RSV Prefusion F Vaccine for Prevention of Hospitalizations in Older Adults

Results from the DAN-RSV Study
Clinicaltrials.gov: NCT06684743

Pfizer Medical Affairs

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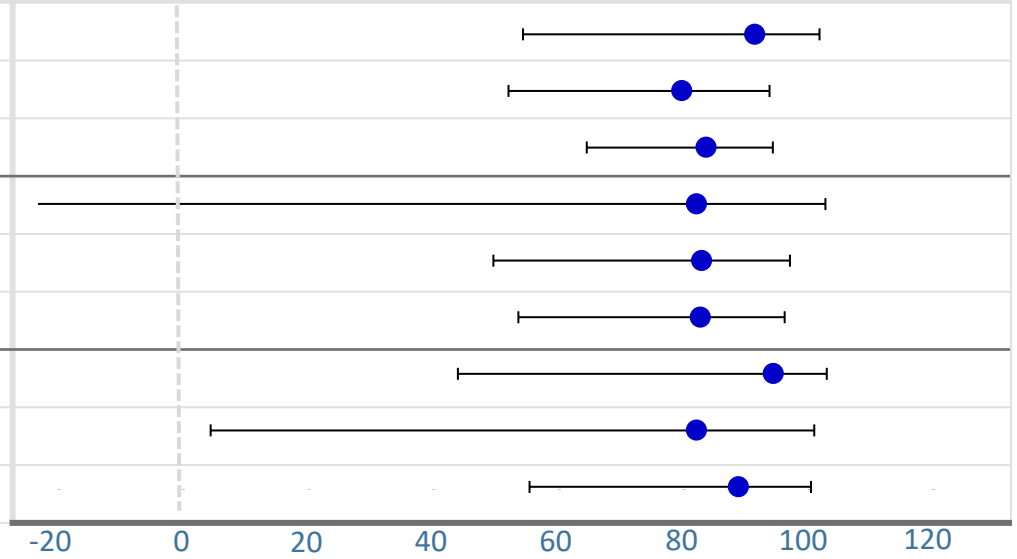
38,863 participants enrolled and randomized to receive RSVpreF 120 µg or placebo

Stratified by age group
60-69 years | 70-79 years | ≥80 years

2-year participant follow-up ARI surveillance through 2 RSV seasons

RSV-LRTI with ≥3 symptoms,		Cases (V:P)	Vaccine efficacy, % (95% CI)
Overall	Season 1 efficacy	2:18	88.9% (53.6, 98.7)
	Season 2 efficacy	8:36	77.8% (51.4, 91.1)
	Efficacy across 2 seasons	10:54	81.5% (63.3, 91.6)
RSV-A	Season 1 efficacy	1:5	80.0% (-78.7, 99.6)
	Season 2 efficacy	5:26	80.8% (49.1, 94.2)
	Efficacy across 2 seasons	6:31	80.6% (52.9, 93.4)
RSV-B	Season 1 efficacy	1:12	91.7% (43.7, 99.8)
	Season 2 efficacy	2:10	80.0% (6.1, 97.9)
	Efficacy across 2 seasons	3:22	86.4% (54.6, 97.4)



Protection against primary study outcome of RSV-associated LRTI with ≥3 solicited symptoms was evident for both RSV-A and RSV-B[4]

Cases of RSV-associated hospitalizations were recorded, but not enough to demonstrate efficacy against severe outcomes[1]

LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus; RSVpreF, RSV prefusion F protein; VE, vaccine efficacy; V:P, vaccine:placebo.

1. Walsh EE, et al. *N Engl J Med*. 2023;388(16):1465-1477. 2. Walsh EE, et al. *N Engl J Med*. 2024;391(15):1459-1460. 3. Supplement to: Walsh EE, et al. *N Engl J Med*. 2024;391(15):1459-1460. 4. Walsh EE, et al. *Clin Infect Dis*. 2025 doi:10.1093/cid/ciaf061

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Data Gap and Rationale for DAN-RSV

	RENOIR	DAN-RSV
RSV-associated LRTD with ≥3 signs/symptoms[1]	☑	n/a
RSV-associated LRTD with ≥2 signs/symptoms[2]	☑	n/a
Severe RSV-related RTD or LRTD[3]	Not met	☑
All-cause outcomes	n/a	☑

Too few events in RENOIR to determine RSVpreF efficacy against severe outcomes (i.e., hospitalizations, ED visits, ICU admissions, death)[4]; efficacy against severe RSV-LRTI endpoints not currently in label.

Effectiveness of RSVpreF vaccination against severe RSV-related and all-cause respiratory and cardiorespiratory hospitalizations have not been evaluated in a randomized trial

1. RSV-associated lower respiratory tract illness (LRTI) with ≥3 signs or symptoms (i.e., cough, wheezing, sputum production, shortness of breath, or tachypnea) lasting more than 1 day and RSV infection confirmed via RT-PCR assay (or nucleic acid amplification test if RT-PCR testing unavailable) within 7 days after the onset of signs or symptoms.; 2. RSV-associated LRTI with ≥2 signs or symptoms lasting more than 1 day and RSV infection confirmed via RT-PCR assay (or by means of nucleic acid amplification test if RT-PCR testing unavailable) within 7 days after the onset of signs or symptoms.; 3. In RENOIR, severe RSV-LRTI was a subset of RSV-LRTI with ≥2 signs/symptoms that included cases hospitalized for RSV-LRTI, requiring new or increased oxygen supplementation, or requiring new or increased mechanical ventilation (including CAP, NIPPV, or BiPAP) ; 4. Walsh EE, et al. *N Engl J Med* 2023;388(16):1465-1477.; 5 Walsh EE, et al. Open Forum Infect Dis 2023; 10(Suppl 2):ofad500.1468

RSVpreF Vaccine Efficacy and RWE Effectiveness in Adults ≥ 60 years – First Season

	RSV-related Endpoint	Vaccine Efficacy (95% CI)
RENOIR[1]	**RSV- LRTD***	**89%** (54, 99)
		Vaccine Effectiveness (95% CI)
Kaiser Permanente Southern California[2]	**Hospitalisation**	**90%** (22, 99)
	Severe RSV†	91% (28, 99)
	ED/Urgent Care	89% (8, 99)
VISION (CDC)[3]	**Hospitalisation**	**73%** (52, 85)
	ED/Urgent Care	79% (59, 89)
Veterans Health Administration (VHA)[4]	RSV Infection‡	77% (70, 82)
HARISS Network (UK)[5]	**Hospitalisation**	**82%** (71, 90)
	Severe RSV†	87% (75, 94)
	Immunosuppressed§	73% (40, 89)

CDC, Centers for Disease Control and Prevention; ED, emergency department; EHR, electronic health record; ESRD, end-stage renal disease; LRTD, Lower respiratory tract disease; RSV, respiratory syncytial virus.
*Defined as ≥3 or more signs/symptoms of LRTD; †Severe hospitalization or ED events defined as requiring supplemental oxygen; ‡RSV infection defined as any positive RSV test result occurring from day 14 following the index date until the end of the study period; §Includes individuals with immunosuppression due to disease or treatment as defined by UK's immunization against infectious disease Green Book.

1. Walsh EE, et al. *N Engl J Med* 2023;388(16):1465-1477; 2. Tartof SY, et al. *JAMA Netw Open*. 2024; 7(12):e2450832; 3. Payne AB, et al. *The Lancet.* 2024; 404(10462):1547-1559;
4. Bajema KL, et al. *The Lancet Inf Dis.* 2025. Published online January 20, 2025. https://doi.org/10.1016/S1473-3099(24)00796-5; 6. Symes R et al. https://www.medrxiv.org/content/10.1101/2025.06.13.25329583v1.

CID will publish season 1 ARI results shortly, including finer age groups with stable VE estimates.

Zhanna's slide

Comparison of Traditional RCT and a PCT

Continuum

Traditional Clinical Trials		Pragmatic Clinical Trials
Demonstrate efficacy and safety	**Purpose**	Inform clinical decision-making
Extensive I/E	**Eligibility**	Minimal I/E
Homogenous and selected population to maximize internal validity.	**Recruitment**	Diverse, inclusive, and representative of actual use population. High external validity.
Patients are randomized to treatment. Protocol-required study visits. Specialist centers and study sites.	**Setting & Delivery**	Patients are randomized to treatment. Limited additional visits outside of usual care. Embedded in clinical practice.
CRFs and extensive electronic data capture.	**Data Source**	EHRs with limited PRO collection.
Data capture requiring new infrastructure (costly, little value for reuse); Well-established standards for quality and accuracy. Associated high costs.	**Data Collection & Follow-Up**	Data collected prospectively during routine care (via EHR or registries); can be automated, Data quality structures already exist. Biggest challenge and costs are here.
Specific to mechanism of action and treatment effects. Capture and definition per protocol. Can be extensive in number.	**Outcomes**	Minimal and relevant to patients and real-world clinical practice; Ideally captured in EHRs.

Modified from: The need for increased pragmatism in cardiovascular clinical trials. *Nat Rev Cardiol* **19**, 737–750 (2022).

DAN-RSV Study Objectives and Methods[1,2]

Objective: To evaluate the vaccine effectiveness of RSVpreF against RSV-related and all-cause hospitalizations in adults ≥60 years

Study Design

- Pragmatic, open-label, parallel-group, individually randomized clinical trial in Denmark
- 2024/2025 season: November 2024 to May 31, 2025

Outcomes

- **Primary:** VE for RSV-related respiratory tract disease hospitalization* (ITT population)†
- **Key Secondary:** RSV-related LRTD hospitalization using as-treated dataset†, hospitalization for RSV-related LRTD†, and all-cause respiratory tract disease hospitalizations
- **Additional Secondary:** RSV-related and all-cause cardiorespiratory hospitalizations, all-cause LRTD hospitalization, all-cause hospitalization, all-cause death, stratification of primary endpoint by age groups (60-74, 75+; subsequent RSV seasons‡)
- Multiple exploratory endpoints including any hospitalization with RSV infection

Analysis

- VE calculated as (1 − infection rate of vaccine group/infection rate of control group) × 100%
- VE point estimate and a 95% confidence interval (CI) reported for all endpoints

ITT, intention to treat; LTRD, lower respiratory tract disease; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; VE, vaccine effectiveness.
*Defined as hospitalization with a primary discharge diagnosis code of RSV infection or primary diagnosis code of respiratory tract disease combined with RSV infection confirmed by specific ICD-10 code for RSV or a positive RSV test performed within 7 days prior to 2 days after date of hospitalization; †Analyzed at a two-sided alpha of 0.05 and a minimum VE of 20%; ‡2025/2026 and 2026/2027 seasons.
1. Lassen MCH, et al. NEJM. Published online 30 August. Doi:10.1056/NEJMoa2509810.

DAN-RSV: Eligible Study Participants Aged ≥60 Years Were Randomized to Receive RSVpreF[1,2]

Study Flowchart

Nationwide Health Registries	Identification of all eligible Danish citizens – No RSVpreF contraindications
Electronic Mail Invitations	Electronic invitation letters sent to **1,500,000** eligible Danish citizens
Governmental Electronic E-mail System	Secure nationwide delivery of trial invitation letters
Link in Electronic Invitation Letter	Electronic invitation letter contains link to trial website
Directed to Trial Website	Detailed information about trial, participant information leaflet, information video etc.
Electronic Informed Consent	After watching video & reading about the trial, informed consent is obtained electronically
Instant Randomization	After consent obtained, participants notified about trial assignment

RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F.

1. Lassen MCH, et al. *Am Heart J*. 2025 Jul 28;291:14-25. doi: 10.1016/j.ahj.2025.07.068; 2. Lassen MCH, et al. *N Engl J Med*. 2025. Published online; doi:10.1056/NEJMoa2509810.

RSVpreF Significantly Reduced RSV-related and All-cause Respiratory Tract Disease Hospitalizations in the Intention-to-Treat Analysis

	RSVpreF Vaccine Group (N=65,642)			Control Group (N=65,634)			Vaccine Effectiveness	
Endpoint	**N Events**	**Total Follow-up (Participant-years)**	**Incidence Rate (N Events/ 1000 PY)**	**N Events**	**Total Follow-up (Participant-years)**	**Incidence Rate (N Events/ 1000 PY)**	**Absolute rate reduction per 1000 PY**	**VE (95% CI)**
Primary								
Hospitalization for RSV-related RTD*	3	27,320	0.11	18	27,330	0.66	0.55	**83.3% (42.9%, 96.9%)**
Secondary								
Hospitalization for RSV-related Lower RTD*	1	27,321	0.04	12	27,332	0.44	0.40	**91.7% (42.7%, 99.8%)**
All-cause RTD Hospitalizations*	284	27,257	10.42	335	27,268	12.29	1.87	**15.2% (0.5%, 27.9%)**
RSV-related Hospitalizations (ICD-10 Coded)**	1	27,321	0.04	8	27,333	0.29	0.25	**87.5% (6.8%, 99.7%)**
RSV-related Cardio-respiratory Disease Hospitalization**	3	27,320	0.11	19	27,330	0.70	0.59	**84.2% (46.4%, 97.0%)**
All-cause Cardio-respiratory Hospitalization**	715	27,167	26.32	794	27,171	29.22	2.90	**9.9% (0.3%, 18.7%)**
All-cause Lower RTD Hospitalization**	236	27,269	8.65	298	27,278	10.92	2.27	**20.8% (5.8%, 33.6%)**

Alpha-controlled endpoints

CI, confidence interval; ICD-10, 10th revision of the International Classification of Diseases; ITT, intention to treat; PY, person-years; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; VE, vaccine effectiveness.
*Analyzed at a two-sided alpha of 0.05 and a minimum VE of 20% **95% confidence intervals have not been adjusted for multiplicity and should not be used to make inference.
Lassen MCH, et al. *N Engl J Med*. 2025. Published online; doi:10.1056/NEJMoa2509810.

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Alpha-controlled endpoints

Absolute rate reductions were several fold higher for all-cause outcomes compared to the corresponding RSV-related outcomes due to undiagnosed RSV disease

CI, confidence interval; ICD-10, 10th revision of the International Classification of Diseases; ITT, intention to treat; PY, person-years; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; VE, vaccine effectiveness.
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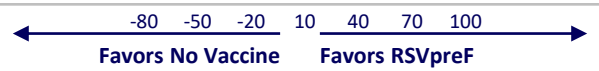
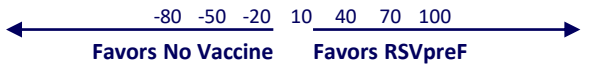
Lassen MCH, et al. *N Engl J Med*. 2025. Published online; doi:10.1056/NEJMoa2509810.

VE Against Hospitalization for RSV-related Respiratory Tract Disease by Subgroup

		RSVpreF (No./total no.)	No Vaccine (No./total no.)	VE (95% CI)
Overall		3/65,642	18/65,634	83.3 (42.9, 96.7)
Age	60-74 years	1/51,803	10/51,781	90.0 (29.7, 99.8)
	≥75 years	2/13,839	8/13,853	75.0 (-25.0, 97.4)
	<median	0/32,890	4/32,751	NA
	≥median	3/32,752	14/32,883	78.5 (23.6, 96.1)
Sex	Males	2/32,931	9/33,082	77.7 (-6.8, 97.7)
	Females	1/32,711	9/32,552	88.9 (19.4, 99.8)
Presence of at Least One Chronic Disease	No	0/38,080	5/38,080	NA
	Yes	3/27,562	13/27,554	76.9 (16.0, 95.8)
Chronic Lung Disease	No	3/60,834	13/60,832	76.9 (16.1, 95.8)
	Yes	0/4808	5/4802	NA
Cardiovascular Disease	No	1/51,265	11/51,349	90.9 (37.6, 99.8)
	Yes	2/14,377	7/14,285	71.6 (-51.1, 97.1)
Overall		3/65,642	18/65,634	83.3 (42.9, 96.7)
Diabetes	No	2/58,452	17/58,385	88.2 (50.4, 98.7)
	Yes	1/7190	1/7249	NA
Cancer	No	2/58,093	12/58,087	83.3 (25.2, 98.2)
	Yes	1/7549	6/7547	83.3 (-37.4, 99.6)
Chronic Kidney Disease	No	1/58,982	12/58,930	91.7 (43.7, 99.8)
	Yes	2/6660	6/6704	66.4 (-85.2, 96.7)
Immuno-suppression	No	1/63023	13/63054	92.3 (48.8, 99.8)
	Yes	2/2619	5/2580	60.5 (-147.3, 96.1)
Influenza Vaccination Same Season	No	0/12,634	1/12,816	NA
	Yes	3/53,008	17/52,818	82.4 (38.8, 96.7)
Prior pneumococcal Vaccination	No	0/23,565	3/23,638	NA
	Yes	3/42,077	15/41,996	80.0 (29.2, 96.3)





Overall, the effect of RSVpreF was similar across pre-specified subgroups including participants with chronic lung disease or cardiovascular disease; not shown but rate reductions higher in higher risk groups

CI, confidence interval; ITT, intention to treat; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; VE, vaccine effectiveness.

Lassen MCH, et al. *N Engl J Med*. 2025. Published online; doi:10.1056/NEJMoa2509810.

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No Statistical Difference in Incidence Rates Between RSVpreF Group and Control Group for Exploratory Outcomes

Endpoint	RSVpreF Vaccine Group				Control Group				Vaccine Effectiveness		P-value‡
	N Participants	N Events	Total Follow-up (Participant-years)	Incidence Rate (N Events/ 1000 PY)	N Participants	N Events	Total Follow-up (Participant-years)	Incidence Rate (N Events/ 1000 PY)	Absolute Rate Reduction per 1000 PY (95% CI)†	VE (95% CI)	
Exploratory Outcomes											
All-cause Cardiovascular spitalization									**1.32** (-0.88, 3.51)	**7.4%** (-5.5%, 18.8%)	0.24
Heart Failure Hospitalization									**-0.08** (-0.74, 0.60)	**-4.7%** (-62.7%, 32.7%)	0.83
Myocardial Infarction									**0.03** (-0.71, 0.78)	**1.8%** (-45.5%, 33.9%)	0.93
Stroke Hospitalization									**0.73** (-0.25, 1.71)	**19.4%** (-8.6%, 40.4%)	0.14
Atrial Fibrillation (Any Hospital Contact)*	**65,642**	**1150**	5,650	0.35	**65,634**	**1124**	27,086	41.50	**-0.99** (-4.45, 2.46)	**-2.4%** (-11.1%, 5.9%)	0.57

- **The direction of effect estimates for all-cause cardiovascular hospitalization and stroke suggest a potential beneficial effect of vaccination, but further data are required to confirm this**

CI, confidence interval; ITT, intention to treat; PY, person-years; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; VE, vaccine effectiveness.
*Atrial fibrillation was defined as any hospital contact with an atrial fibrillation diagnosis code to capture events such as same-day cardioversions without overnight stays; †Absolute rate reductions were calculated as the difference in incidence rates between the control and RSVpreF groups, with 95% confidence intervals derived using the Wald method based on a normal approximation; ‡All p-values are with respect to a null of 0% VE.
Lassen MCH, et al. *JAMA*. Published online: August 30, 2025. doi: 10.1001/jama.2025.15405.

SAEs Were Balanced Between RSVpreF and Control Groups in the As-treated Analysis

Serious Adverse Events	RSVpreF Vaccine Group (N=63,045)	No Vaccine Group (N=68,334)
Any SAE	1341 (2.1%)	1670 (2.4%)
Total Number of SAEs	1,497	1 937
Any Cardiovascular SAE	224 (0.4%)	286 (0.4%)
Any Respiratory SAE	116 (0.2%)	113 (0.2%)
Any Gastrointestinal SAE	136 (0.2%)	172 (0.3%)
Any Neurological SAE	41 (0.1%)	40 (0.1%)
Any Cancer SAE	61 (0.1%)	85 (0.1%)
Any Infection-related SAE	40 (0.1%)	57 (0.1%)
Any Injury-related SAE	156 (0.2%)	205 (0.3%)
Fatal SAE	17 (<0.1%)	33 (<0.1%)
Any Serious Adverse Reaction	5 (<0.1%)	N/A

RSVpreF, respiratory syncytial virus prefusion F; SAE, serious adverse event.
Lassen M, et al. Presented at the European Society of Cardiology, 29 August to 1 September 2025, Madrid, Spain.

Summary: DAN-RSV Study

DAN-RSV is the largest RSV vaccine trial ever conducted and the first pragmatic, individually randomized trial to measure the effectiveness of the RSVpreF vaccine, including cardio-respiratory outcomes, in older adults in a real-world setting[1-3]

- RSVpreF vaccine helped prevent RSV-related respiratory tract disease hospitalization (primary endpoint), RSV-related LRTD hospitalization, and all-cause respiratory tract disease (alpha-controlled secondary endpoints)
- RSVpreF was effective against multiple secondary and exploratory endpoints including all-cause cardio-respiratory and LRTD hospitalizations
- Absolute rate reductions for all-cause cardiorespiratory hospitalizations greater than all-cause respiratory hospitalization suggesting of RSVpreF prevented some cardiovascular events
- Greater rate reductions in all-cause vs RSV-related endpoints indicate the presence of undetected RSV disease
- SAEs were balanced between vaccine and control groups
- The study will be extended to look at additional seasons and expanded to allow for assessment of post-revaccination VE to support product label updates

LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F; SAE, serious adverse event.

1. Lassen MCH, et al. *Am Heart J*. 2025 Jul 28;291:14-25. doi: 10.1016/j.ahj.2025.07.0684; 2. Lassen MCH, et al. *N Engl J Med*. 2025. Published online; doi:10.1056/NEJMoa2509810; 3. Lassen MCH, et al. *JAMA*. Published online: August 30, 2025. doi: 10.1001/jama.2025.15405.

DAN-RSV publications and commentaries to date:

1. Main results in NEJM: https://www.nejm.org/doi/full/10.1056/NEJMoa2509810
2. Cardiovascular results in JAMA
   a. Bivalent RSV Prefusion F Protein–Based Vaccine for Preventing Cardiovascular Hospitalizations in Older Adults: A Prespecified Analysis of the DAN-RSV Trial | Vaccination | JAMA | JAMA Network
   b. Accompanying Commentary by Helen Chu and Alistair Murray: Bivalent RSV Prefusion F Protein–Based Vaccine for Preventing Cardiovascular Hospitalizations in Older Adults: A Prespecified Analysis of the DAN-RSV Trial | Vaccination | JAMA | JAMA Network
3. Heart Failure results in A Journal of the American College of Cardiology
   a. Effect of RSV Vaccine on Heart Failure Hospitalizations: A Prespecified Analysis of the DAN-RSV Trial - ScienceDirect
   b. New article in JACC: New Research Underscores Benefits of Influenza and RSV Vaccinations - American College of Cardiology
4. Atherosclerotic results in European Heart Journal
   a. Effectiveness of bivalent respiratory syncytial virus prefusion F protein-based vaccine in individuals with or without atherosclerotic cardiovascular disease: the DAN-RSV trial | European Heart Journal | Oxford Academic

Commentary by Bettina Heidecker and Thomas F Lüscher: Respiratory Viruses, Vaccines, and the Heart: Lessons from DANFLU-2, DAN-RSV, and Beyond | European Heart Journal | Oxford Academic