Arexvy™, (GSK Inc.) to prevent RSV LRTD

Prevenzione delle infezioni da Virus Respiratorio Sinciziale nella popolazione italiana

Società Scientifiche proponenti:

SItI- Società Italiana Igiene, Medicina Preventiva e Sanità Pubbli

SIMIT- Società Italiana Malattie Infettive e Tropicali

- Considerare che i nuovi vaccini contro RSV oggi disponibili rappresentano una opzione preventiva innovativa nei confronti di un bisogno medico ad oggi insoddisfatto
- Prevedere di inserire la vaccinazione contro RSV nel calendario vaccinale, raccomandando la vaccinazione negli adulti ≥60 anni di età con co-morbosità e negli anziani ≥75 anni di età

Lack of evidence in immunocompromised patient: an unmet medical need

American Society of Transplantation and Cellular Therapy Series: #7 - Management of Respiratory Syncytial Virus Infections in Hematopoietic Cell Transplant Recipients

Firas El Chaer[1,*], Daniel R. Kaul[2], Janet A. Englund[3], Michael Boeckh[4,†], Marjorie V. Batista[5,†], Susan K. Seo[6], Paul A. Carpenter[7], David Navarro[8], Hans H. Hirsch[9,10,11,†], Michael G. Ison[12,†], Genovefa A. Papanicolaou[6,†], Roy F. Chemaly[13,†]

- Only few RSV-vaccine clinical trials has included HCT recipients or other immunosuppressed patients
- **no evidence-based** recommendations can be made for these groups at this time
- There are **no data or guidelines** yet to inform the use of this vaccine in **other individuals <60 years,** including those who are immunocompromised
- RSV vaccine can be considered in HCT recipients age >60 years who are eligible for **routine** vaccination post-HCT
- **Dedicated studies** in HCT recipients/immunosuppressed patient are needed to evaluate the immunogenicity and efficacy of RSV vaccines

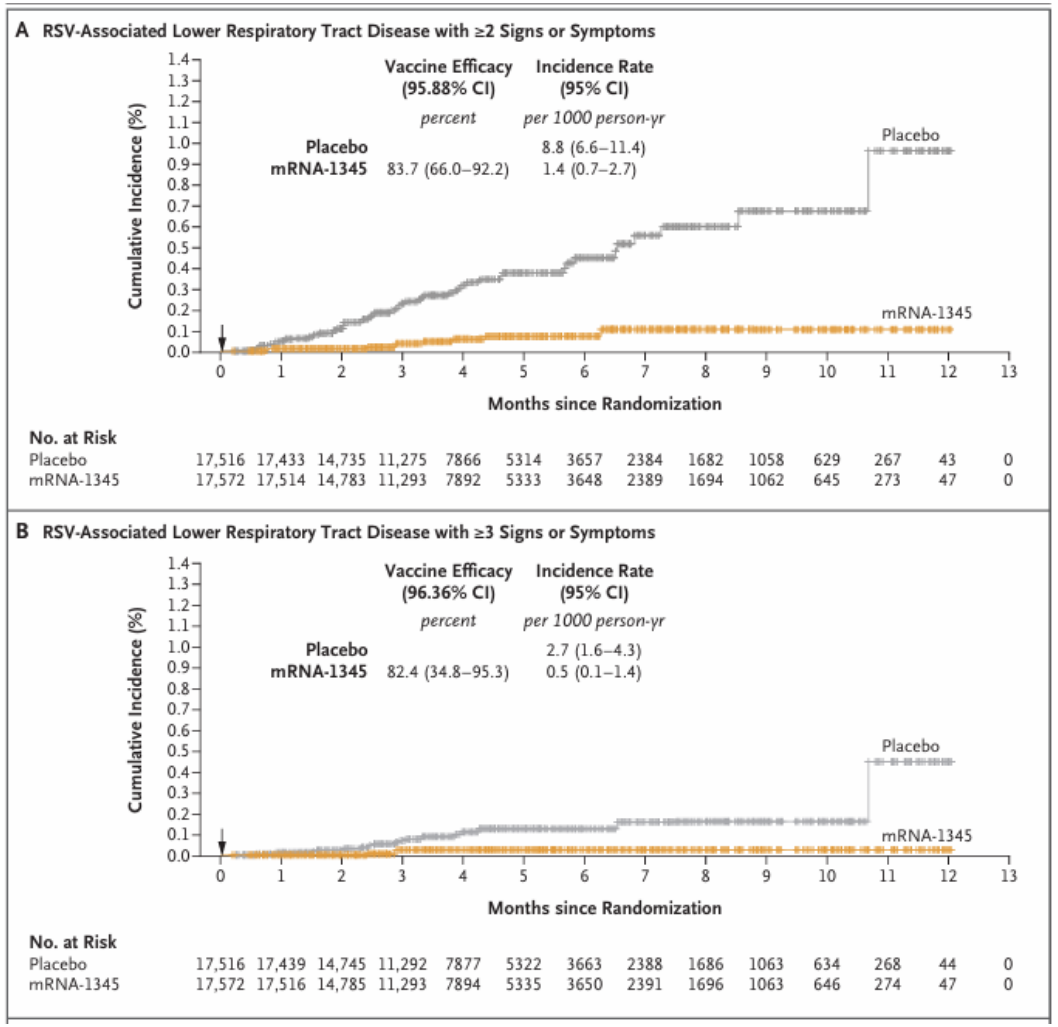
m-RNA 1345

- encapsulated mRNA based vaccine
- encoding the membrane-anchored **RSV-F glycoprotein** derived from an RSV **A** strain, and stabilized in the **preF** conformation (as the previously approved vaccine)
- phase 1 clinical trial of this vaccine did not show safety concerns and showed immunogenicity in younger and older adults

ORIGINAL ARTICLE

Efficacy and Safety of an mRNA-Based RSV PreF Vaccine in Older Adults

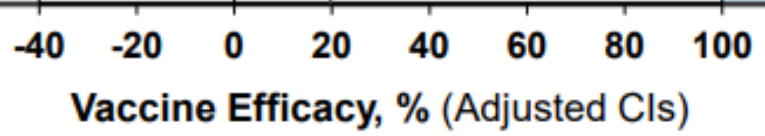
- randomized, double-blind, placebo-controlled, **phase 2–3 trial**
- randomly assigned, in a 1:1 ratio, adults **60 years of age or older** to receive **one** dose of mRNA-1345 (50 µg) or placebo
- **35,541** participants
- The trial included persons with stable chronic medical conditions and **excluded** persons with certain **immunocompromising conditions.**
- RSV LRTD with ≥ 2 sign o symptoms: vaccine efficacy **83.7%**
- RSV LRTD with ≥ 3 sign o symptoms: vaccine efficacy **82.4%**
- RSV-associated acute respiratory disease: vaccine efficacy **68.4%**
- **no** evident safety concerns



Efficacia del vaccino in base all'età al momento dell'arruolamento per endpoint

Primary Analysis

RSV LRTD with ≥ 2 Symptoms		Numbers of Events: RSV Vaccine (mRNA-1345) (N = 17,572)	Numbers of Events: Placebo (N = 17,516)	Vaccine Efficacy (CI)
Overall		**9** / 17,572	**55** / 17,516	**83.7%** (66.0, 92.2)
Age	60 – 69 Years	**8** / 11,168	**33** / 11,118	**76.0%** (48.0, 88.9)
	70 – 79 Years	**1** / 5,440	**22** / 5,416	**95.4%** (65.9, 99.4)
	≥ 80 Years	**0** / 964	**0** / 982	–
Comorbidities	No Comorbidities	**7** / 12,377	**38** / 12,431	**81.6%** (58.8, 91.8)
	≥ 1 Comorbidities	**2** / 5,195	**17** / 5,085	**88.4%** (49.9, 97.3)
Frailty Status	Fit (0-3)	**8** / 13,396	**45** / 13,250	**82.3%** (62.5, 91.7)
	Vulnerable/Frail (≥ 4)	**0** / 3,781	**6** / 3,858	**100.0%** (NE, 100.0)



Perché un vaccino a mRNA per prevenire l'infezione da RSV?

- Negli studi clinici di Fase 1, l'immunogenicità umorale e cellulare di mRNA-1345 è apparsa generalmente simile tra gli adulti più anziani e quelli più giovani.[7]

- Efficacia di mRNA-1345 nei soggetti di **70-79** anni di età pari a **95.4%** (65.9, 99.4) nell'analisi primaria e a **78%** (56.3, 88.9) nell'analisi addizionale

- Finora non è stata riscontrata alcuna evidenza di sindrome di Guillain Barre o di encefalomielite acuta disseminata (ADEM) per mRNA-1345; non sono stati identificati problemi di sicurezza per altri disturbi neurologici, tra cui paralisi di Bell/paralisi facciale.

- L'mRNA-1345 è attualmente in fase di valutazione per il suo potenziale di protezione da RSV per tutte le popolazioni vulnerabili.

1. Cherukuri et al. *J Clin Vacc Immunol*. 2013;20:239-47; 2. Walsh et al. *J Infect Dis.* 2004;190: 373-78; 3. Duncan et al. *J Infect Dis.* 2009;200:1242-46; 4. Walsh et al. *J Infect Dis.* 2013;207:1424-32; 5. Piedra et al. *Vaccine.* 2003;21:3479-82; 6. Luchsinger et al. *Clin Infect Dis.* 2012;54:905-12; 7. Aliprantis et al. *Human Vaccines Immunother.* 2021;17:1248-61; 8. Urdaneta et al. *Open Forum Infect Dis.* 2024;11:ofae067; 9. Makwana S, et al. *Int J Pharm Investig*. 2011;1: 200.

Raccomandazioni Board Calendario per la Vita

Raccomandazioni del Board del Calendario per la Vita sulla vaccinazione contro Virus Respiratorio Sinciziale (VRS o RSV) nella popolazione anziana e negli adulti a rischio

Il Board del Calendario della Vita, sulla base delle evidenze di efficacia e sicurezza ad oggi disponibili, e considerando le informazioni atualmente in fase di raccolta sulla durata della protezione conferita dai vaccini anti-RSV, ne ***raccomanda l'utilizzo ai soggetti di età pari o superiore ai 75 anni****, popolazione nella quale è peraltro molto frequente la co-esistenza di condizioni di cronicità che rendono l'infezione da RSV ancora più a rischio di complicanze gravi.*
Per le stesse motivazioni, ***raccomanda l'estensione della vaccinazione ai soggetti affetti da patologie croniche di età superiore o uguale ai 60 anni.***

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