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Efficacy and Safety of Respiratory Syncytial Virus Prefusion F Protein Vaccines: a Systematic Review and Meta-analysis

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Background & Objectives

Human RSV is a globally prevalent cause of lower respiratory tract infection in children under 5 years old and adults at 65 years or above. There is a need for high-quality, safe, effective, affordable and accessible RSV vaccines. Vaccine efficacy and safety are therefore critical to vaccine development, testing and evaluation.

Methods

Here, we performed a systematic review to synthesize data from those published studies estimating the efficacy and safety for RSV prefusion F (pre-F) protein vaccines. All searches were conducted on Nov 11, 2023 in PubMed for published articles and ClicinalTrial.gov for clinical trials.

Results

We identified 22 studies meeting the inclusion requirements for this review, 6 reported efficacy results and 22 reported safety results.
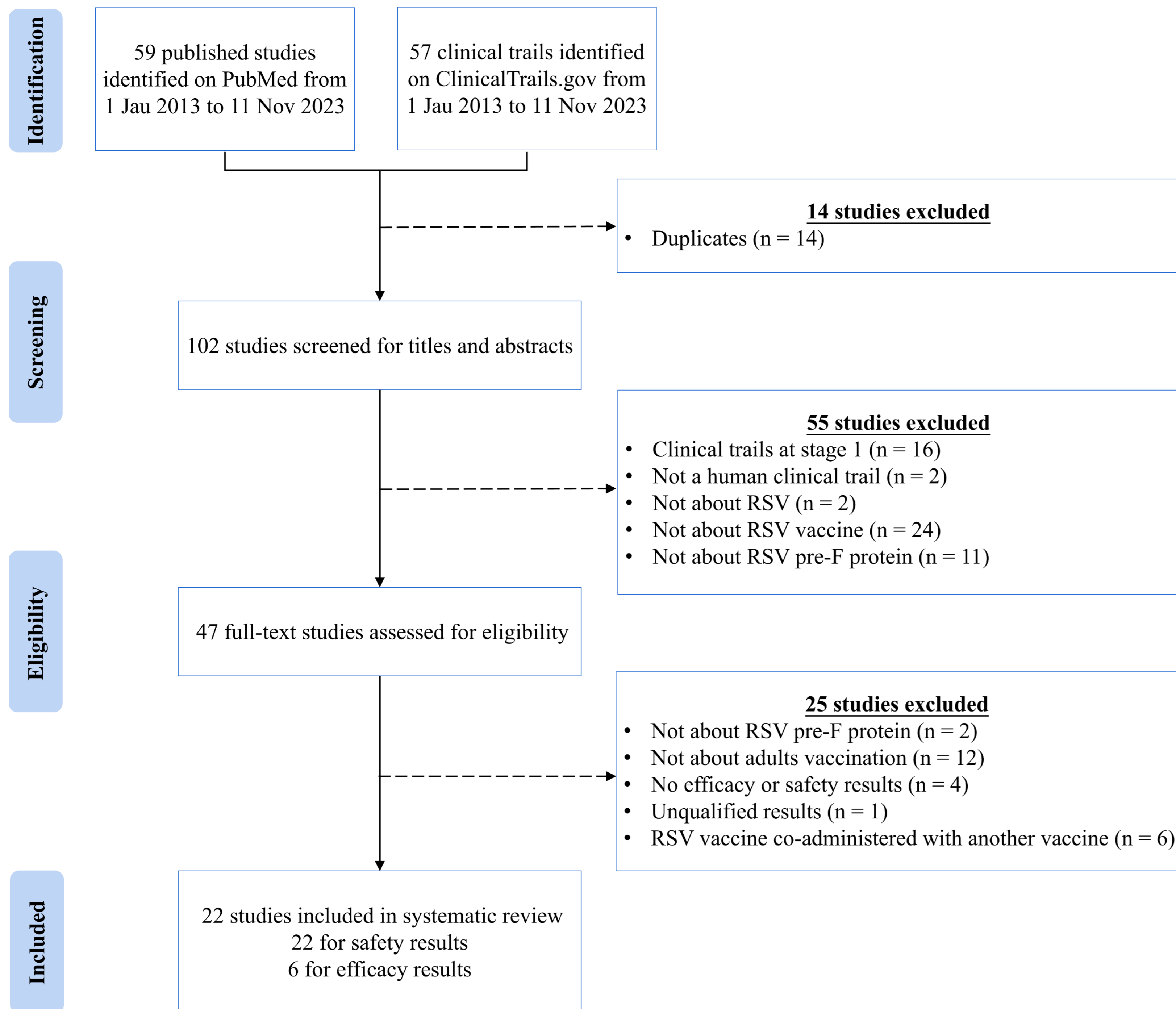

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram for searching and selecting studies that reported the prophylactic efficacy and safety outcomes of RSV pre-F protein vaccines under development.

Conclusion

RSV vaccine development is the outcome of extensive research and rigorous clinical trials conducted over several decades. The recent approval of RSV pre-F protein vaccines marks a major breakthrough in preventing RSV-related illnesses, especially among vulnerable populations.

References

1. Sadoff, J. et al. Prevention of Respiratory Syncytial Virus Infection in Healthy Adults by a Single Immunization of Ad26.RSV.preF in a Human Challenge Study. J. Infect. Dis. 226, 396–406 (2022).

Acknowledgements

Results (Cont.)

The efficacy results of phase 3 clinical trials for the vaccines of RSVPreF for older adults [OA] and RSVpreF show that a variety of RSV-associated illnesses were significantly reduced in the vaccine group. RSVPreF OA has 82.6% vaccine efficacy.

The safety results suggest that the incidence of adverse events [AEs] were similar across treatment groups and the control groups in adults. The RSVpreF OA vaccine resulted in a non-significant 1% higher risk of systemic AEs in the treatment group than in the placebo group among older adults.

Table 1. Summary of the efficacy results for the pre-F protein vaccines in development

| Vaccine | Phase as of 30 August 2023 | Outcome | Population | | | Efficacy Period |
			Newborns (maternal vaccination) [a]	Adults [b]	Older adults [c]	
GSK's RSVPreF3 OA	Approved for older adults	LRTD [d]			82.6 (57.9, 94.1)[#]	Follow-up of 6.7 months on average
Pfizer's RSVpreF	Approved for older adults and maternal vaccination	MA-LRTI [e]	44.9 (17.9, 63.5)[$]			Follow-up of 210 days after birth
		LRTI [f]			85.7 (32.0, 98.7)[&]	Follow-up of 11 months from day 15 after vaccination until the end of season 1
		Symptomatic infection [g]		86.7 (53.8, 96.5)		Follow-up of 12 days after challenge
Janssen's Ad26.RSV.preF	Phase 2	Infection [h]		47.1 (2.2, 71.3)[l]		Follow-up of 12 days after challenge
		LRTD [i]			80.0 (52.2, 92.9)[*]	Follow-up of 21 months from 1 Sep 2019 to 6 June 2022
Novavax's RSV-F vaccine (ResVax)	Phase 3, and failed	MS-LRTI [j]	39.4 (5.3, 61.2)			Follow-up of 90 days after birth
		MS-LRTI	41.4 (18.0, 58.1)			Follow-up of 90 days after birth

Note, the values and 95% confidence interval for the efficacy of RSV vaccines against RSV infection/illness were summarized in this table.
[a] Newborns, could be born to healthy pregnant women aged 18-49 or 18-40, and 24-36 or 28-36 weeks of gestation in different studies
[b] Adults aged 18-40, or 18-50 in different studies.
[c] Older adults, could be aged 60 or older, 65 or older, or 60-80 in different studies.
[d] RSV-related lower respiratory tract disease (RSV LRTD) were identified by the adjudication committee.
[e] MA-LRTI is a medically-attended visit AND ≥1 of the following RTI signs and symptoms and RSV-positive test result* AND ≥1 of the following: Fast breathing (RR ≥60 bpm for <2 months of age [<60 days of age], ≥50 bpm for 2–<12 months of age, or ≥40 bpm for 12–24 months of age); SpO2 <95%; Chest wall indrawing.
[f] RSV-LRTI is an ARI with 3 or more of the lower respiratory signs/symptoms lasting more than 1 day during the same illness, plus RT-PCR-confirmed RSV infection within 7 days of ARI symptom onset.
[g] qRT-PCR−confirmed symptomatic RSV infection (Variant 1). Any 2 detectable (quantifiable OR detectable and <LLOQ) qRT-PCR results from nasal swabs obtained on ≥2 consecutive days from Day 2 to Day 12 AND symptoms from 2 different categories (URT, LRT, systemic) or any grade 2 symptom (bothersome but not interfering with daily activity)
[h] Liberal RSV infection is defined as ≥2 quantifiable rt-PCR measurements above the LLOQ plus any clinical symptom of any severity.
[i] RSV LRTD definition is ≥3 symptoms of lower respiratory tract infection (LRTI).
[j] Medically-significant RSV-associated lower respiratory tract infection (RSV MS-LRTI) was defined as the presence of RSV infection confirmed by detection of the RSV genome by RT-PCR on respiratory secretions (obtained within the continuous illness episode which fulfilled the other criteria listed below); AND at least one manifestation of LRTI from among the following: cough, nasal flaring, lower chest wall indrawing, subcostal retractions, stridor, rales, rhonchi, wheezing, crackles/crepitations, or observed apnea; AND evidence of medical significance as defined by the presence of: EITHER hypoxemia (peripheral oxygen saturation [SpO2] < 95% at sea level or < 92% at altitudes > 1800 meters) OR tachypnea (≥ 70 breaths per minute [bpm] in infants 0 to 59 days of age and ≥ 60 bpm in infants ≥ 60 days of age).
[$] The CI of the efficacy results are for 99.17% Confidential Interval.
[#] The CI of the efficacy results are for 96.5% Confidential Interval.
[&] The CI of the efficacy results are for 96.66% Confidential Interval.
[*] The CI of the efficacy results are for 94.2% Confidential Interval.