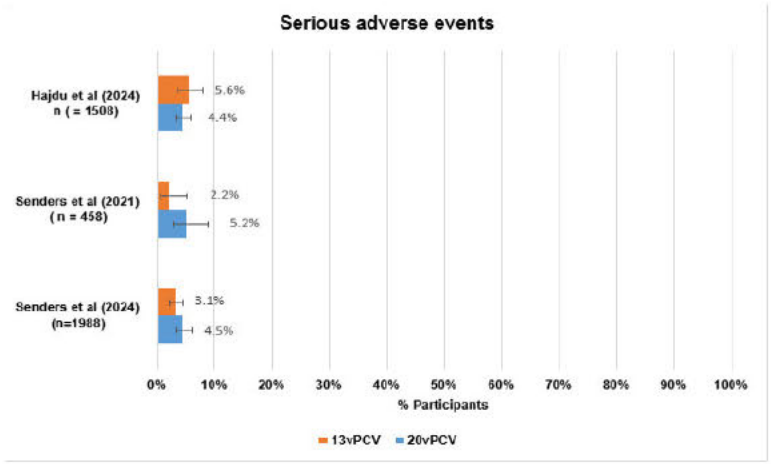
GRADE tables: Comparison of 20vPCV vs 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children with a risk condition† in a 3+1 schedule

NCIRS is conducting GRADE assessments in support of the Australian Technical Advisory Group on Immunisation (ATAGI) and making pilot results available on the NCIRS Centre's website. Please read this material as a supplement to the Australian Immunisation Handbook pneumococcal disease chapter.

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
CRITICAL OUTCOMES				
Serious adverse events (SAE) Follow-up: 6 months		3,949 (3 RCTs)[1-3]	⊕⊕⊕◯ Moderate[a,b]	20vPCV likely results in little to no difference in SAE compared to 13vPCV

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
IMPORTANT OUTCOMES				
Difference in IgG response rate post dose 4 Assessed with: % participants with IgG ≥0.35ug/mL Follow-up: 30 days		1,500 (1 RCT)[4]	⨁⨁◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG response rate for all shared ST post dose 4, except for [redacted] which did not meet the non-inferiority margin. 20vPCV may increase IgG response rates for 20v-non-13v ST.

Study	B7471011*	
PCV	20v	13v
N	755	745
Shared serotypes		
1	[redacted]	
3		
4		
5		
6A		
6B		
7F		
9V		
14		
18C		
19A		
19F		
23F		

*Cells shaded red did not meet non-inferiority margin, yellow met the non-inferiority margin: LCI>-10% points; blue met the superiority margin: LCI>10% points

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
continued **Difference in IgG response rate post dose 4** Assessed with: % participants with IgG ≥0.35ug/mL Follow-up: 30 days	*continued* **Study** B7471011* **PCV** 20v 13v **N** 755 745 **20v-non13 serotypes** 8 [redacted] 10A 11A 12F 15B 22F 33F *Cells shaded red did not meet non-inferiority margin, yellow met the non-inferiority margin: LCI>-10% points; blue met the superiority margin: LCI>10% points	1,500 (1 RCT)[4]	⊕⊕◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG response rate for all shared ST post dose 4, except for [redacted] which did not meet the non-inferiority margin. 20vPCV may increase IgG response rates for 20v-non-13v ST.

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
Difference in IgG response rate post dose 3 Assessed with: % participants with IgG ≥0.35ug/mL Follow-up: 30 days	**Study** B7471011* **PCV** 20v / 13v **N** 833 / 803 **Shared serotypes** 1: -12.5, 5.1 3: -20.1, -10.8 4: -12.0, -4.9 5: -7.8, -.08 6A: -4.6, -0.2 6B: -7.0, -1.2 7F: -2.7, -0.7 9V: -11.3, -4.6 14: -3.1, 1.6 18C: -3.1, 1.9 19A: -2.6, 0.5 19F: -1.5, 2.0 23F: -11.4, -3.9 *Cells shaded red did not meet non-inferiority margin, yellow met the non-inferiority margin: LCI>-10% points; blue met the superiority margin: LCI>10% points	1,636 (1 RCT)[4]	⊕⊕◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG response rate for most shared STs post dose 3, except for [redacted] and [redacted] which did not meet the non-inferiority margin. 20vPCV may increase IgG response rates for 20v-non-13v STs.

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
continued **Difference in IgG response rate post dose 3** Assessed with: % participants with IgG ≥0.35ug/mL Follow-up: 30 days	*continued* **20v-non13 serotypes** 8 10A 11A 12F 15B 22F 33F [redacted] *Cells shaded red did not meet non-inferiority margin, yellow met the non-inferiority margin: LCI>-10% points; blue met the superiority margin: LCI>10% points	1,636 (1 RCT)4	⨁⨁◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG response rate for most shared STs post dose 3, except for [redacted] and [redacted] which did not meet the non-inferiority margin. 20vPCV may increase IgG response rates for 20v-non-13v STs.

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
IgG Geometric Mean Concentration (GMC) ratio post dose 4 Follow-up: 30 days	See table below	1,500 (1 RCT)[4,5]	⊕⊕◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG GMC ratios for all shared ST post dose 4. 20vPCV may increase IgG GMC ratios for 20v-non-13v ST.

Study	**B7471011***	
PCV	20v	13v
N	755	745
Shared serotypes		
1	0.63, 0.76	
3	0.61, 0.73	
4	0.70, 0.86	
5	0.67, 0.82	
6A	0.70, 0.85	
6B	0.62, 0.79	
7F	0.70, 0.82	
9V	0.73, 0.88	
14	0.81, 1.00	
18C	0.67, 0.82	
19A	0.77, 0.94	
19F	0.78, 0.96	
23F	0.57, 0.72	

*Cells shaded yellow met the non-inferiority margin: LCI>0.5; cells shaded blue met the superiority margin: LCI>2.0

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
continued **IgG Geometric Mean Concentration (GMC) ratio post dose 4** Follow-up: 30 days	*continued* **Study** B7471011* **PCV** 20v 13v **N** 755 745 **20v-non-13v serotypes** 8 [redacted] 10A 11A 12F 15B 22F 33F *Cells shaded yellow met the non-inferiority margin: LCI>0.5; cells shaded blue met the superiority margin: LCI>2.0	1,500 (1 RCT)[4,5]	⨁⨁◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG GMC ratios for all shared ST post dose 4. 20vPCV may increase IgG GMC ratios for 20v-non-13v ST

IgG Geometric Mean Concentration (GMC) ratio post dose 3 Follow-up: 30 days	<table><tr><td>**Study**</td><td colspan="2">**B7471011***</td></tr><tr><td>**PCV**</td><td>20v</td><td>13v</td></tr><tr><td>**N**</td><td>833</td><td>803</td></tr><tr><td colspan="3">**Shared serotypes**</td></tr><tr><td>1</td><td colspan="2">0.59, 0.72</td></tr><tr><td>3</td><td colspan="2">0.64, 0.76</td></tr><tr><td>4</td><td colspan="2">0.63, 0.78</td></tr><tr><td>5</td><td colspan="2">0.61, 0.7</td></tr><tr><td>6A</td><td colspan="2">0.65, 0,81</td></tr><tr><td>6B</td><td colspan="2">0.51, 0.7</td></tr><tr><td>7F</td><td colspan="2">0.69, 0.81</td></tr><tr><td>9V</td><td colspan="2">0.65, 0.80</td></tr><tr><td>14</td><td colspan="2">0.71, 0.89</td></tr><tr><td>18C</td><td colspan="2">0.70, 0.84</td></tr><tr><td>19A</td><td colspan="2">0.72, 0.86</td></tr><tr><td>19F</td><td colspan="2">0.73, 0.86</td></tr><tr><td>23F</td><td colspan="2">0.58, 0.75</td></tr><tr><td colspan="3">**20v-non13 serotypes**</td></tr><tr><td>8</td><td colspan="2" rowspan="8"></td></tr><tr><td>10A</td></tr><tr><td>11A</td></tr><tr><td>12F</td></tr><tr><td>15B</td></tr><tr><td>22F</td></tr><tr><td>33F</td></tr></table> *Cells shaded red did not meet non-inferiority margin, yellow met the non-inferiority margin: LCI>0.5; cells shaded blue met the superiority margin: LCI>2.0	1,635 (1 RCT)[4,5]	⊕⊕◯◯ Low[a,b,c,d]	20vPCV may result in no difference in IgG GMC ratios for all shared ST post dose 3. 20vPCV may increase IgG GMC ratios for 20v-non-13v ST.

OPA response rate post dose 4 Assessed with: % participants ≥LLOQ Follow-up: 30 days	**Study**	**B7471011***		214 (1 RCT)[4]	⊕◯◯◯ Very low[a,b,c,d,e]	20vPCV may result in little to no difference in OPA response rate for shared STs except [redacted] post dose 4, which was statistically significantly lower for 20vPCV. However, the evidence is very uncertain. 20vPCV may increase OPA response rates for 20v-non-13v ST post dose 4. However, the evidence is very uncertain.
	PCV	20v	13v			
	N	[redacted]	109			
	Shared serotypes					
	1	[redacted]				
	3					
	4					
	5					
	6A					
	6B					
	7F					
	9V					
	14					
	18C					
	19A					
	19F					
	23F					
	20v-non-13v serotypes					
	8	[redacted]				
	10A					
	11A					
	12F					
	15B					
	22F					
	33F					

*Cells shaded red have a lower point estimate for 20vPCV and non-overlapping confidence intervals, green have higher point estimate for 20vPCV and non-overlapping confidence intervals

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

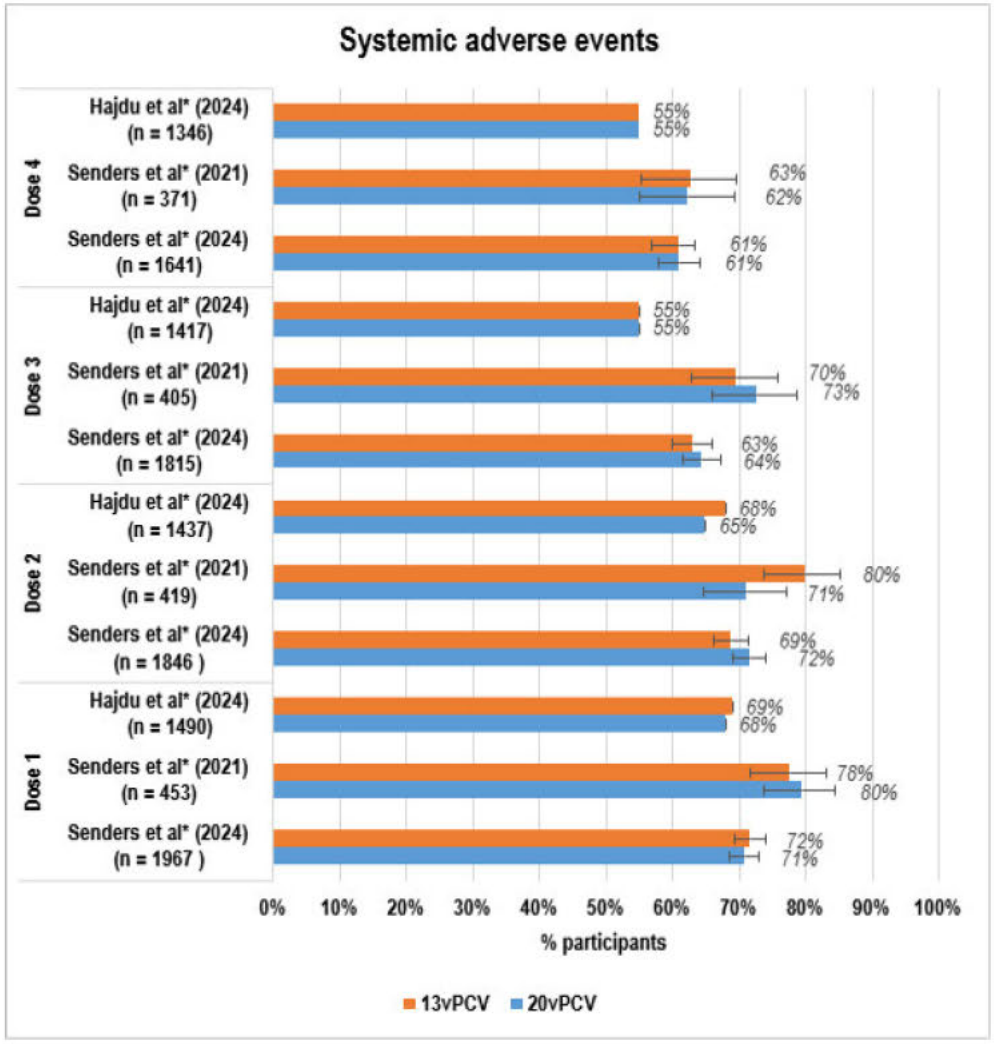
Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

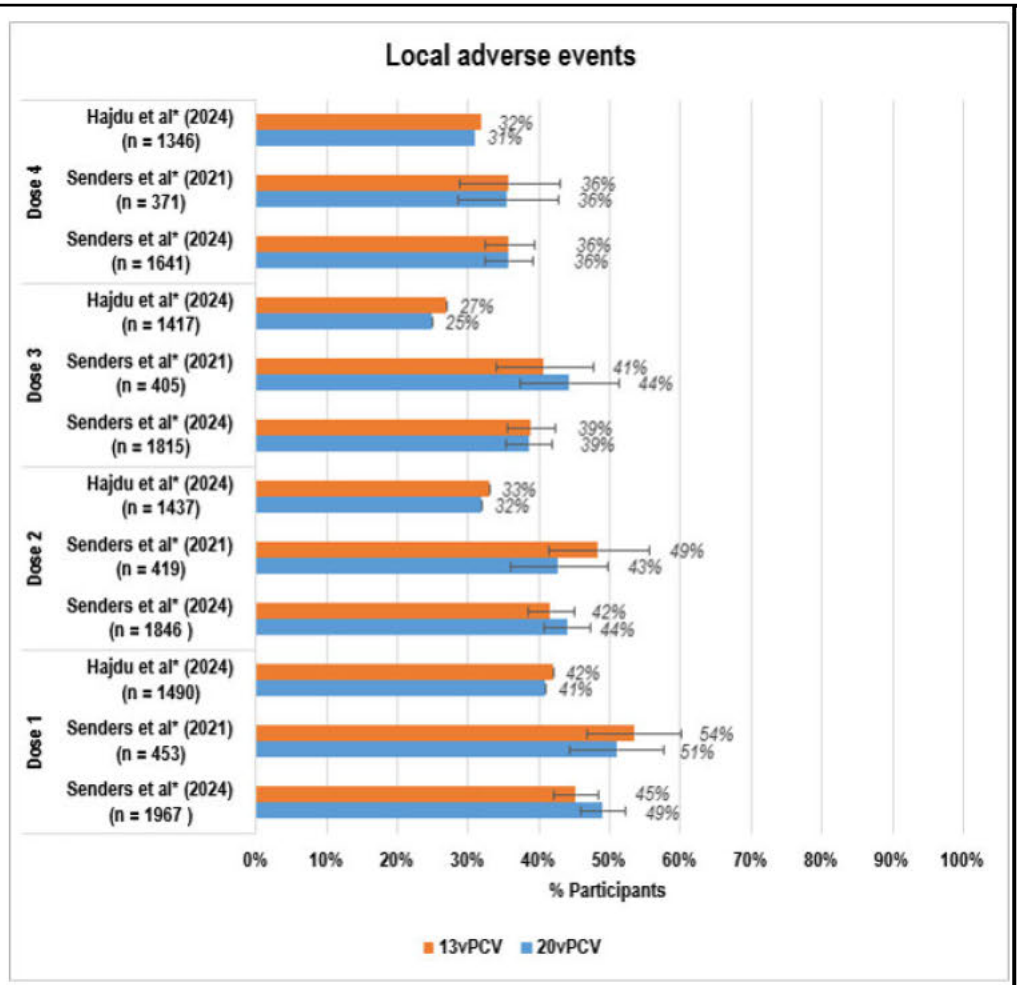
Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
OPA response rate post dose 3 Assessed with: % participants ≥LLOQ Follow-up: 30 days	**Study** B7471011* **PCV** 20v 13v **N** [redacted] **Shared serotypes** 1 [redacted] 3 4 5 6A 6B 7F 9V 14 18C 19A 19F 23F *Cells shaded red have a lower point estimate for 20vPCV and non-overlapping confidence intervals, green have higher point estimate for 20vPCV and non-overlapping confidence intervals	216 (1 RCT)[4]	⊕◯◯◯ Very low[a,b,c,d,e]	20vPCV may result in little to no difference in OPA response rates for shared STs post dose 3. However, the evidence is very uncertain. 20vPCV may increase in OPA response rates for 20v-non13v ST post dose 3. However, the evidence is very uncertain.

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement
continued **OPA response rate post dose 3** Assessed with: % participants ≥LLOQ Follow-up: 30 days	*continued* **Study** B7471011* **PCV** 20v 13v **N** [redacted] **20v-non-13v serotypes** 8 [redacted] 10A 11A 12F 15B 22F 33F *Cells shaded red have a lower point estimate for 20vPCV and non-overlapping confidence intervals, green have higher point estimate for 20vPCV and non-overlapping confidence intervals	216 (1 RCT)[4]	⊕◯◯◯ Very low[a,b,c,d,e]	20vPCV may result in little to no difference in OPA response rates for shared STs post dose 3. However, the evidence is very uncertain. 20vPCV may increase in OPA response rates for 20v-non13v ST post dose 3. However, the evidence is very uncertain.

Systemic adverse events post each dose Follow-up: 7 days	 *Study did not report overall rates of systemic adverse events; irritability was used as a proxy measure	3,960 (3 RCTs)[1-3]	⊕⊕⊕◯ Moderate[a,b]	20vPCV likely results in little to no difference in systemic AE compared to 13vPCV

Local adverse events post each dose Follow-up: 7 days	 *Study did not report overall rates of local adverse events; injection site pain was used as a proxy measure	3,924 (3 RCTs)[1-3]	⊕⊕⊕◯ Moderate[a,b]	20vPCV likely results in little to no difference in local adverse events compared to 13vPCV
Explanations				

20vPCV compared with 13vPCV+23vPPV in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule

Patient or population: Aboriginal and Torres Strait Islander infants and infants and children diagnosed with a risk condition† in a 3+1 schedule
Intervention: 20vPCV
Comparison: 13vPCV+23vPPV

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretive statement

a. Downgraded as study population not reflective of population of interest (infants with risk conditions including indigenous or Aboriginal and Torres Strait Islander infants)
b. Downgraded as comparator in study (13vPCV) not comparator of interest in PICO (13vPCV+23vPPV)
c. Some concerns in the domain of risk of bias in the selection of the reported results
d. Inconsistency cannot be assessed as only one study reported on this outcome
e. Downgraded due to small sample size n is <400

Abbreviations: 13vPCV=13-valent pneumococcal conjugate vaccine; 20vPCV=20-valent pneumococcal conjugate vaccine; 23vPPV=23-valent pneumococcal polysaccharide vaccine; AE=adverse event; CI=confidence interval; GMC=geometric mean concentrations; GMT=geometric mean titres; ID=identification; IgG=Immunoglobulin G; LCI=lower confidence interval; LLOQ = lower limit of quantification; NR=not reported; OPA, opsonophagocytic activity; PD=post dose; RCTs=randomised controlled trials; SAE=serious adverse events; ST=serotype; UCI=upper confidence interval.

† see The Australia Immunisation Handbook pneumococcal disease chapter for a list of risk conditions recommended to receive pneumococcal vaccination

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.

GRADE evidence profile

Evidence profile: 20vPCV compared to 13vPCV for Aboriginal and Torres Strait Islander infants and infants and children diagnosed with certain risk condition† in a 3+1 schedule

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Serious adverse events (SAE) (follow-up: 6 months)									
3	Randomised trials	Not serious	Not serious	Serious[a,b]	Not serious	None	The rates of serious adverse events ranged from 4.4% to 5.2% for 20vPCV recipients and 2.2% to 5.6% for 13vPCV recipients.[1-3]	⨁⨁⨁◯ Moderate	CRITICAL
Difference in IgG response rate post dose 4 (follow-up: 30 days; assessed with: % participants with IgG ≥0.35ug/mL)									
1	Randomised trials	Serious[c]	N/a[d]	Serious[a,b]	Not serious	None	The difference in the proportion of participants with IgG ≥0.35 ug/mL at 30 days post dose 4 for shared serotypes ranges from [redacted] percentage points to [redacted] percentage points. All shared serotypes except [redacted] met a non-inferiority margin of LCI > -10 percentage points.[4] For 20v-non13v serotypes the difference in proportion of participants with IgG ≥0.35 ug/mL at 30 days post dose 4 was [redacted] percentage points to [redacted] percentage points. All 20v-non13v serotypes met the superiority margin of LCI>10% points.[4]	⨁⨁◯◯ Low	IMPORTANT

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Difference in IgG response rate post dose 3 (follow-up: 30 days; assessed with: % participants with IgG ≥0.35ug/mL)									
1	Randomised trials	Serious[c]	N/a[d]	Serious[a,b]	Not serious	None	The difference in the proportion of participants with IgG ≥0.35 ug/mL at 30 days post dose 3 for shared serotypes ranges from [redacted] percentage points to [redacted] percentage points. [redacted] shared STs [redacted] did not meet a non-inferiority margin of LCI > -10% points. The remaining [redacted] STs met this margin after dose 3.[4] For 20v-non13v serotypes the difference in proportion of participants with IgG ≥0.35 ug/mL at 30 days post dose 3 was [redacted] percentage points to [redacted] percentage points. [redacted] 20v-non13v serotypes met the superiority margin of LCI>10% points.[4]	⊕⊕◯◯ Low	IMPORTANT
IgG Geometric Mean Concentration (GMC) ratio post dose 4 (follow-up: 30 days)									
1	Randomised trials	Serious[c]	N/a[d]	Serious[a,b]	Not serious	None	The IgG GMC ratio 30 days post dose 4 for shared serotypes ranges from 0.64 to 0.90. All serotypes met a non-inferiority margin of LCI>0.5.[4,6] For 20v-non13v serotypes the IgG GMCs ranged from [redacted] to [redacted] All 20v-non13v serotypes IgG GMCs met the superiority margin of LCI>2.0.[4]	⊕⊕◯◯ Low	Important

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
IgG Geometric Mean Concentration (GMC) ratio post dose 3 (follow-up: 30 days)									
1	Randomised trials	Serious[c]	N/a[d]	Serious[a,b]	Not serious	None	The IgG GMC ratio 30 days post dose 3 for shared serotypes ranges from 0.60 to 0.79. All serotypes met a non-inferiority margin of LCI>0.5.[4,6] For 20v-non13v serotypes the IgG GMCs ranged from [redacted] to [redacted]. All 20v-non13v serotypes IgG GMCs met the superiority margin of LCI>2.0.[4]	⨁⨁◯◯ Low	IMPORTANT
OPA response rate post dose 4 (follow-up: 30 days; assessed with: % participants ≥LLOQ)									
1	Randomised trials	Serious[d]	N/a[d]	Serious[a,b,c]	Serious[e]	None	The OPA response rate 30 days post dose 4 for shared serotypes ranged from [redacted] to [redacted] for 20vPCV and [redacted] to [redacted] for 13vPCV. Serotype 1 was statistically significantly lower for 20vPCV compared to 13vPCV as the based on non-overlapping confidence intervals.[4] For the 20v-non13v serotypes the OPA response rate ranged from [redacted] to [redacted] for 20vPCV and [redacted] to [redacted] for 13vPCV. All 20v-non13 serotypes had statistically significantly higher response rates for 20vPCV compared to 13vPCV based on non-overlapping CI.[4]	⨁◯◯◯ Very low	IMPORTANT

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
OPA response rate post dose 3 (follow-up: 30 days; assessed with: % participants ≥LLOQ)									
1	Randomised trials	Serious[d]	N/a[d]	Serious[a,b,c]	Serious[e]	None	The OPA response rate 30 days post dose 3 for shared serotypes ranged from [redacted] to [redacted] for 20vPCV and [redacted] to [redacted] for 13vPCV. All serotypes had overlapping confidence intervals.[4] For the 20v-non13v serotypes the OPA response rate ranged from [redacted] to [redacted] for 20vPCV and [redacted] to [redacted] for 13vPCV. All 20v-non13 serotypes had statistically significantly higher response rates for 20vPCV compared to 13vPCV based on non-overlapping CI.[4]	⊕◯◯◯ Very low	IMPORTANT
Systemic adverse events post each dose (follow-up: 7 days)									
3	Randomised trials	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The rate of systemic adverse events ranged from 55% to 85.9% for 20vPCV recipients and 55% to 84.5% for 13vPCV recipients. Systemic adverse events were highest after dose 1 of both 20vPCV and 13vPCV.[1-3]	⊕⊕⊕◯ Moderate	IMPORTANT

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Local adverse events post each dose (follow-up: 7 days)									
3	Randomised trials	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The rate of local adverse events ranged from 25% to 59.8% for 20vPCV recipients and 27% to 56.5% for 13vPCV recipients. Local adverse events were highest after dose 1 of both 20vPCV and 13vPCV. [1-3]	⨁⨁⨁◯ Moderate	IMPORTANT

Explanations

a. Downgraded as study population not reflective of population of interest (infants with risk conditions including indigenous or Aboriginal and Torres Strait Islander infants)
b. Downgraded as comparator in study (13vPCV) not comparator of interest in PICO (13vPCV+23vPPV)
c. Some concerns in the domain of risk of bias in the selection of the reported results
d. Inconsistency cannot be assessed as only one study reported on this outcome
e. Downgraded due to small sample size n is <400

Abbreviations: 13vPCV=13-valent pneumococcal conjugate vaccine; 20vPCV=20-valent pneumococcal conjugate vaccine; AE=adverse event; CI=confidence interval; GMC=geometric mean concentrations; GMT=geometric mean titres; ID=identification; IgG=Immunoglobulin G; LCI=lower confidence interval; LLOQ = lower limit of quantification; NR=not reported; OPA=opsonophagocytic activity; PD=post dose; RCTs=randomised controlled trials; SAE=serious adverse events; ST=serotype; UC=upper confidence interval.

Evidence to Decision Framework: individual perspective

Should 20vPCV (3+1 schedule) be used in Aboriginal and Torres Strait Islander infants and infants and children diagnosed with certain risk conditions† for the prevention of pneumococcal disease?	
Population	Aboriginal and Torres Strait Islander infants and infants and children diagnosed with certain risk conditions
Intervention	20-valent pneumococcal conjugate vaccine (20vPCV) in a 3+1 schedule
Comparison	13-valent pneumococcal conjugate vaccine (13vPCV) in a 3+1 schedule, followed by 23vPPV (2-doses)
Main outcomes	*Immunogenicity* • Difference in IgG response rate (30-days post dose 4) – Important • Difference in IgG response rate (30-days post dose 3) – Important • IgG GMC ratios (30-days post dose 4) – Important • IgG GMC ratios (30-days post dose 3) – Important • OPA response rate (30-days post dose 4) – Important • OPA response rate (30-days post dose 3) – Important *Safety* • Severe adverse events (SAE) – Critical • Local adverse events – Important • Systemic adverse events – Important
Setting	Multicentre (USA, Australia, Belgium, Czechia, Denmark, Estonia, Finland, Italy, Netherlands, Norway, Russia, Slovakia)
Perspective	Individual
ASSESSMENT	
Problem *Is the problem a priority?*	

Don't know	Varies	No	Probably No	Probably Yes	Yes

- Pneumococcal disease incidence is high in younger children. In Australia in 2016 there were 1,666 IPD notifications of which 234 (14%) were in children under 5 years. Of the 2,434 hospitalisations for pneumonia in 2016, 5% were in children under 5 years.7
- People with certain medical conditions and Aboriginal and Torres Strait Islander children are at higher risk of IPD and require additional doses of pneumococcal vaccines.7,8
- Rates of IPD fell after vaccination with 13vPCV was introduced for infants, however non-13v serotypes contribute to IPD burden.
- Extended valency PCVs would likely improve pneumococcal disease prevention in children.

Desirable effects
How substantial are the desirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- Overall, there is improved immunogenicity outcomes for 20v-non13v serotypes.
- There is downward drift towards lower immunogenicity for shared serotypes between 20vPCV and 13vPCV.
- There is no evidence available on the efficacy or effectiveness against clinical outcomes after 20vPCV in children.

Undesirable Effects
How substantial are the undesirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- Undesirable effects include frequent rates of local adverse events and systemic adverse events which are mostly of mild to moderate severity. The rates were similar between 20vPCV and 13vPCV.
- The rates of serious adverse events were low for both 20vPCV and 13vPCV.

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 low. Out of the nine outcomes, three were moderate, four were low and two were very low.
- Outcomes were downgraded due to serious indirectness as the studies did not include Aboriginal and Torres Strait Islander children and did not include all populations with medical conditions that increase the risk of IPD. The studies also did not provide data for the comparator of interest (13vPCV+23vPPV). The only available study on immunogenicity was downgraded due to serious risk of bias. The outcome of OPA response rate was downgraded due to imprecision due to the small sample size.

Values
Is 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

- There is an overall improvement in immune response from 20vPCV for the 20v-non-13v serotypes, which likely balances out the downward drift towards lower immunogenicity for 20vPCV for the shared serotypes.
- Undesirable effects are minor and comparable between 20vPCV and 13vPCV.
- The evidence is very uncertain due to a single study for immunogenicity outcomes and the design of this study varying significantly from the currently recommended schedule and population groups.

Acceptability
Is the intervention acceptable to key stakeholders?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- Vaccination against pneumococcal disease appears to be acceptable in the Australian setting. In 2022 the vaccination uptake of pneumococcal vaccination in infants aged one and two years was 95.7% and 95.3%, respectively.9

Feasibility
Is the intervention feasible to implement?

Don't know	Varies	No	Probably No	Probably Yes	Yes

- Minimal barriers in implementation, as vaccine delivery system already in use and this vaccine would likely replace current vaccines or be an alternative vaccine for the individuals receiving it.

ATAGI RECOMMENDATION

20vPCV is recommended in preference to 13vPCV in Aboriginal and Torres Strait Islander infants AND infants and children diagnosed with certain risk condition for the prevention of pneumococcal disease.

JUSTIFICATION AND CONSIDERATIONS
For 20v-non-13v serotypes (8, 10A, 11A, 12F, 15B, 22F and 33F), 20vPCV results in improved protection based on immunogenicity outcomes compared to 13vPCV. The evidence suggests that 20vPCV results in little difference in the immunogenicity outcomes for the shared serotypes compared to 13vPCV. Safety outcomes are comparable between 20vPCV and 13vPCV. There is currently no data available for the specific populations of interest (Aboriginal and Torres Strait Islander infants or children with risk conditions) or the comparator (13vPCV+23vPPV) of interest. Therefore, the evidence for this PICO is uncertain.

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