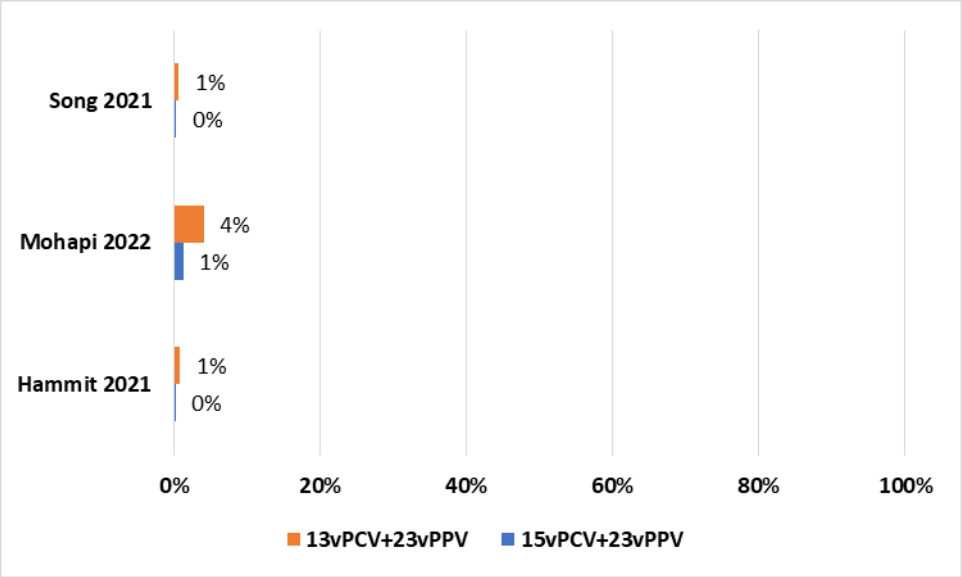
NCIRS is conducting GRADE in support of ATAGI and making pilot results available on the NCIRS website. Please read this material as a supplement to the Australian Immunisation Handbook Pneumococcal Chapter

Summary of findings: 15vPCV+23vPPV compared to 13vPCV+23vPPV for Indigenous Australian adults ≥50 years without special risk factors

Patient or population: Indigenous Adults ≥50 years without special risk factors
Intervention: 15vPCV+23vPPV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Serious adverse events (SAE)		2465 (3 RCTs)	⨁⨁◯◯ Low[a,b,c,d]	15vPCV+23vPPV may result in little to no difference in SAE compared to 13vPCV+23vPPV

<table>
<tr>
<td>OPA GMT ratios follow-up: 30 days</td>
<td>
Table 1: 95% CI for OPA GMT ratios (15vPCV+23vPPV vs. 13vPCV+23vPPV) for shared and unique serotypes at Day 30 a) shaded by non-inferiority and superiority margins^ b) shaded by estimated that favour 15vPCV or 13vPCV†
a)
<table>
<tr><th>Study ID</th><th colspan="2">Hammit 2021*</th><th colspan="2">Mohapi 2022*</th><th colspan="2">Song 2021*</th></tr>
<tr><td>Population</td><td colspan="2">Age 18-49 years
Pneumococcal vaccine naïve
Immunocompetent with RFs (Non Native Americans) or without (Native American).</td><td colspan="2">Age ≥18 years
Pneumococcal vaccine naïve
Adults living with HIV</td><td colspan="2">Age ≥50 years
Pneumococcal vaccine naïve
Immunocompetent</td></tr>
<tr><td>PCV</td><td>15</td><td>13</td><td>15</td><td>13</td><td>15</td><td>13</td></tr>
<tr><td>N</td><td>1133</td><td>379</td><td>152</td><td>150</td><td>326</td><td>325</td></tr>
<tr><td>1</td><td colspan="2">1.12, 1.58</td><td colspan="2">0.94, 2.04</td><td colspan="2">1.1, 1.74</td></tr>
<tr><td>3</td><td colspan="2">0.85, 1.12</td><td colspan="2">0.82, 1.39</td><td colspan="2">0.9, 1.29</td></tr>
<tr><td>4</td><td colspan="2">0.79, 1.01</td><td colspan="2">0.72, 1.36</td><td colspan="2">0.85, 1.32</td></tr>
<tr><td>5</td><td colspan="2">0.86, 1.19</td><td colspan="2">0.93, 1.95</td><td colspan="2">0.94, 1.56</td></tr>
<tr><td>6A</td><td colspan="2">0.87, 1.16</td><td colspan="2">0.75, 1.49</td><td colspan="2">0.95, 1.43</td></tr>
<tr><td>6B</td><td colspan="2">1.06, 1.36</td><td colspan="2">1.01, 1.95</td><td colspan="2">0.93, 1.35</td></tr>
<tr><td>7F</td><td colspan="2">0.89, 1.12</td><td colspan="2">0.83, 1.41</td><td colspan="2">0.9, 1.25</td></tr>
<tr><td>9V</td><td colspan="2">0.84, 1.08</td><td colspan="2">0.98, 1.61</td><td colspan="2">0.91, 1.33</td></tr>
<tr><td>14</td><td colspan="2">0.97, 1.26</td><td colspan="2">1.12, 2.02</td><td colspan="2">1.05, 1.53</td></tr>
<tr><td>18C</td><td colspan="2">1.25, 1.57</td><td colspan="2">1.17, 2.09</td><td colspan="2">0.95, 1.34</td></tr>
<tr><td>19A</td><td colspan="2">0.93, 1.2</td><td colspan="2">0.82, 1.45</td><td colspan="2">0.96, 1.38</td></tr>
<tr><td>19F</td><td colspan="2">0.97, 1.22</td><td colspan="2">0.91, 1.52</td><td colspan="2">0.89, 1.2</td></tr>
<tr><td>23F</td><td colspan="2">0.9, 1.21</td><td colspan="2">0.9, 1.9</td><td colspan="2">1.01, 1.61</td></tr>
<tr><td>22F</td><td colspan="2">0.77, 1.05</td><td colspan="2">0.81, 1.64</td><td colspan="2">1.29, 2.06</td></tr>
<tr><td>33F</td><td colspan="2">0.63, 0.85</td><td colspan="2">0.67, 1.21</td><td colspan="2">0.77, 1.17</td></tr>
</table>
^Non-inferiority: orange=LCI>0.67[6]; yellow=LCI>0.5[7] Superiority: blue=LCI>0.1[7]
*study not powered to detect a difference between 15vPCV and 13vPCV
b)
<table>
<tr><th>Study ID</th><th colspan="2">Hammit 2021*</th><th colspan="2">Mohapi 2022*</th><th colspan="2">Song 2021*</th></tr>
<tr><td>PCV</td><td>15</td><td>13</td><td>15</td><td>13</td><td>15</td><td>13</td></tr>
<tr><td>N</td><td>1133</td><td>379</td><td>152</td><td>150</td><td>326</td><td>325</td></tr>
<tr><td>1</td><td colspan="2">1.12, 1.58</td><td colspan="2">0.94, 2.04</td><td colspan="2">0.92, 1.53</td></tr>
<tr><td>3</td><td colspan="2">0.85, 1.12</td><td colspan="2">0.82, 1.39</td><td colspan="2">1.29, 1.9</td></tr>
<tr><td>4</td><td colspan="2">0.79, 1.01</td><td colspan="2">0.72, 1.36</td><td colspan="2">0.57, 0.9</td></tr>
<tr><td>5</td><td colspan="2">0.86, 1.19</td><td colspan="2">0.93, 1.95</td><td colspan="2">0.78, 1.33</td></tr>
<tr><td>6A</td><td colspan="2">0.87, 1.16</td><td colspan="2">0.75, 1.49</td><td colspan="2">0.93, 1.41</td></tr>
<tr><td>6B</td><td colspan="2">1.06, 1.36</td><td colspan="2">1.01, 1.95</td><td colspan="2">1.16, 1.77</td></tr>
<tr><td>7F</td><td colspan="2">0.89, 1.12</td><td colspan="2">0.83, 1.41</td><td colspan="2">0.8, 1.11</td></tr>
<tr><td>9V</td><td colspan="2">0.84, 1.08</td><td colspan="2">0.98, 1.61</td><td colspan="2">0.81, 1.18</td></tr>
</table>
</td>
<td>2465
(3 RCTs)</td>
<td>⨁⨁◻◻
Low[b,c,d,e]</td>
<td>15vPCV+23vPPV may result in little difference in OPA GMT ratios

Note: OPA GMT ratios all met a non-inferiority margin of LCI>0.5. Across all studies, 15vPCV is statistically significantly higher than 13vPCV for ST 6B and 18C</td>
</tr>
</table>

Summary of findings: 15vPCV+23vPPV compared to 13vPCV+23vPPV for Indigenous Australian adults ≥50 years without special risk factors

	14	0.97, 1.26	1.12, 2.02	0.9, 1.36			
	18C	1.25, 1.57	1.17, 2.09	1.05, 1.55			
	19A	0.93, 1.2	0.82, 1.45	0.91, 1.31			
	19F	0.97, 1.22	0.91, 1.52	0.91, 1.29			
	23F	0.9, 1.21	0.9, 1.9	1.06, 1.76			
	22F	0.77, 1.05	0.81, 1.64	9.44, 17.34			
	33F	0.63, 0.85	0.67, 1.21	2.73, 3.84			

†Green=LCI>1; red=UCI<1
*study not powered to detect a difference between 15vPCV and 13vPCV

% of participants ≥ 4-fold rise of GMT pre PCV to post PPV vaccination

Table 2: Proportion of participants with a ≥ 4-fold rise of GMT pre PCV to post PPV vaccination*

Study ID	Hammit 2021*		Mohapi 2022*		Song 2021*	
PCV	15	13	15	15	13	15
N	1133	379	152	1133	379	152
1	88% (85,90)	84% (79,88)	84% (76,90)	73% (63,81)	88% (83,92)	79% (73,84)
3	67% (63,70)	67% (61,72)	50% (41,60)	52% (43,62)	79% (73,84)	76% (70,81)
4	84% (82,87)	86% (82,90)	85% (77,91)	81% (73,88)	84% (79,88)	84% (79,89)
5	87% (84,89)	87% (83,91)	82% (74,89)	70% (61,78)	80% (75,84)	81% (76,85)
6A	74% (70,77)	80% (75,85)	76% (67,84)	69% (59,78)	68% (62,74)	65% (58,71)
6B	76% (73,79)	74% (69,79)	83% (74,89)	79% (71,86)	78% (73,83)	77% (72,82)
7F	60% (56,63)	60% (54,66)	71% (62,79)	71% (62,79)	72% (66,78)	65% (58,70)
9V	51% (47,54)	52% (46,58)	44% (35,54)	45% (36,55)	56% (50,62)	51% (45,57)
14	65% (62,68)	59% (53,65)	68% (59,76)	57% (48,67)	64% (58,70)	59% (53,65)
18C	78% (75,80)	76% (71,81)	76% (67,83)	69% (59,77)	76% (70,81)	74% (68,79)
19A	68% (65,71)	71% (65,76)	80% (72,87)	69% (59,77)	70% (64,76)	66% (60,72)
19F	61% (58,64)	63% (57,69)	72% (62,80)	57% (48,67)	68% (62,74)	62% (56,68)
23F	74% (70,77)	72% (66,77)	84% (75,90)	70% (60,78)	74% (69,80)	66% (60,72)
22F	59% (55,63)	65% (59,71)	74% (64,82)	75% (66,83)	80% (74,85)	63% (56,69)
33F	53% (50,57)	61% (55,67)	61% (51,70)	68% (58,76)	56% (50,62)	52% (45,58)

*Hammit 2022: Proportion of participants with ≥4-fold rise in OPA antibodies from Day 1 (pre PCV) to Month 7 (post 23vPPV); Mohapi 2022: Proportion of participants with ≥4-fold rise in OPA antibodies from Day 1 (pre PCV) to Week 12 (post 23vPPV); Song 2021 Proportion of participants with ≥4-fold rise in OPA antibodies from Day 1 (pre PCV) to Month 13 (post 23vPPV)

2465 (3 RCTs)	⨁⨁⨁◯ Moderate[b,c,d]	15vPCV+23vPPV likely results in little difference in ≥ 4-fold rise of GMT pre to post vaccination compared to 13vPCV+23vPPV

IgG GMC ratios follow-up: 30 days

Table 3: 95% CI for IgG GMC ratios (15vPCV+23vPPV vs. 13vPCV+23vPPV) for shared and unique serotypes at Day 30 a) shaded by non-inferiority and superiority margins^ b) shaded by estimated that favour 15vPCV or 13vPCV†

a)

Study ID	Hammit 2021*		Mohapi 2022*		Song 2021*	
PCV	15	13	15	13	15	13
N	1133	379	152	150	326	325
1	0.81, 1.01		0.59, 0.98		0.79, 1.07	
3	0.85, 1.04		0.83, 1.21		0.87, 1.16	
4	0.65, 0.82		0.63, 0.99		0.74, 1.02	
5	0.84, 1.08		0.85, 1.36		0.84, 1.18	
6A	0.78, 1.04		0.81, 1.45		0.96, 1.41	
6B	0.96, 1.27		0.9, 1.6		0.96, 1.4	
7F	0.8, 1		0.7, 1.12		0.85, 1.16	
9V	0.81, 1.01		0.78, 1.21		0.89, 1.22	
14	0.91, 1.17		0.76, 1.35		0.98, 1.39	
18C	1.15, 1.46		0.86, 1.39		1, 1.36	
19A	0.8, 1.01		0.73, 1.17		0.95, 1.29	
19F	0.89, 1.12		0.79, 1.28		0.93, 1.27	
23F	0.94, 1.21		0.67, 1.23		0.96, 1.35	
22F	0.93, 1.23		0.79, 1.44		1.16, 1.77	
33F	0.6, 0.77		0.6, 0.99		0.67, 0.95	

^ orange=LCI>0.67[6] yellow=LCI>0.5; blue=LCI>1.0 (non-inferiority and superiority margins for IgG GMC ratio in Stacey et al 2019[7])
*study not powered to detect a difference between 15vPCV and 13vPCV

b)

Study ID	Hammit 2021*		Mohapi 2022*		Song 2021*	
PCV	15	13	15	13	15	13
N	1133	379	152	150	326	325
1	0.81, 1.01		0.59, 0.98		0.79, 1.07	
3	0.85, 1.04		0.83, 1.21		0.87, 1.16	
4	0.65, 0.82		0.63, 0.99		0.74, 1.02	
5	0.84, 1.08		0.85, 1.36		0.84, 1.18	
6A	0.78, 1.04		0.81, 1.45		0.96, 1.41	
6B	0.96, 1.27		0.9, 1.6		0.96, 1.4	
7F	0.8, 1		0.7, 1.12		0.85, 1.16	
9V	0.81, 1.01		0.78, 1.21		0.89, 1.22	
14	0.91, 1.17		0.76, 1.35		0.98, 1.39	
18C	1.15, 1.46		0.86, 1.39		1, 1.36	

2454 (3 RCTs)

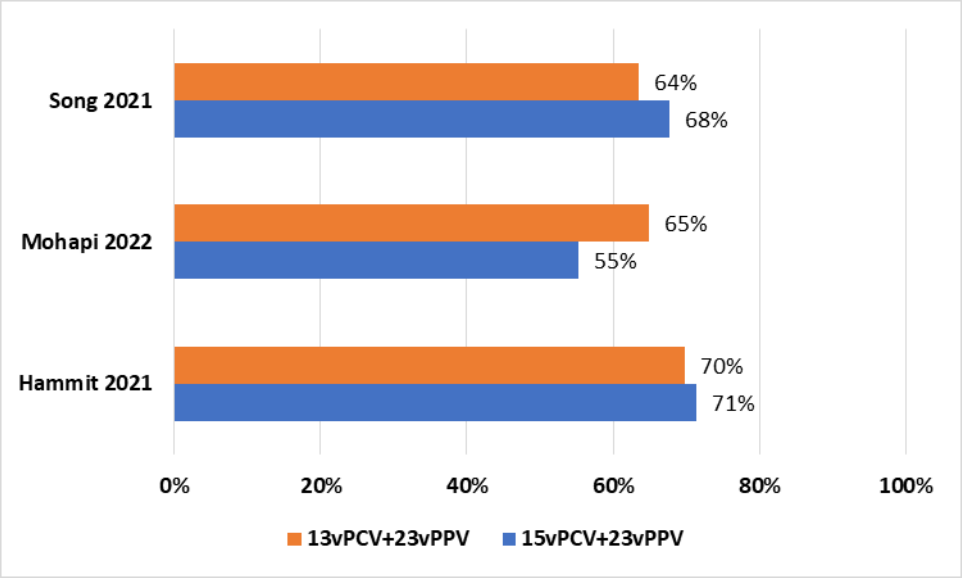
⨁⨁◯◯ Low[b,c,d,e]

15vPCV+23vPPV may result in little to no difference in IgG GMC ratios

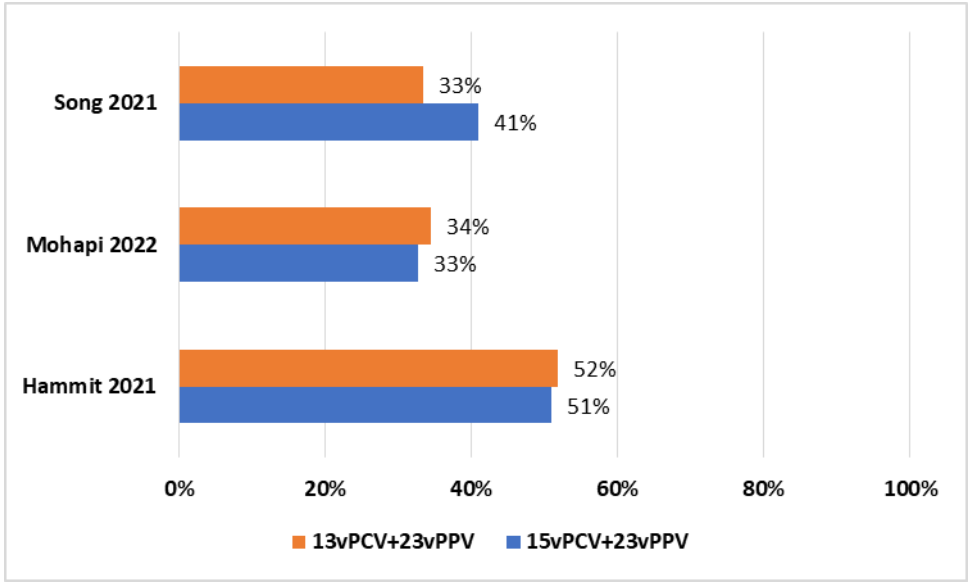
Note: All ST across all studies met a non-inferiority margin (LCI>0.5). This is consistent with OPA GMT ratio
Across all studies, 15vPCV is statistically significantly lower than 13vPCV for ST 33f

Summary of findings: 15vPCV+23vPPV compared to 13vPCV+23vPPV for Indigenous Australian adults ≥50 years without special risk factors

	19A	0.8, 1.01	0.73, 1.17	0.95, 1.29			
	19F	0.89, 1.12	0.79, 1.28	0.93, 1.27			
	23F	0.94, 1.21	0.67, 1.23	0.96, 1.35			
	22F	0.93, 1.23	0.79, 1.44	1.16, 1.77			
	33F	0.6, 0.77	0.6, 0.99	0.67, 0.95			
	†Green=LCI>1; red=UCI<1 *study not powered to detect a difference between 15vPCV and 13vPCV						
% of participants ≥ 4-fold rise of GMC pre to post vaccination	Table 4: Proportion of participants with a ≥ 4-fold rise of GMC pre PCV to post PPV vaccination*						
	Study ID	**Hammit 2021***		**Mohapi 2022***		**Song 2021***	
	PCV	15	13	15	15	13	15
	N	1133	379	152	1133	379	152
	1	81% (79,84)	84% (79,88)	81% (73,87)	89% (82,94)	80% (74,84)	79% (73,83)
	3	41% (37,44)	46% (40,52)	50% (42,59)	45% (36,54)	73% (67,78)	69% (63,74)
	4	71% (68,74)	82% (77,86)	71% (63,79)	84% (76,90)	77% (71,82)	76% (70,80)
	5	49% (45,52)	52% (46,58)	44% (36,53)	44% (35,53)	60% (54,66)	60% (54,66)
	6A	82% (79,84)	82% (77,86)	83% (75,89)	80% (72,86)	81% (76,85)	77% (72,82)
	6B	86% (84,89)	85% (81,89)	81% (74,88)	81% (73,87)	81% (76,85)	77% (72,82)
	7F	77% (74,80)	84% (80,88)	81% (73,87)	86% (79,91)	82% (77,86)	81% (76,86)
	9V	72% (69,75)	77% (72,80)	76% (68,83)	78% (70,85)	76% (71,81)	73% (68,79)
	14	77% (74,80)	71% (65,76)	67% (58,75)	70% (62,78)	69% (63,74)	64% (58,70)
	18C	83% (80,85)	80% (75,85)	82% (75,88)	84% (76,90)	78% (73,83)	71% (65,76)
	19A	66% (63,69)	75% (69,80)	68% (59,76)	73% (65,81)	70% (64,75)	66% (61,72)
	19F	75% (71,78)	79% (74,84)	78% (70,85)	84% (77,90)	77% (72,82)	74% (68,79)
	23F	78% (75,81)	78% (73,83)	75% (67,82)	78% (70,85)	72% (66,77)	70% (64,75)
	22F	69% (66,72)	66% (60,71)	84% (76,90)	86% (79,91)	81% (75,85)	72% (66,77)
	33F	68% (65,71)	76% (70,81)	77% (69,84)	86% (79,91)	76% (70,80)	77% (71,82)
	*Hammit 2022: Proportion of participants with ≥4-fold rise in IgG antibodies from Day 1 (pre PCV) to Month 7 (post 23vPPV); Mohapi 2022: Proportion of participants with ≥4-fold rise in IgG antibodies from Day 1 (pre PCV) to Week 12 (post 23vPPV); Song 2021 Proportion of participants with ≥4-fold rise in IgG antibodies from Day 1 (pre PCV) to Month 13 (post 23vPPV)						
	2465 (3 RCTs))	⨁⨁⨁◯ Moderate[b,c,d]	15vPCV+23vPPV likely results in little difference in ≥ 4-fold rise of GMC pre to post vaccination compared to 13vPCV+23vPPV				

Summary of findings: 15vPCV+23vPPV compared to 13vPCV+23vPPV for Indigenous Australian adults ≥50 years without special risk factors				
Injection site adverse event		2465 (3 RCTs)	⨁⨁⨁◯ Moderate[b,c,d]	15vPCV+23vPPV likely results in little difference in injection site adverse events compared to 13vPCV+23vPPV

Summary of findings: 15vPCV+23vPPV compared to 13vPCV+23vPPV for Indigenous Australian adults ≥50 years without special risk factors

Systemic Adverse Events		2465 (3 RCTs)	⊕⊕⊕? Moderate[b,c,d]	15vPCV+23vPPV likely results in little difference in systemic adverse events compared to 13vPCV+23vPPV

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Abbreviations: 13vPCV, 13-Valent pneumococcal conjugate vaccine; 15vPCV, 15-Valent pneumococcal conjugate vaccine; 23vPPV, pneumococcal polysaccharide vaccine; CI, confidence interval; GMC, geometric mean concentrations; GMT, geometric mean titres; ID, identification; IgG, Immunoglobulin G; LCI, lower confidence interval; OPA, opsonophagocytic activity; RCTs, randomised controlled trials; SAE, serious adverse events; UCI, upper confidence interval

Explanations

a. Downgraded due to low number of events
b. No studies included Indigenous Australian adults
c. One study included Native Americans aged 18-49 years, age range not applicable
d. Two of the studies had an interval of 2 and 6 months between PCV and PPV vaccines. This differs to the 12 months interval recommended in the Australian Immunisation Handbook
e. No studies were powered to detect a difference between PCV15+23PPV and PCV13+23PPV

Evidence Profile: Indigenous Adults >50 years without special risk factors

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Serious adverse events									
3	randomised trials	not serious	not serious	serious[b,c,d]	serious[a]	none	The rates of serious adverse events ranged from 0% to 1% for 15vPCV+23vPPV recipients and 1% to 4% for 13vPCV+23vPPV recipients. None were considered by study investigators to be related to the vaccine.	⨁⨁◯◯ Low	CRITICAL
OPA GMT ratios (follow-up: 30 days)									
3	randomised trials	not serious	not serious	serious[b,c,d]	serious[e]	none	The OPA GMT ratio 30 days following vaccination for shared serotypes ranges from 0.89 to 1.57. For 15v-non13v serotypes (22F and 33F) OPA GMT ratios ranged from 0.9 to 1.63. Majority of serotypes across studies met a non-inferiority margin of 0.67.[6]	⨁⨁◯◯ Low	IMPORTANT
% of participants ≥ 4-fold rise of GMT pre to post vaccination									
3	randomised trials	not serious	not serious	serious[b,c,d]	not serious	none	The proportion of participants with ≥4-fold rise of GMT pre PCV to post PPV vaccination for shared serotypes ranged from 44% to 88% for 15vPCV+23vPPV recipients and 45% to 87% for 13vPCV+23vPPV recipients. For 15v-non13v serotypes (22F and 33F) the proportion of participants with ≥4-fold rise of GMT pre PCV to post PPV ranged from 53% to 80% for 15vPCV+23vPPV recipients and 52% to 75% for 13vPCV+23vPPV recipients.	⨁⨁⨁◯ Moderate	IMPORTANT
IgG GMC ratios (follow-up: 30 days)									
3	randomised trials	not serious	not serious	serious[b,c,d]	serious[e]	none	The IgG GMC ratio 30 days following vaccination for shared serotypes ranges from 0.73 to 1.30. For 15v-non13v serotypes (22F and 33F) the IgG GMC ratio 30 days following vaccination ranged from 0.68 to 1.43. Majority of serotypes across studies met a non-inferiority margin of 0.67.[6]	⨁⨁◯◯ Low	IMPORTANT
% of participants ≥ 4-fold rise of GMC pre to post vaccination									

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
3	randomised trials	not serious	not serious	serious[b,c,d]	not serious	none	The proportion of participants with ≥4-fold rise of GMC pre PCV to post PPV vaccination for shared serotypes ranged from 41% to 86% for 15vPCV+23vPPV recipients and 44% to 89% for 13vPCV+23vPPV recipients. For 15v-non13v serotypes (22F and 33F) the proportion of participants with ≥4-fold rise of GMC pre PCV to post PPV ranged from 68% to 84% for 15vPCV+23vPPV recipients and 66% to 86% for 13vPCV+23vPPV recipients.	⊕⊕⊕◯ Moderate	IMPORTANT
Solicited local adverse event									
3	randomised trials	not serious	not serious	serious[b,c,d]	not serious	none	The rate of injection site adverse events ranged from 55% to 71% for 15vPCV+23vPPV recipients and 70% to 65% for 13vPCV+23vPPV recipients	⊕⊕⊕◯ Moderate	IMPORTANT
Solicited Systemic Adverse Events									
3	randomised trials	not serious	not serious	serious[b,c,d]	not serious	none	The rates of systemic adverse events ranged from 33% to 51% for 15vPCV+23vPPV recipients and 33% to 52% for 13vPCV+23vPPV recipients	⊕⊕⊕◯ Moderate	IMPORTANT

Abbreviations: 13vPCV, 13-Valent pneumococcal conjugate vaccine; 15vPCV, 15-Valent pneumococcal conjugate vaccine; 23vPPV, pneumococcal polysaccharide vaccine; CI, confidence interval; GMC, geometric mean concentrations; GMT, geometric mean titres; ID, identification; IgG, Immunoglobulin G; LCI, lower confidence interval; OPA, opsonophagocytic activity; RCTs, randomised controlled trials; SAE, serious adverse events; UCI, upper confidence interval

Explanations

a. Downgraded due to low number of events
b. No studies included Indigenous Australian adults
c. One study included Native Americans aged 18-49 years, age range not applicable
d. Two of the studies had an interval of 2 and 6 months between PCV and PPV vaccines. This differs to the 12 months interval recommended in the Australian Immunisation Handbook
e. No studies were powered to detect a difference between PCV15+23PPV and PCV13+23PPV

Evidence to Decision Framework: Individual perspective

Should 15vPCV+23vPPV vaccination be used in Indigenous Australian adults ≥50 years old without risk conditions for Pneumococcal disease for the prevention of pneumococcal disease?	
Population	Indigenous Australian adults ≥50 years without special risk factors
Intervention	15-valent pneumococcal conjugate vaccine with subsequent 23-valent pneumococcal polysaccharide vaccine
Comparison	13-valent pneumococcal conjugate vaccine with subsequent 23-valent pneumococcal polysaccharide vaccine
Main outcomes	Immunogenicity: OPA and IgG geometric mean titres - OPA GMT ratios (follow-up: 30 days) - % of participants ≥ 4-fold rise of GMT pre to post vaccination - IgG GMC ratios (follow-up: 30 days) - % of participants ≥ 4-fold rise of GMC pre to post vaccination Safety: 23vPPV after previous 15vPCV or 13vPCV delivery - Severe adverse events (SAE) - Injection site adverse events - Systematic adverse events
Setting	USA, South Korea, Spain, Taiwan, Canada, Chile, Poland, Australia, New Zealand, France, Peru, South Africa, Thailand
Perspective	Individual

ASSESSMENT

Problem
Is the problem a priority?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- Aboriginal and Torres Strait Islander people have a disproportionately higher incidence of pneumococcal disease than others. Invasive pneumococcal disease starts to rise at a much younger age in Aboriginal and Torres Strait Islander adults compared to other adults.
- The serotypes that cause pneumococcal disease in Aboriginal and Torres Strait Islander adults is more diverse than in others.
- Following several years of PCV use with high uptake certain non- PCV serotypes have emerged to cause increased incidence of IPD. This serotype replacement disease is particularly marked among Aboriginal and Torres Strait Islander adults.

- New PCVs with extended valencies will likely improve the protection against pneumococcal disease in Aboriginal and Torres Strait Islander adults.

Desirable effects
How substantial are the desirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- There is variability in the evidence of immunogenicity outcomes of 15vPCV+23vPPV compared with 13vPCV+23vPPV. Although there are small effects at improving immunogenicity outcomes in the 15v-non13v serotypes from the 15vPCV vaccine, these benefits are diminished following 23vPPV vaccine.
- There is no evidence available on clinical outcomes after 15vPCV and no evidence available on the persistence of 15vPCV+23vPPV vaccination

Undesirable Effects
How substantial are the undesirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- Undesirable effects include frequent rates of injection site adverse events and systemic adverse events which are mostly of mild to moderate severity. Rates are similar to those seen after 13vPCV+23vPPV.
- There were no vaccine-related serious adverse events in the included studies.

Certainty of evidence
What is the overall certainty of the evidence of effects?

No Included Studies	Very Low	Low	Moderate	High

- The certainty of evidence is moderate due to imprecision as some studies were not powered to detect a different between 15vPCV and 13vPCV

Values
I*s there important uncertainty about or variability in how much people value the main outcomes?*

Important uncertainty	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

- Unlikely to be important uncertainty in how people value protection against pneumococcal disease.

Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?

Don't Know	Varies	Favours comparison	Probably favours comparison	Does not favour either comparison or intervention	Probably favours intervention	Favours intervention

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- 15vPCV+23vPPV was found to have similar desirable and undesirable effects compared to 13vPCV+23vPPV. Although there are small effects at improving immunogenicity outcomes in the 15v-non13v serotypes from the 15vPCV vaccine, these benefits are diminished following 23vPPV vaccine.
- Undesirable effects are minor

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<tr><td colspan="6">Acceptability
Is the intervention acceptable to key stakeholders?</td></tr>
<tr><td>Don’t know</td><td>Varies</td><td>No</td><td>Probably No</td><td>Probably Yes</td><td>Yes</td></tr>
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- Vaccination to prevent pneumococcal disease appears to be acceptable in the Australian setting. In 2016 the vaccination uptake of the 23vPPV vaccine in adults aged ≥65 years was estimated to be 52%[11]

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<tr><td colspan="6">Feasibility
Is the intervention feasible to implement?</td></tr>
<tr><td>Don’t know</td><td>Varies</td><td>No</td><td>Probably No</td><td>Probably Yes</td><td>Yes</td></tr>
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- Minimal barriers in implementation, as vaccine delivery system already in use and this vaccine would likely replace the use of another vaccine for the individuals receiving it

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</table>

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