Coversheet on evidence assessment by ATAGI using the GRADE framework for Arexvy (GSK) and Abrysvo (Pfizer) RSV vaccines in adults aged 60 years and over

A summary of key methods and decisions on evidence assessment using the GRADE framework for developing ATAGI recommendations on the use of Arexvy or Abrysvo in adults 60 years and over for the Australian Immunisation Handbook

Background

- Respiratory syncytial virus (RSV) infection is an increasingly recognised cause of significant hospitalisation, morbidity and mortality in older adults.
- RSV vaccines targeting the prefusion F protein are being investigated for their efficacy in preventing infection and severe disease.
- ATAGI undertook GRADE assessment in 2023 to make relevant recommendations on the use of RSV vaccine in older adults in anticipation of its availability in Australia.
- The Therapeutic Goods Administration (TGA) approved Arexvy (GSK) vaccine in January 2024 and Abrysvo (Pfizer) vaccine in March 2024 for use in older adults.

Research questions

1. Should Arexvy (GSK; Recombinant Respiratory Syncytial Virus pre-fusion F protein vaccine [RSVPreF3] adjuvanted with AS01$_E$) be recommended for adults aged ≥60 years to prevent RSV disease?

Table 1: Population, Intervention, Comparator, Outcomes (PICO) 1 RSV vaccine vs placebo, age 60 and over

Population	Adults aged ≥60 years
Intervention	Arexvy (GSK) adjuvanted RSV vaccine
Comparator	Placebo
Outcomes	*Critical* • RSV (laboratory confirmed) lower respiratory tract illness/disease (LRTI/LRTD) • Severe RSV (laboratory confirmed) LRTI/LRTD • Serious adverse events (SAEs) • Duration of protection (as secondary analysis) *Not included** • RSV (laboratory confirmed) medically attended LRTI/LRTD • Death due to RSV respiratory illness • Adverse events of special interest (AESI) • Hospitalisation for RSV respiratory illness *Important* • RSV – subtype A LRTI/LRTD • RSV – subtype B LRTI/LRTD • RSV (laboratory confirmed) acute respiratory infection (ARI) • Solicited systemic adverse events (AEs) • Solicited local AEs ** Outcomes not included were due to data that was not available or was insufficient for GRADE.*

2. Should Abrysvo (Pfizer; Respiratory Syncytial Virus pre-fusion F protein vaccine [RSVPreF]) be recommended for adults aged ≥60 years to prevent respiratory syncytial virus disease?

Table 1: PICO 2: RSV vaccine vs placebo, age 60 years old and over

Population	Adults aged ≥60 years
Intervention	Abrysvo (Pfizer) non-adjuvanted RSV vaccine
Comparator	Placebo
Outcomes	*Critical* • RSV (laboratory confirmed) LRTI • RSV (laboratory confirmed) severe LRTI • SAEs *Not included** • RSV (laboratory confirmed) medically attended LRTI/LRTD • Death due to RSV respiratory illness • AESI • Hospitalisation for RSV respiratory illness *Important* • RSV – subtype A (laboratory confirmedLRTI/LRTD • RSV – subtype B (laboratory confirmed) LRTI/LRTD • RSV (laboratory confirmed) ARI • Systemic AEs • Local AEs *Not included** • Duration of protection * Outcomes not included were due to data that was not available, insufficient, or not standardised across each GRADE assessment.

Literature search

The literature search was undertaken on 27 June 2023 to identify studies assessing efficacy and/or safety outcomes for **PICO 1**.

The literature search was undertaken on 13 July 2023 to identify studies assessing efficacy and/or safety outcomes for **PICO 2**.

Details of the search methods are presented in Appendix A. The citations were selected for review if they met the following criteria:

- *Study design:* Randomised controlled trial (RCT), observational study, meta-analysis
- *Population:* 18 years old and over
- *Intervention:* RSV vaccine: GSK RSVPreF3 (Arexvy); Pfizer RSVPreF (Abrysvo)
- *Comparator:* Placebo
- *Outcomes:* Effectiveness, efficacy, safety

PICO 1: GSK RSVPreF3 (Arexvy) vaccine vs placebo

The published literature search retrieved a total of 5 citations. Additional company data (unpublished) based on the included study were also incorporated (see References).

PICO 2: Pfizer RSVPreF (Abrysvo) vaccine vs placebo

The published literature search retrieved a total of 2 citations. Of these, one RTC was included for GRADE analysis. Additional company data (unpublished) based on the included study were also incorporated (see References).

Inclusion criteria and rationale

Table 3: Rationale for PICO and inclusion criteria

PICO	Rationale
Study type RCT, observational study, effectiveness studies	Vaccine efficacy and safety studies are available for the PICO question. The search criteria allows for future capture of relevant effectiveness and observational studies.
Population Adults aged 60 years and over	Population of interest for this vaccine.
	Vaccine indicated for and studied in older adult population with increased burden due to severe RSV disease. Includes adults who are healthy and have comorbid conditions. Noting the study search was conducted from 18 years of age to permit inclusion of studies for indirectness by age if necessary.
Intervention Arexvy (GSK) adjuvanted RSV vaccine; Abrysvo (Pfizer) RSV vaccine	Current formulation in terms of dosage and included antigens and presence/absence of adjuvants.
Comparator Placebo /no vaccine	There are no current studies directly comparing the vaccines of interest.

Outcomes	Included outcome as stated above in Tables 1–3. Included iteratively according to outcomes found in the studies.
	Ranking of importance discussed in many iterations with portfolio leads and ATAGI full panel.

	General framework (depending on outcomes measured in studies available):
	
	Critical
	
	    • RSV (laboratory confirmed) LRTI/LRTD
	    • Severe RSV (laboratory confirmed) LRTI/LRTD
	    • RSV (laboratory confirmed) medically attended LRTI/LRTD
	    • Hospitalisation for RSV respiratory illness
	    • Death due to RSV respiratory illness
	    • SAEs and AESI
	
	Important
	
	    • RSV A/B LRTD/LRTI
	    • RSV (laboratory confirmed) acute respiratory infection
	    • Duration of protection
	    • Systemic AEs
	    • Local AEs
	
	Note: some outcomes may be missing in GRADE projects due to no data from available studies. Extra outcomes added due to relevance.

Abbreviations: AE=adverse event; AESI=adverse event of special interest; LRTI/LRTD=lower respiratory tract illness/disease; SAE= serious adverse event; RCT=rondomised controlled trial; RSV=respiratory syncytial virus

Risk of bias assessment

Risk of bias (RoB) was assessed for all selected studies using the standard GRADE criteria. Two assessors independently undertook this using the RoB 2.0 tool for randomised controlled trials (Appendix B).

Appendix A: Literature search strategy

Table A1: PICO 1 – GSK RSVPreF3 (Arexvy) vaccine vs placebo

Cochrane Library Central Register of Controlled Trials (CENTRAL), Issue 6 of 12, June 2023: RSV vaccines – GSK older adults – FINAL (as at 27.06.23)

Notes: No age, language or date limits applied.

ID	Search	Hits
#1	MeSH descriptor: [Respiratory Syncytial Virus, Human] explode all trees	104
#2	MeSH descriptor: [Respiratory Syncytial Virus Infections] explode all trees	449
#3	("respiratory syncytial"):ti,ab,kw	1177
#4	rsv:ti,ab,kw	1054
#5	#1 OR #2 OR #3 OR #4	1415
#6	MeSH descriptor: [Immunization] explode all trees	6891
#7	MeSH descriptor: [Immunization Programs] explode all trees	304
#8	MeSH descriptor: [Vaccines] explode all trees	15898
#9	(immuni* OR vaccin*):ti,ab,kw	39486
#10	#6 OR #7 OR #8 OR #9	39661
#11	#5 AND #10	440
#12	MeSH descriptor: [Respiratory Syncytial Virus Vaccines] explode all trees	65
#13	#11 OR #12	440
#14	(GlaxoSmithKline* OR GSK*):ti,ab,kw	4485
#15	Arexvy*:ti,ab,kw	0
#16	AReSVi*:ti,ab,kw	1
#17	((RSV NEXT 007*) OR RSV-007* OR RSV007*):ti,ab,kw	0
#18	((RSV NEXT pre F3*) OR RSV-pre-F3* OR RSVpreF3*):ti,ab,kw	36
#19	((RSV NEXT PReF30A) OR RSVPreF3OA):ti,ab,kw	0
#20	AS01*:ti,ab,kw	276
#21	NCT04886596*:ti,ab,kw	3
#22	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	4701
#23	#13 AND #22	58
#24	MeSH descriptor: [Immunogenicity, Vaccine] explode all trees	646
#25	immunogen*:ti,ab,kw	16408
#26	MeSH descriptor: [Antibody Formation] explode all trees	1104
#27	(antibod* NEAR/3 (respons* OR form*)):ti,ab,kw	5927

ID	Search	Hits
#28	(immun* NEAR/3 (respon* OR protect*)):ti,ab,kw	18396
#29	MeSH descriptor: [Antibodies, Viral] explode all trees	4405
#30	MeSH descriptor: [Antibodies, Neutralizing] explode all trees	753
#31	MeSH descriptor: [Treatment Outcome] explode all trees	180743
#32	MeSH descriptor: [Vaccine Efficacy] explode all trees	44
#33	efficac*:ti,ab,kw	430845
#34	effective*:ti,ab,kw	408372
#35	MeSH descriptor: [Safety] explode all trees	18465
#36	MeSH descriptor: [Safety-Based Drug Withdrawals] explode all trees	11
#37	MeSH descriptor: [Product Surveillance, Postmarketing] explode all trees	434
#38	MeSH descriptor: [Drug Evaluation] explode all trees	5966
#39	MeSH descriptor: [Population Surveillance] explode all trees	779
#40	MeSH descriptor: [Adverse Drug Reaction Reporting Systems] explode all trees	157
#41	(adverse NEAR/3 (effect* OR event*)):ti,ab,kw	309942
#42	(safe OR safety OR aefi OR aesi):ti,ab,kw	328136
#43	MeSH descriptor: [Mortality] explode all trees	21870
#44	MeSH descriptor: [Death] explode all trees	8020
#45	(mortalit* OR death* OR fatal* OR case-fatal* OR lethal* or died)	185380
#46	#24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45	1037038
#47	#23 AND #46	58

DSR – 0

CENTRAL – 58

EMBASE: RSV vaccines – GSK older adults – FINAL (as at 27.06.23)

Notes: No age, language or date limits applied.

Database: Embase <1974 to 2023 June 23>
Search Strategy:

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1 exp Human respiratory syncytial virus/ (8881)
2 exp respiratory syncytial virus infection/ (7821)
3 (respiratory adj2 syncytial).tw. (20519)
4 rsv.tw. (20102)
5 1 or 2 or 3 or 4 (31866)
6 exp Immunization/ (372629)
7 exp vaccine/ (414713)
8 (immuni$ or vaccin$).tw. (800987)
9 6 or 7 or 8 (947748)
10 5 and 9 (7648)
11 exp respiratory syncytial virus vaccine/ (1941)
12 10 or 11 (7945)
13 (GlaxoSmithKline$ or GSK$).tw. (44315)
14 Arexvy$.tw. (1)
15 AReSVi$.tw. (2)
16 ("RSV 007$" or RSV-007$ or RSV007$).tw. (2)
17 ("RSV pre F3$" or RSV-pre-F3$ or RSVpreF3$).tw. (23)
18 ("RSVPreF3 OA" or "RSVPreF3-OA" or "RSVPreF3OA").tw. (10)
19 AS01$.tw. (720)
20 NCT04886596$.tw. (3)
21 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (44975)
22 12 and 21 (52)
23 exp vaccine immunogenicity/ (6754)

24 immunogen$.tw. (122566)
25 exp antibody production/ (62555)
26 exp antibody response/ (64121)
27 (antibod$ adj3 (respons$ or form$)).tw. (82171)
28 (immun$ adj3 (respon$ or protect$)).tw. (508644)
29 exp virus antibody/ (108124)
30 exp neutralizing antibody/ (52769)
31 exp drug efficacy/ (1024339)
32 efficac$.tw. (1618898)
33 effective$.tw. (3319696)
34 exp safety/ (565897)
35 exp postmarketing surveillance/ (39284)
36 exp drug surveillance program/ (26710)
37 exp adverse drug reaction/ (638745)
38 (adverse adj3 (effect$ or event$)).tw. (742914)
39 (safe or safety or aefi or aesi).tw. (1574282)
40 exp mortality/ (1382258)
41 exp death/ (819469)
42 (mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (3139876)
43 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 (9803986)
44 22 and 43 (43)

MEDLINE: RSV vaccines – GSK older adults – FINAL (as at 27.06.23)

Notes: No age, language or date limits applied.

Database: MEDLINE(R) All including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946-current>
Search Strategy:

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1   exp Respiratory Syncytial Virus, Human/ (3891)
2   exp Respiratory Syncytial Virus Infections/ (8651)
3   (respiratory adj syncytial).tw. (16331)
4   rsv.tw. (14709)
5   1 or 2 or 3 or 4 (22089)
6   exp Immunization/ (208917)
7   exp Immunization Programs/ (16037)
8   exp Vaccines/ (276867)
9   (immuni$ or vaccin$).tw. (665476)
10   6 or 7 or 8 or 9 (766316)
11   5 and 10 (4829)
12   exp Respiratory Syncytial Virus Vaccines/ (899)
13   11 or 12 (4859)
14   (GlaxoSmithKline$ or GSK$).tw. (24410)
15   Arexvy$.tw. (1)
16   AReSVi$.tw. (2)
17   ("RSV 007$" or RSV-007$ or RSV007$).tw. (0)
18   ("RSV pre F3$" or RSV-pre-F3$ or RSVpreF3$).tw. (10)
19   ("RSVPreF3 OA" or "RSVPreF3-OA" or "RSVPreF3OA").tw. (2)
20   AS01$.tw. (482)
21   NCT04886596$.tw. (1)
22   14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 (24852)
23   13 and 22 (14)
24   exp Immunogenicity, Vaccine/ (3312)

25   immunogen$.tw. (91382)
26   exp Antibody Formation/ (63639)
27   (antibod$ adj3 (respons$ or form$)).tw. (69513)
28   (immun$ adj3 (respon$ or protect$)).tw. (383836)
29   exp Antibodies, Viral/ (122689)
30   exp Antibodies, Neutralizing/ (18352)
31   exp Treatment Outcome/ (1243014)
32   exp Vaccine Efficacy/ (759)
33   efficac$.tw. (1087377)
34   effective$.tw. (2511970)
35   exp Safety/ (88737)
36   exp Safety-Based Drug Withdrawals/ (416)
37   exp Product Surveillance, Postmarketing/ (18205)
38   exp Drug Evaluation/ (42061)
39   exp Population Surveillance/ (74468)
40   exp Adverse Drug Reaction Reporting Systems/ (8816)
41   (adverse adj3 (effect$ or event$)).tw. (461451)
42   (safe or safety or aefi or aesi).tw. (1021183)
43   exp Mortality/ (423288)
44   exp Death/ (164221)
45   (mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (2155557)
46   24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 (7139473)
47   23 and 46 (13)

Table A2: PICO 2 – Pfizer RSVPreF (Abrysvo) vaccine vs placebo

Cochrane Library Central Register of Controlled Trials (CENTRAL), Issue 6 of 12, June 2023: RSV vaccines – Pfizer older adults – FINAL (as at 13.06.23)

Notes: No age, language or date limits applied.

ID	Search	Hits
#1	MeSH descriptor: [Respiratory Syncytial Virus, Human] explode all trees	104
#2	MeSH descriptor: [Respiratory Syncytial Virus Infections] explode all trees	449
#3	("respiratory syncytial"):ti,ab,kw	1177
#4	rsv:ti,ab,kw	1054
#5	#1 OR #2 OR #3 OR #4	1415
#6	MeSH descriptor: [Immunization] explode all trees	6890
#7	MeSH descriptor: [Immunization Programs] explode all trees	304
#8	MeSH descriptor: [Vaccines] explode all trees	15898
#9	(immuni* OR vaccin*):ti,ab,kw	39485
#10	#6 OR #7 OR #8 OR #9	39660
#11	#5 AND #10	440
#12	MeSH descriptor: [Respiratory Syncytial Virus Vaccines] explode all trees	65
#13	#11 OR #12	440
#14	Pfizer*:ti,ab,kw	2742
#15	Abrysvo*:ti,ab,kw	0
#16	("PF 06928316*" OR "PF-06928316*" OR PF06928316*):ti,ab,kw	3
#17	("RSV pre F*" OR "RSV-pre-F*" OR RSVpreF*):ti,ab,kw	91
#18	(bivalen* NEAR/3 ("prefusion F" OR "prefusion-F" OR prefusionF)):ti,ab,kw	7
#19	(bivalen* NEAR/3 recombinant):ti,ab,kw	29
#20	(bivalen* NEAR/3 (protein* OR subunit*)):ti,ab,kw	15
#21	RENOIR:ti,ab,kw	3
#22	"RSV vaccine Efficacy study iN Older adults Immunized against RSV disease":ti,ab,kw	0
#23	NCT05035212*:ti,ab,kw	2
#24	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	2870
#25	#13 AND #24	90
#26	MeSH descriptor: [Immunogenicity, Vaccine] explode all trees	646

ID	Search	Hits
#27	immunogen*:ti,ab,kw	16408
#28	MeSH descriptor: [Antibody Formation] explode all trees	1104
#29	(antibod* NEAR/3 (respons* OR form*)):ti,ab,kw	5927
#30	(immun* NEAR/3 (respon* OR protect*)):ti,ab,kw	18396
#31	MeSH descriptor: [Antibodies, Viral] explode all trees	4405
#32	MeSH descriptor: [Antibodies, Neutralizing] explode all trees	753
#33	MeSH descriptor: [Treatment Outcome] explode all trees	180744
#34	MeSH descriptor: [Vaccine Efficacy] explode all trees	44
#35	efficac*:ti,ab,kw	430845
#36	effective*:ti,ab,kw	408367
#37	MeSH descriptor: [Safety] explode all trees	18462
#38	MeSH descriptor: [Safety-Based Drug Withdrawals] explode all trees	11
#39	MeSH descriptor: [Product Surveillance, Postmarketing] explode all trees	434
#40	MeSH descriptor: [Drug Evaluation] explode all trees	5966
#41	MeSH descriptor: [Population Surveillance] explode all trees	779
#42	MeSH descriptor: [Adverse Drug Reaction Reporting Systems] explode all trees	157
#43	(adverse NEAR/3 (effect*OR event*)):ti,ab,kw	147277
#44	(safe OR safety OR aefi OR aesi):ti,ab,kw	328133
#45	MeSH descriptor: [Mortality] explode all trees	21868
#46	MeSH descriptor: [Death] explode all trees	8019
#47	(mortalit* OR death* OR fatal* OR case-fatal* OR lethal* OR died):ti,ab,kw	179778
#48	#26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47	976713
#49	#25 AND #48	90

EMBASE: RSV vaccines – Pfizer older adults – FINAL (as at 13.06.23)

Notes: No age, language or date limits applied.

Database: Embase <1974 to 2023 June 09>
Search Strategy:
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1	exp Human respiratory syncytial virus/ (8824)	25	exp vaccine immunogenicity/ (6695)
2	exp respiratory syncytial virus infection/ (7776)	26	immunogen$.tw. (122360)
3	(respiratory adj2 syncytial).tw. (20471)	27	exp antibody production/ (62492)
4	rsv.tw. (20045)	28	exp antibody response/ (63968)
5	1 or 2 or 3 or 4 (31771)	29	(antibod$ adj3 (respons$ or form$)).tw. (82057)
6	exp Immunization/ (371391)	30	(immun$ adj3 (respon$ or protect$)).tw. (507523)
7	exp vaccine/ (413510)	31	exp virus antibody/ (107992)
8	(immuni$ or vaccin$).tw. (798907)	32	exp neutralizing antibody/ (52586)
9	6 or 7 or 8 (945208)	33	exp drug efficacy/ (1022252)
10	5 and 9 (7624)	34	efficac$.tw. (1614212)
11	exp respiratory syncytial virus vaccine/ (1939)	35	effective$.tw. (3308213)
12	10 or 11 (7921)	36	exp safety/ (564546)
13	Pfizer$.tw. (44826)	37	exp postmarketing surveillance/ (39239)
14	Abrysvo$.tw. (0)	38	exp drug surveillance program/ (26706)
15	("PF 06928316$" or PF-06928316$ or PF06928316$).tw. (0)	39	exp adverse drug reaction/ (637468)
16	("RSV pre F$" or RSV-pre-F$ or RSVpreF$).tw. (45)	40	(adverse adj3 (effect$ or event$)).tw. (740106)
17	(bivalen$ adj3 ("prefusion F" or prefusion-F or prefusionF)).tw. (8)	41	(safe or safety or aefi or aesi).tw. (1568598)
18	(bivalen$ adj3 recombinant).tw. (132)	42	exp mortality/ (1377984)
19	(bivalen$ adj3 (protein$ or subunit$)).tw. (271)	43	exp death/ (818097)
20	RENOIR$.tw. (57)	44	(mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (3131082)
21	"RSV vaccine Efficacy study iN Older adults Immunized against RSV disease".tw. (0)	45	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 (9776234)
22	NCT05035212$.tw. (2)	46	24 and 45 (99)
23	13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 (45304)		
24	12 and 23 (115)		

MEDLINE: RSV vaccines – Pfizer older adults – FINAL (as at 07.06.23)
Notes: No age, language or date limits applied.

Database: MEDLINE(R) All including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946-current>
Search Strategy:

1	exp Respiratory Syncytial Virus, Human/ (3866)	26	exp Immunogenicity, Vaccine/ (3297)
2	exp Respiratory Syncytial Virus Infections/ (8621)	27	immunogen$.tw. (91078)
3	(respiratory adj syncytial).tw. (16286)	28	exp Antibody Formation/ (63612)
4	rsv.tw. (14656)	29	(antibod$ adj3 (respons$ or form$)).tw. (69388)
5	1 or 2 or 3 or 4 (22025)	30	(immun$ adj3 (respon$ or protect$)).tw. (382494)
6	exp Immunization/ (208388)	31	exp Antibodies, Viral/ (122428)
7	exp Immunization Programs/ (16022)	32	exp Antibodies, Neutralizing/ (18236)
8	exp Vaccines/ (276160)	33	exp Treatment Outcome/ (1241047)
9	(immuni$ or vaccin$).tw. (663119)	34	exp Vaccine Efficacy/ (749)
10	6 or 7 or 8 or 9 (763858)	35	efficac$.tw. (1083264)
11	5 and 10 (4807)	36	effective$.tw. (2502333)
12	exp Respiratory Syncytial Virus Vaccines/ (895)	37	exp Safety/ (88684)
13	11 or 12 (4837)	38	exp Safety-Based Drug Withdrawals/ (416)
14	Pfizer$.tw. (6311)	39	exp Product Surveillance, Postmarketing/ (18179)
15	Abrysvo$.tw. (0)	40	exp Drug Evaluation/ (42056)
16	("PF 06928316$" or PF-06928316$ or PF06928316$).tw. (0)	41	exp Population Surveillance/ (74452)
17	("RSV pre F$" or RSV-pre-F$ or RSVpreF$).tw. (29)	42	exp Adverse Drug Reaction Reporting Systems/ (8806)
18	(bivalen$ adj3 ("prefusion F" or prefusion-F or prefusionF)).tw. (7)	43	(adverse adj3 (effect$ or event$)).tw. (459481)
19	(bivalent adj3 recombinant).tw. (117)	44	(safe or safety or aefi or aesi).tw. (1017093)
20	(bivalen$ adj3 (protein$ or subunit$)).tw. (238)	45	exp Mortality/ (423121)
21	RENOIR$.tw. (46)	46	exp Death/ (164028)
22	"RSV vaccine Efficacy study iN Older adults Immunized against RSV disease".tw. (0)	47	(mortalit$ or death$ or fatal$ or case-fatal$ or lethal$ or died).tw. (2148984)
23	NCT05035212$.tw. (1)	48	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 (7117434)
24	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 (6718)	49	25 and 48 (37)
25	13 and 24 (38)		

Appendix B

Table B1: Risk of bias assessment using ROB 2.0

Study	Outcome	Randomisation process	Deviations from intervention	Missing data	Measurement of outcomes	Selection of the reported results	Overall bias
PICO 1							
Papi 2023*	Efficacy	Low	Low	Low	Low	Low	Low
	Safety	Low	Low	Low	Low	Low	Low
PICO 2							
Walsh 2023	Efficacy	Low	Low	Low	Low	Low	Low
	Safety	Low	Low	Low	Low	Low	Low

References

1. Papi A, Ison MG, Langley JM, et al. Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults. *New England Journal of Medicine* 2023;388(7):595-608.
2. Ison MG, Papi A., Athan E, et al; ReSVi-006 study group. Efficacy and safety of respiratory syncytial virus prefusion F protein vaccine (RSVPreF3 OA) in older adults over 2 RSV seasons. *Clinical Infectious Diseases* 2024:78(6):1732-1744.
3. GSK CSR(2). OA=ADJ-006 Study Report (VE Analysis 2) 30 Mar 2023 Synopsis - CONFIDENTIAL.
4. GlaxoSmithKline. RSVPreF3 Vaccine for Respiratory Syncytial Virus (RSV) in Older Adults. 2023. Available from: https://www.fda.gov/media/165649/download (Accessed 17 May 2024).
5. Walsh EE, Perez Marc G, Zareba AM, et al. Efficacy and safety of a bivalent RSV Prefusion F vaccine in older adults. *New England Journal of Medicine* 2023;388(16):1465-7.
6. Pfizer Clinical Study Report (CSR) (2). Through End of Season 1 – Study C3671013. 23 June 2023.