Grading of Recommendations, Assessment, Development, and Evaluation (GRADE): Pfizer's Pentavalent Meningococcal Vaccine (MenACWY-TT/MenB-FHbp)

Introduction

On October 20, 2023, the U.S. Food and Drug Administration approved the use of a pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya, Pfizer]) for prevention of invasive disease caused by *Neisseria meningitidis* serogroups A, B, C, W, and Y among persons aged 10–25 years.[1] On October 25, 2023, CDC's Advisory Committee on Immunization Practices (ACIP) recommended MenACWY-TT/MenB-FHbp may be used when both MenACWY and MenB are indicated at the same visit for 1) healthy individuals aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccination and 2) individuals aged 10 years and older at increased risk of meningococcal disease (e.g., due to persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia).

A systematic review and Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to inform ACIP's deliberations regarding use of MenACWY-TT/MenB-FHbp. The policy questions under consideration were 1) Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY and MenB?, 2) Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?, and 3) Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only? (Tables 1a–c).

Methods

Members of ACIP's Meningococcal Vaccines Work Group ("Work Group") selected policy questions and prespecified and rated the importance of relevant outcomes (including benefits and harms) before the GRADE assessment (Tables 1a–c, Table 2). All Work Group members and CDC staff participating in the GRADE assessment met ACIP requirements for reporting conflicts of interest.

A systematic literature search was conducted using Medline, Embase, Global Health, CINAHL, Cochrane, Scopus, and clinicaltrials.gov databases. Efforts also were made to obtain unpublished or other relevant data. Two reviewers independently screened titles and abstracts and reviewed full-text records. Records were included if they presented primary data on Pfizer's pentavalent meningococcal vaccine. Characteristics of all included studies are shown in Appendix 1, and evidence retrieval methods are shown in Appendix 2.[2–4]

The GRADE evidence certainty assessment addressed risk of bias, inconsistency, indirectness, imprecision, and other characteristics. The evidence certainty categories include high, moderate, low, or very low certainty.

Results

A summary of the GRADE assessment was presented to ACIP on June 23, 2023. Overall, 48 records were identified and screened; 29 records were excluded based on the title and abstract, and 10 records were excluded based on full text review. The remaining nine records described results from three randomized controlled clinical trials and were included in the evidence synthesis and GRADE assessment (Appendix 1).

No data were identified regarding the outcomes "disease caused by serogroups A, B, C, W, and Y" or "interference with other recommended vaccines administered concurrently." Data on the remaining outcomes are summarized in the tables below. When the available data applied to all 3 policy questions, only one table is shown; separate tables were created when the data varied by policy question.

Summary

For all outcomes, the initial evidence level was high because the available data were from randomized control trials. The final evidence certainty was the same for all three policy questions. The evidence certainty for short-term immunity was moderate for healthy persons and low for persons at increased risk. The evidence certainty for persistent immunity was low for serogroups A, C, W, and Y for healthy persons, moderate for serogroup B for healthy persons, and low for all serogroups for those at increased risk. For both serious and non-serious adverse events, the level of certainty was low for healthy persons, and very low for those at increased risk.

Table 1a: Policy Question and PICO 1

Policy Question	Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY and MenB?
Population	All individuals aged 10 years or older currently recommended to receive MenACWY and MenB vaccine
Intervention	Vaccination with the pentavalent vaccine
Comparison	Vaccination with currently licensed MenACWY and MenB vaccine
Outcomes	• Disease caused by serogroups A, B, C, W, and Y • Short-term immunity • Persistent immunity • Interference with other recommended vaccines administered concurrently • Serious adverse events • Non-serious adverse events

Table 1b: Policy Question and PICO 2

Policy Question	Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?
Population	All individuals aged 10 years or older currently recommended to receive MenACWY vaccine
Intervention	Vaccination with the pentavalent vaccine
Comparison	Vaccination with currently licensed MenACWY vaccine
Outcomes	• Disease caused by serogroups A, C, W, and Y • Short-term immunity • Persistent immunity • Interference with other recommended vaccines administered concurrently • Serious adverse events • Non-serious adverse events

Table 1c: Policy Question and PICO 3

Policy Question	Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only?
Population	All individuals aged 10 years or older currently recommended to receive MenB vaccine
Intervention	Vaccination with the pentavalent vaccine
Comparison	Vaccination with currently licensed MenB vaccine

Outcomes	• Disease caused by serogroup B • Short-term immunity • Persistent immunity • Interference with other recommended vaccines administered concurrently • Serious adverse events • Non-serious adverse events

Table 2: Outcomes and Rankings

Outcome	Importance	Included in Profile
Meningococcal disease caused by serogroups A, B, C, W, and Y	Critical	No
Short-term immunity	Critical	Yes
Persistent immunity	Important	Yes
Interference with other recommended vaccines administered concurrently	Important	No
Serious adverse events	Critical	Yes
Non-serious adverse events	Important	Yes

Table 3a: Summary of Studies Reporting Short-Term Immunity — PICOs 1, 2, and 3

Author, pub year	Age or other characteristic	Serogroup (test strain)	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	Effect estimate — RR (95% CI)	Study limitations (risk of bias)
Seroresponse based on hSBA titer[a] 1 month after 1 intervention dose								
		A	484/499	242/254			1.02 (0.99–1.05)	Not serious

Pfizer CT (NCT04440163), 2020	10–25 years; ACWY naïve	C	315/501	132/252	MenABCWY (1 dose)	MenACWY-CRM (1 dose) + MenB-FHbp (1 dose)	1.20 (1.05–1.38)	
		W	390/492	178/244			1.09 (0.99–1.19)	
		Y	405/494	175/248			1.16 (1.06–1.27)	
	10–25 years; ACWY primed	A	416/439	220/227			0.98 (0.95–1.01)	
		C	410/439	214/226			0.99 (0.95–1.03)	
		W	417/428	214/222			1.01 (0.98–1.04)	
		Y	417/442	209/223			1.01 (0.97–1.05)	
Seroresponse based on hSBA titer 1 month after 2 intervention doses								
Pfizer CT (NCT04440163), 2020	10–25 years; ACWY naïve	A	437/447	242/254	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	1.03 (1.00–1.06)	Not serious
		C	421/451	132/252			1.78 (1.58–2.01)	
		W	427/439	178/244			1.33 (1.23–1.44)	
		Y	421/446	175/248			1.34 (1.23–1.45)	
	10–25 years; B naïve[b]	B (A22)	646/778	313/396			1.05 (0.99–1.12)	
		B (A56)	774/807	378/400			1.02 (0.99–1.05)	
		B (B24)	567/833	239/418			1.19 (1.08–1.31)	
		B (B44)	731/845	332/419			1.09 (1.03–1.15)	
		B (composite)	591/755	263/419			1.25 (1.15–1.36)	
	10–25 years; ACWY primed	A	361/385	220/227			0.97 (0.93–1.00)	
		C	362/386	214/226			0.99 (0.95–1.03)	
		W	365/376	214/222			1.01 (0.98–1.04)	
		Y	360/387	209/223			0.99 (0.95–1.04)	

[a] hSBA stands for serum bactericidal assay using human complement. For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8 (<1:16 for A22), seroresponse is a titer ≥4 times the 1:8 (1:16 for A22). For those with a baseline hSBA titer ≥1:8 (≥1:16 for A22), seroresponse is a titer ≥4 times the baseline titer.

[b] Serogroup B primed was not assessed.

Table 3b: Summary of Studies Reporting Persistent Immunity — PICOs 1, 2, and 3

Author, pub year	Age or other characteristic	Serogroup (test strain)	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	Effect estimate — RR (95% CI)	Study limitations (risk of bias)
Seroprotection (defined as hSBA titer ≥1:8 for all but A22 which is ≥1:16) at 12 months (18 months for MenACWY-CRM) after last dose[a]								
Pfizer CT (NCT03135834), 2017	10–25 years; ACWY naïve	A	102/112	42/59	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	1.28 (1.08–1.52)	Not serious
		C	86/112	32/62			1.49 (1.15–1.93)	
		W	111/112	52/62			1.18 (1.06–1.32)	
		Y	112/112	61/62			1.02 (0.98–1.05)	
	10–25 years; B naïve[b]	B (A22)	53/162	22/83			1.23 (0.81–1.88)	
		B (A56)	54/162	27/83			1.03 (0.70–1.50)	
		B (B24)	51/165	24/85			1.10 (0.73–1.65)	
		B (B44)	31/166	13/85			1.22 (0.68–2.21)	
	10–25 years; ACWY primed	A	47/48	22/22			0.98 (0.94–1.02)	
		C	52/54	21/23			1.06 (0.92–1.21)	
		W	48/48	21/22			1.05 (0.96–1.15)	
		Y	48/48	22/22			1.00 (1.00–1.00)	
Seroprotection (defined as hSBA titer ≥1:8 for all but A22 which is ≥1:16) at 24 months (30 months for MenACWY-CRM) after last dose								
Pfizer CT (NCT03135834), 2017	10–25 years; ACWY naïve	A	89/101	42/60	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	1.26 (1.05–1.51)	Not serious
		C	76/101	29/61			1.58 (1.19–2.11)	
		W	102/103	48/61			1.26 (1.10–1.44)	
		Y	102/102	57/61			1.07 (1.00–1.14)	
	10–25 years; B naïve	B (A22)	72/196	37/128			1.27 (0.92–1.76)	
		B (A56)	68/196	44/131			1.03 (0.76–1.41)	
		B (B24)	65/196	36/131			1.21 (0.86–1.70)	
		B (B44)	36/200	24/132			0.99 (0.62–1.58)	
	10–25 years; ACWY primed	A	61/61	37/37			1.00 (1.00–1.00)	
		C	94/97	67/71			1.03 (0.96–1.10)	
		W	61/61	35/37			1.06 (0.98–1.14)	
		Y	61/61	37/37			1.00 (1.00–1.00)	
Seroprotection (defined as hSBA titer ≥1:8 for all but A22 which is ≥1:16) at 36 months (42 months for MenACWY-CRM) after last dose								

Pfizer CT (NCT03135834), 2017	10–25 years; ACWY naïve	A	84/95	39/54	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	1.22 (1.02–1.47)	Not serious
		C	64/95	24/54			1.52 (1.09–2.11)	
		W	92/97	42/54			1.22 (1.05–1.42)	
		Y	97/97	49/54			1.10 (1.01–1.20)	
	10–25 years; B naïve	B (A22)	54/185	30/116			1.13 (0.77–1.65)	
		B (A56)	54/186	40/118			0.86 (0.61–1.20)	
		B (B24)	68/192	34/120			1.25 (0.89–1.76)	
		B (B44)	39/193	24/121			1.02 (0.65–1.61)	
	10–25 years; ACWY primed	A	57/57	32/33			1.03 (0.97–1.10)	
		C	93/96	64/67			1.01 (0.95–1.08)	
		W	57/57	32/33			1.03 (0.97–1.10)	
		Y	57/57	32/33			1.03 (0.97–1.10)	
Seroprotection (defined as hSBA titer ≥1:8 for all but A22 which is ≥1:16) at 48 months (54 months for MenACWY-CRM) after last dose								
Pfizer CT (NCT03135834), 2017	10–25 years; ACWY naïve	A	58/71	26/41	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	1.29 (1.00–1.67)	Not serious
		C	44/71	16/42			1.63 (1.06–2.49)	
		W	64/70	29/41			1.29 (1.05–1.59)	
		Y	71/71	40/42			1.05 (0.98–1.12)	
	10–25 years; B naïve	B (A22)	39/139	30/94			0.88 (0.59–1.31)	
		B (A56)	50/145	29/98			1.17 (0.80–1.70)	
		B (B24)	53/145	26/98			1.38 (0.93–2.04)	
		B (B44)	27/148	16/99			1.13 (0.64–1.98)	
	10–25 years; ACWY primed	A	40/40	23/23			1.00 (1.00–1.00)	
		C	75/76	52/58			1.10 (1.01–1.21)	
		W	40/40	21/23			1.10 (0.97–1.24)	
		Y	40/40	22/22			1.00 (1.00–1.00)	
Seroprotection (defined as hSBA titer ≥1:8) at 13 months (12 months for MenACWY-CRM) after last dose								
Pfizer CT (NCT04440176), 2020, and Pfizer	11–14 years for NCT04440176	A	102/126	42/59	1 dose of MenABCWY	1 dose of MenACWY-CRM	1.14 (0.95–1.37)	Not serious
		C	92/127	32/62			1.40 (1.08–1.83)	

CT (NCT03135834), 2017	and 10–25 years for NCT03135834; both groups ACWY naive	W	125/128	52/62			1.16 (1.04–1.30)	
		Y	122/126	61/62			0.98 (0.94–1.03)	

[a] Seroprotection analyses are staggered for ACWY comparisons with the single dose MenACWY-CRM group starting 6 months after the 2 dose MenABCWY group (e.g., 18 months after the single dose of MenACWY-CRM versus 12 months after the 2 doses of MenABCWY). Seroprotection for the MenB component analyses is not staggered.
[b] Serogroup B primed was not assessed.

Table 3c: Summary of Studies Reporting Serious Adverse Events[a] — PICOs 1, 2, and 3

Author, pub year	Age or other characteristic	Type of event	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	Effect estimate — RR (95% CI)	Study limitations (risk of bias)
Pfizer CT (NCT04440163), 2020	10–25 years	All serious adverse events (SAE) during vaccination phase[b]	7/1763[c]	0/649	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) and MenB-FHbp (2 doses 6 months apart)	5.53 (0.32–96.64)	Not serious
Pfizer CT (NCT04440176), 2020[d]	11–14 years	All SAEs during vaccination phase	0/146	N/A	MenABCWY (2 doses 12 months apart)	N/A	N/A	Not serious
Pfizer CT (NCT03135834), 2017	10–25 years	All SAEs during primary vaccination phase	6/543[e]	8/1057	MenABCWY 2 dose primary series (6 months apart)	MenACWY-CRM 1 dose + MenB-FHbp 2 doses primary series (6 months apart)	1.46 (0.51–4.19)	Not serious

Pfizer CT (NCT03135834), 2017	10–25 years	All SAEs during booster vaccination phase	0/144	1/96	MenABCWY 2 dose primary series (6 months apart) followed by 1 dose booster at 54 months	MenACWY-CRM 1 dose + MenB-FHbp 2 dose primary series (6 months apart) followed by 1 dose booster at 54 months	0.22 (0.01–5.42)	Not serious

[a] Serious adverse events were any undesirable experience associated with vaccination in which the patient outcome was death, was life-threatening, required or prolonged hospitalization, caused disability or permanent damage, was a congenital anomaly/birth defect, or was another serious or important medical events as defined by Pfizer.[5]

[b] Vaccination phase refers to the time from the first study vaccination visit through 1 month after the last study vaccination.

[c] Nine SAEs occurred in 7 patients: *Salmonella* gastroenteritis (1 patient), depression (1 patient), anxiety (1 patient), suicide attempt (1 patient), postural orthostatic tachycardia syndrome (1 patient), dyspnea (1 patient), head injury due to motor vehicle accident (1 patient), traumatic spinal cord injury (1 patient), and depression with suicidal ideation (1 patient).

[d] Not included in GRADE table 4 given no comparison group.

[e] Eight SAEs occurred in 6 patients: cyst (1 patient), tendon injury (1 patient), dyskinesia (1 patient), migraine with aura (1 patient), aggression (1 patient), conversion disorder (1 patient), and suicidal ideation (2 patients).

Table 3d: Summary of Studies Reporting Non-Serious Adverse Events[a] — PICOs 1, 2, and 3

Author, pub year	Age or other characteristic	Type of event	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	Effect estimate — RR (95% CI)	Study limitations (risk of bias)
Pfizer CT (NCT04440163), 2020	10–25 years	All nonserious adverse events (AEs) during vaccination phase[b]	361/1763	132/649	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) and MenB-FHbp (2 doses 6 months apart)	1.00 (0.84–1.20)	Not serious
Pfizer CT (NCT04440176), 2020	11–14 years	All nonserious AEs during vaccination phase	51/146	N/A	MenABCWY (2 doses 12 months apart)	None	N/A	Not serious
Pfizer CT (NCT03135834), 2017	10–25 years	All nonserious AEs during primary vaccination phase	207/543	422/1057	MenABCWY 2 dose primary series (6 months apart)	MenACWY-CRM 1 dose + MenB-FHbp 2 dose primary series (6 months apart)	0.95 (0.84–1.09)	Not serious

Pfizer CT (NCT03135834), 2017	10–25 years	All AEs during booster vaccination phase	17/144	14/96	MenABCWY 2 dose primary series (6 months apart) followed by 1 dose booster at 54 months	MenACWY-CRM 1 dose + MenB-FHbp 2 dose primary series (6 months apart) followed by 1 dose booster at 54 months	0.81 (0.42–1.56)	Not serious

[a] Nonserious adverse events included all adverse events during the vaccination phase except for serious adverse events. As defined by Pfizer, all adverse events included serious adverse events, nonserious adverse events, medically attended events (nonserious adverse events that resulted in evaluation at a medical facility), and newly diagnosed chronic medical conditions (a disease or medical condition, not previously identified, that is expected to be persistent or is otherwise long-lasting in its effects).

[b] Vaccination phase refers to the time from the first study vaccination visit through 1 month after the last study vaccination.

Table 4: GRADE Summary of Findings for Healthy Persons — PICOs 1, 2, and 3

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pfizer MenABCWY	MenACWY and MenB	Relative (95% CI)	Absolute (95% CI)		
Short-term immunity for MenACWY (follow-up: 1 month)												
1	Randomized trials	Not serious	Not serious	Serious[a]	Not serious	None	In naïve participants, short-term immunity increases slightly for serogroups A, C, W, and Y at 1 month after 1 dose of MenABCWY versus 1 dose of MenACWY-CRM: Serogroup A (n=753), RR of 1.02 (95% CI: 0.99–1.05) Serogroup C (n=753), RR: 1.20 (95% CI: 1.05–1.38) Serogroup W (n=736), RR 1.09 (95% CI: 0.99–1.19) Serogroup Y (n=742), RR 1.16 (95% CI: 1.06–1.27)				Moderate	Critical

							In primed participants, little or no difference was observed in short-term immunity for serogroups A, C, W, and Y at 1 month after 1 dose of MenABCWY versus 1 dose of MenACWY-CRM: Serogroup A (n=666), RR of 0.98 (95% CI: 0.95–1.01) Serogroup C (n=665), RR: 0.99 (95% CI: 0.95–1.03) Serogroup W (n=650), RR 1.01 (95% CI: 0.98–1.04) Serogroup Y (n=665), RR 1.01 (95% CI: 0.97–1.05)					
Short-term immunity for MenB (follow-up: 1 month)												
1	Randomized trials	Not serious	Not serious	Serious[a]	Not serious	None	591/755 (78.3%)[b]	263/419 (62.8%)[b]	RR 1.25 (1.15 to 1.36)	15,692 more per 100,000 (from 9,415 to 22,597 more)	Moderate	Critical
Persistent immunity for MenACWY (follow-up: 48 months)												
1	Randomized trials	Not serious	Not serious	Very serious[a,c]	Not serious	None	In naïve participants, seroprotection probably increases for serogroups A, C, W, and Y at 48 months after 2 doses of MenABCWY versus 54 months after 1 dose of MenACWY-CRM: Serogroup A (n=112), RR of 1.29 (95% CI: 1.00–1.67) Serogroup C (n=113), RR: 1.63 (95% CI: 1.06–2.49) Serogroup W (n=111), RR 1.29 (95% CI: 1.05–1.59) Serogroup Y (n=113), RR 1.05 (95% CI: 0.98–1.12)				Low	Important

							In primed participants, little or no difference was observed in seroprotection for serogroups A, C, W, and Y at 48 months after 2 doses of MenABCWY versus 54 months after 1 dose of MenACWY-CRM: Serogroup A (n=63), RR of 1.00 (95% CI: 1.00–1.00) Serogroup C (n=134), RR: 1.10 (95% CI: 1.01–1.21) Serogroup W (n=63), RR 1.10 (95% CI: 0.97–1.24) Serogroup Y (n=62), RR 1.00 (95% CI: 1.00–1.00)				
Persistent immunity for MenB (follow-up: 48 months)												
1	Randomized trials	Not serious	Not serious	Serious[a]	Not serious	None	In naïve participants, little or no difference was observed in seroprotection for serogroup B at 48 months after 2 doses of MenABCWY versus 48 months after 2 doses of MenB-FHbp: Serogroup B (A22) (n=233), RR of 0.88 (95% CI: 0.59–1.31) Serogroup B (A56) (n=243), RR: 1.17 (95% CI: 0.80–1.70) Serogroup B (B24) (n=243), RR 1.38 (95% CI: 0.93–2.04) Serogroup B (B44) (n=247), RR 1.13 (95% CI: 0.64–1.98)				Moderate	Important
Serious Adverse Events[d]												
2	Randomized trials	Not serious	Not serious	Serious[e]	Serious[f]	None	13/2306 (0.6%)	8/1706 (0.5%)	RR 1.20 (0.50 to 2.89)	94 more per 100,000 (from 234 fewer to 886 more)	Low	Critical
Non-Serious Adverse Events[d]												

2	Randomized trials	Not serious	Not serious	Serious[e]	Serious[g]	None	568/2306 (24.6%)	554/1706 (32.5%)	RR 0.76 (0.69 to 0.84)	7,794 fewer per 100,000 (from 10,067 fewer to 5,196 fewer)	, Low	Important

[a] hSBA titers are the established correlate of protection for serogroup C meningococcal disease. This correlation is assumed to extend to other serogroups, but direct evidence for these serogroups is limited.[6]

[b] Calculated based on serogroup B composite data.

[c] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM. Comparisons also were staggered by 6 months.

[d] Following primary vaccination.

[e] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM plus 2 doses of MenB-FHbp.

[f] Downgraded because the relative effect confidence intervals are wide.

[g] Downgraded because the absolute effect confidence intervals are wide.

Table 4: GRADE Summary of Findings for Persons at Increased Risk due to Underlying Medical Conditions — PICOs 1, 2, and 3

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Pfizer MenABCWY	MenACWY and MenB	Relative (95% CI)	Absolute (95% CI)		
Short-term immunity for MenACWY (follow-up: 1 month)												
1	Randomized trials	Not serious	Not serious	Very serious[a,b]	Not serious	None	In naïve participants, short-term immunity increases slightly for serogroups A, C, W, and Y at 1 month after 1 dose of MenABCWY versus 1 dose of MenACWY-CRM: Serogroup A (n=753), RR of 1.02 (95% CI: 0.99–1.05) Serogroup C (n=753), RR: 1.20 (95% CI: 1.05–1.38) Serogroup W (n=736), RR 1.09 (95% CI: 0.99–1.19) Serogroup Y (n=742), RR 1.16 (95% CI: 1.06–1.27) In primed participants, little or no difference was observed in short-term immunity for serogroups A, C, W, and Y at 1 month after 1 dose of MenABCWY versus 1 dose of MenACWY-CRM:				Low	Critical

							Serogroup A (n=666), RR of 0.98 (95% CI: 0.95–1.01) Serogroup C (n=665), RR: 0.99 (95% CI: 0.95–1.03) Serogroup W (n=650), RR 1.01 (95% CI: 0.98–1.04) Serogroup Y (n=665), RR 1.01 (95% CI: 0.97–1.05)					
Short-term immunity for MenB (follow-up: 1 month)												
1	Randomized trials	Not serious	Not serious	Very serious[a,b]	Not serious	None	591/755 (78.3%)[c]	263/419 (62.8%)[c]	RR 1.25 (1.15 to 1.36)	15,692 more per 100,000 (from 9,415 to 22,597 more)	Low	Critical
Persistent immunity for MenACWY (follow-up: 48 months)												
1	Randomized trials	Not serious	Not serious	Very serious[a,b,d]	Not serious	None	In naïve participants, seroprotection probably increases for serogroups A, C, W, and Y at 48 months after 2 doses of MenABCWY versus 54 months after 1 dose of MenACWY-CRM: Serogroup A (n=112), RR of 1.29 (95% CI: 1.00–1.67) Serogroup C (n=113), RR: 1.63 (95% CI: 1.06–2.49) Serogroup W (n=111), RR 1.29 (95% CI: 1.05–1.59) Serogroup Y (n=113), RR 1.05 (95% CI: 0.98–1.12) In primed participants, little or no difference was observed in seroprotection for serogroups A, C, W, and Y at 48 months after 2 doses of MenABCWY versus 54 months after 1 dose of MenACWY-CRM: Serogroup A (n=63), RR of 1.00 (95% CI: 1.00–1.00) Serogroup C (n=134), RR: 1.10 (95% CI: 1.01–1.21) Serogroup W (n=63), RR 1.10 (95% CI: 0.97–1.24) Serogroup Y (n=62), RR 1.00 (95% CI: 1.00–1.00)				Low	Important

Persistent immunity for MenB (follow-up: 48 months)												
1	Randomized trials	Not serious	Not serious	Very serious[a,b]	Not serious	None	In naïve participants, little or no difference was observed in seroprotection for serogroup B at 48 months after 2 doses of MenABCWY versus 48 months after 2 doses of MenB-FHbp: Serogroup B (A22) (n=233), RR of 0.88 (95% CI: 0.59–1.31) Serogroup B (A56) (n=243), RR: 1.17 (95% CI: 0.80–1.70) Serogroup B (B24) (n=243), RR 1.38 (95% CI: 0.93–2.04) Serogroup B (B44) (n=247), RR 1.13 (95% CI: 0.64–1.98)				Low	Important
Serious Adverse Events[e]												
2	Randomized trials	Not serious	Not serious	Very serious[a,f]	Serious[g]	None	13/2306 (0.6%)	8/1706 (0.5%)	RR 1.20 (0.50 to 2.89)	94 more per 100,000 (from 234 fewer to 886 more)	Very low	Critical
Non-Serious Adverse Events[e]												
2	Randomized trials	Not serious	Not serious	Serious[a,f]	Serious[h]	None	568/2306 (24.6%)	554/1706 (32.5%)	RR 0.76 (0.69 to 0.84)	7,794 fewer per 100,000 (from 10,067 fewer to 5,196 fewer)	Very low	Important

[a] Clinical trials did not include patients at increased risk for invasive disease.

[b] hSBA titers are the established correlate of protection for serogroup C meningococcal disease. This correlation is assumed to extend to other serogroups, but direct evidence for these serogroups is limited.[6]

[c] Calculated based on serogroup B composite data.

[d] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM. Comparisons also were staggered by 6 months.

[e] Following primary vaccination.

[f] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM plus 2 doses of MenB-FHbp.

[g]Downgraded because the relative effect confidence intervals are wide.

[h] Downgraded because the absolute effect confidence intervals are wide.

Table 5: Summary of Evidence, PICO 1

Outcome	Importance	Included in Evidence Profile	Certainty for Healthy Individuals	Certainty for Individuals at Increased Risk
Meningococcal disease caused by serogroups A, B, C, W, and Y	Critical	No	–	–
Short-term immunity	Critical	Yes	Moderate	Low
Persistent immunity	Important	Yes	Low	Low
Interference with other recommended vaccines administered concurrently	Important	No	–	–
Serious adverse events	Critical	Yes	Low	Very low
Non-serious adverse events	Important	Yes	Low	Very low

Table 5: Summary of Evidence, PICO 2

Outcome	Importance	Included in Evidence Profile	Certainty for Healthy Individuals	Certainty for Individuals at Increased Risk
Meningococcal disease caused by serogroups A, B, C, W, and Y	Critical	No	–	–
Short-term immunity	Critical	Yes	Moderate	Low
Persistent immunity	Important	Yes	Low	Low

Interference with other recommended vaccines administered concurrently	Important	No	–	–
Serious adverse events	Critical	Yes	Low	Very low
Non-serious adverse events	Important	Yes	Low	Very low

Table 5: Summary of Evidence, PICO 3

Outcome	Importance	Included in Evidence Profile	Certainty for Healthy Individuals	Certainty for Individuals at Increased Risk
Meningococcal disease caused by serogroups A, B, C, W, and Y	Critical	No	–	–
Short-term immunity	Critical	Yes	Moderate	Low
Persistent immunity	Important	Yes	Moderate	Low
Interference with other recommended vaccines administered concurrently	Important	No	–	–
Serious adverse events	Critical	Yes	Low	Very low
Non-serious adverse events	Important	Yes	Low	Very low

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Appendix 1: Studies Included in Review of Evidence

Author, Year	Study Design	Country	Age	Number of Participants	Number Intervention	Number Comparison	Data Sources
Pfizer (NCT04440163), 2020[2]	RCT	US, Czech R., Denmark, Hungary, Poland	10–25 years	2412	1763	649	Clinicaltrials.gov, Pfizer WG and ACIP presentations, Pfizer correspondence, Pfizer preliminary results presentations
Pfizer (NCT03135834), 2017[3]	RCT	US, Czech R., Finland, Poland	10–25 years	1600	543	1057	
Pfizer (NCT04440176), 2020[4]	RCT	US	11–14 years	294	294	N/A	

Appendix 2: Search Strategies

Database	Search terms	Records

Medline, Embase, Global Health, CINAHL, Cochrane, Scopus, and clinicaltrials.gov	meningococcal pentavalent, pentavalent meningococcal, Pfizer pentavalent meningococcal, MenABCWY, Pfizer MenABCWY, pentavalent MenABCWY, ABCWY, MenABCWY meningococcal, Neisseria meningitidis group A, B, C, W, and Y, Neisseria meningitidis A, B, C, W, and Y, Neisseria meningitidis pentavalent, bivalent RLP2086-containing pentavalent, NCT03135834, B1971057, NCT04440163, C3511001, NCT04440176, C3511004, and “vaccin*”	43