GRADE/Evidence to Recommendations Framework (EtR) for GSK Pentavalent (MenABCWY) Vaccine

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October 24, 2024

Meningococcal Vaccine Recommendations

- Routine schedule
  - One MenACWY* dose at age 11–12 years and a booster at age 16 years
  - Two MenB** doses at age 16–23 years (shared clinical decision-making [SCDM])
    - Preferred age range: 16–18 years

- Increased risk, MenACWY*
  - Asplenia, complement deficiency, complement inhibitor use, and HIV infection
  - Some microbiologists
  - Exposure during an outbreak
  - Travel to hyperendemic areas
  - First-year college students (if not previously vaccinated at age ≥16 years)

- Increased risk, MenB**
  - Asplenia, complement deficiency, and complement inhibitor use
  - Some microbiologists
  - Exposure during an outbreak

*MenACWY vaccines *are* interchangeable; **MenB vaccines *are not* interchangeable

Pentavalent MenABCWY Vaccines

- Two new MenABCWY vaccines:
  - Pfizer (Penbraya, ACIP vote October 2023)
  - GSK (ACIP vote anticipated February 2025)

- Each vaccine is a combination of an existing:
  - MenACWY vaccine
  - *and*
  - MenB vaccine

- Each vaccine assessed separately by Work Group
  - Lack of data directly comparing Pfizer and GSK Pentavalent vaccines

Pfizer and GSK MenABCWY Vaccines

	Pfizer (Penbraya)	GSK*
ACWY component	Nimenrix (not licensed in U.S.)	Menveo
B component	Trumenba	Bexsero
Schedule	2 doses, 6 months apart	2 doses, 6 months apart*
Age	10–25 years	10–25 years*

*Vaccine not yet licensed in U.S. and this slide represents anticipated schedule and age indications

Policy Questions

PICO 1:

- Should the GSK pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines at the same visit?
  - For example, 16 year-olds*

PICO 2:

- Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?
  - For example, 11–12 year-olds

PICO 3:

- Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenB only?
  - For example, during a serogroup B outbreak

*16 year-olds who decide to receive the MenB vaccine based on shared clinical decision-making

Combined Policy and PICO Questions

Policy Question	Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY and MenB, MenACWY only, or MenB only?
Population	All individuals aged ≥10 years currently recommended to receive MenACWY+MenB, MenACWY, or MenB vaccine
Intervention	Vaccination with the pentavalent vaccine
Comparison	Vaccination with currently licensed MenACWY+MenB, MenACWY, or MenB vaccine
Outcomes	• Meningococcal 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

Outcomes Table

Outcome	Importance*	Included in Evidence Profile
Meningococcal disease caused by serogroups A, B, C, W, and Y	Critical	Yes
Persistent immunity	Important	Yes
Short-term immunity	Critical	Yes
Interference with other recommended vaccines administered concurrently	Important	Yes
Serious adverse events	Critical	Yes
Non-serious adverse events	Important	Yes

*Three options: critical, important but not critical, of limited importance for decision making

How PICOs Translate into Schedule Options for Healthy Adolescents

Options	Dose at age 11—12 years	Dose at age 16 years	Dose at age 16 years
Standard of care (MenACWY only)	Q	Q	-
Standard of care (MenACWY + MenB)	Q	Q+B	B
PICO 1 (MenABCWY as option for MenACWY + MenB)	Q	P	B
PICO 2 (MenABCWY as option for MenACWY)	P	P	B
PICO 3 (MenABCWY as option for MenB)	Q	P	P
Combination of all 3 PICOs	P	P	P

Legend
Q = MenACWY (quadrivalent)
B = MenB
P = MenABCWY (pentavalent)

EtR Domain	Question
Public health problem	Is invasive meningococcal disease a problem of public health importance?
Benefits and harms	How substantial are the *desirable* anticipated effects?
	How substantial are the *undesirable* anticipated effects?
	Do the desirable anticipated effects outweigh the undesirable effects?
	What is the overall certainty of the evidence for the critical outcomes?
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?
	Is there important variability in how patients value the outcome?
Acceptability	Is the intervention acceptable to key stakeholders?
Resource use	Is the intervention a reasonable and efficient allocation of resources?
Equity	What would be the impact of the intervention on health equity?
Feasibility	Is the intervention feasible to implement?

Public health problem

Is invasive meningococcal disease a problem of public health importance?

Meningococcal Disease

- Most often presents as meningitis or bacteremia
- Progresses rapidly
- 10–15% of cases are fatal (even with appropriate antibiotic therapy)
- ~20% of survivors experience long-term sequelae
  - Cognitive deficits
  - Hearing loss
  - Limb amputations

Public Health Problem

- Is invasive meningococcal disease a problem of public health importance?

	No	Probably no	Probably yes	Yes	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY				X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB				X		
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY				X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB				X		

Grey area = previous determinations for Pfizer pentavalent vaccine

Benefits and harms

- How substantial are the desirable anticipated effects?
- How substantial are the undesirable anticipated effects?
- Do the desirable effects outweigh the undesirable effects?

Studies Included in Review of Evidence

Study ID(s)	Location(s)	Study Design	Phase	Blinding	Population	Author, year or Study ID	Period
NCT01210885 NCT01367158 NCT02451514	Chile, Colombia, Panama	RCT	II	Observer-blind	Healthy, immuno-naïve individuals aged 11-18 years	Saez-Llorens 2015a	Dec 2010—Jul 2011
						~~Saez-Llorens 2015b~~	~~Jul 2011—Jul 2012~~
				~~Open-label*~~	~~Prior participants + individuals w/o meningococcal vaccine history~~	~~Saez-Llorens 2018~~	~~Jun 2015—Dec 2015~~
NCT01272180 NCT01992536	Poland, USA	RCT	II	Observer-blind	Healthy, immuno-naïve individuals aged 10-25 years	Block 2015	Aug 2011—Sep 2012
						~~Szenborn 2018~~	~~Dec 2013—Apr 2015~~
NCT02140762 NCT02285777	USA	RCT	IIb	Observer-blind	Healthy, immuno-naïve individuals aged 10-18 years	Welsch 2018	May 2014—Jun 2015
NCT02212457 NCT02946386	Finland, Poland	RCT	IIb	Observer-blind	Healthy, immuno-naïve individuals aged 10-18 years	Vesikari 2021	Aug 2014—Mar 2016 Nov 2016—Feb 2018
NCT03587207	Czechia	RCT	II	Open-label	Healthy, immuno-naïve individuals aged 10-25 years	Beran 2021	Jul 2018—Dec 2018
NCT04502693	Australia, Canada, Czechia, Estonia, Finland, Turkey, USA	RCT	III	Observer-blind	Healthy individuals aged 10-25 years w/o history of meningococcal disease or vaccination	v72_72	Aug 2020—Sep 2022
NCT04707391	Argentina, Australia, Canada, USA	RCT	III	Observer-blind	Healthy individuals aged 15-25 years vaccinated with MenACWY ≥4 years prior and w/o history of meningococcal disease	MenABCWY_019	Jan 2021—Sep 2023

*This extension study did not randomize participants. All prior participants were given a single dose of MenABCWY, while all newly enrolled participants were given two doses of MenABCWY.

Short-term immunity one month after one dose

MenABCWY vs MenACWY

Short-Term Immunity After One Dose for Healthy Persons

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Short-term immunity vs MenACWY (follow-up: 1 month)							**Serogroup A**				Moderate	Critical
4[3]	Randomized trials	Not serious	Not serious	Serious[4]	Not serious	GSK funded	914	1,093	0.94 (0.86, 1.01)	5,437 fewer (11,705 fewer to 832 more)		
							Serogroup C					
							926	1,105	1.03 (0.97, 1.10)	2,726 more (2,545 fewer to 7,997 more)		
							Serogroup W					
							926	1,106	1.02 (1.00, 1.04)	1,930 more (314 to 3,546 more)		
							Serogroup Y					
							929	1,109	0.98 (0.93, 1.03)	1,930 fewer (6,528 fewer to 2,668 more)		

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented.
[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.
[3]Includes one study with concomitant administration of MenB; meta-analysis suggested no statistically significant subgroup differences.
[4]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. Goldschneider et al. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med. 1969;129(6):1307–26.

Short-Term Immunity After One Dose for Persons at Increased Risk

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Short-term immunity vs MenACWY (follow-up: 1 month)							**Serogroup A**				Low	Critical
4[3]	Randomized trials	Not serious	Not serious	Very serious[4,5]	Not serious	GSK funded	914	1,093	0.94 (0.86, 1.01)	5,437 fewer (11,705 fewer to 832 more)		
							Serogroup C					
							926	1,105	1.03 (0.97, 1.10)	2,726 more (2,545 fewer to 7,997 more)		
							Serogroup W					
							926	1,106	1.02 (1.00, 1.04)	1,930 more (314 to 3,546 more)		
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[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.
[3]Includes one study with concomitant administration of MenB; meta-analysis suggested no statistically significant subgroup differences.
[4]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. Goldschneider et al. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med. 1969;129(6):1307–26.
[5]Studies did not include persons at increased risk.

Short-term immunity one month after series completion

Two doses of MenABCWY vs two doses of MenB

Short-Term Immunity After Series* Completion for Healthy Persons

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Short-term immunity after series completion vs MenB series (follow-up: 1 month)							fHbp				Moderate	Critical
1	Randomized trials	Not serious	None[3]	Serious[4]	Not serious	GSK funded	738	707	1.01 (0.99, 1.04)	1,300 more (896 fewer to 3,496 more)		
							NadA					
							734	707	0.98 (0.96, 1.00)	1,800 fewer (3,526 to 74 fewer)		
							NHBA					
							738	711	0.98 (0.96,1.00)	2,200 fewer (4,110 to 290 fewer)		
							PorA					
							709	684	0.91 (0.86, 0.96)	7,300 fewer (11,560 to 3,040 fewer)		

*MenABCWY and MenB given on a 0,6 month schedule

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented.

[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.

[3]Only one study included, therefore results are consistent by default.

[4]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. Goldschneider et al. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med. 1969;129(6):1307–26.

Short-Term Immunity After Series* Completion for Persons at Increased Risk

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Short-term immunity after series completion vs MenB series (follow-up: 1 month)							fHbp				Low	Critical
1	Randomized trials	Not serious	None[3]	Very serious[4,5]	Not serious	GSK funded	738	707	1.01 (0.99, 1.04)	1,300 more (896 fewer to 3,496 more)		
							NadA					
							734	707	0.98 (0.96, 1.00)	1,800 fewer (3,526 to 74 fewer)		
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							738	711	0.98 (0.96,1.00)	2,200 fewer (4,110 to 290 fewer)		
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*MenABCWY and MenB given on a 0,6 month schedule

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented.

[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.

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[5]Studies did not include persons at increased risk.

Long-term immunity two years after series completion

Two doses of MenABCWY vs two doses of MenB

Long-Term Immunity After Series* Completion for Healthy Persons

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Long-term immunity after series completion vs MenACWY (follow-up: 2 years)												
0												
Long-term immunity after series completion vs MenB (follow-up: 2 years							fHbp				Low	Important
1	Randomized trials	Not serious	None[3]	Serious[4]	Serious[5]	GSK funded	70	119	1.46 (0.84, 2.54)	8,000 more (4,379 fewer to 20,379 more)		
							NadA					
							72	121	0.90 (0.77, 1.06)	8,000 fewer (20,228 fewer to 4,228 more)		
							NHBA					
							71	122	1.31 (0.86, 2.00)	9,000 more (4,770 fewer to 22,770 more)		
							PorA					
							71	121	1.17 (0.61, 2.22)	2,000 more (9,069 fewer to 13,069 more)		

*MenABCWY and MenB given on a 0,6 month schedule

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented.

[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.

[3]Only one study included, therefore results are consistent by default.

[4]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. Goldschneider et al. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med. 1969;129(6):1307–26.

[5]Based on both the precision of the relative and absolute effects and the relatively small sample size

Long-Term Immunity After Series* Completion for Persons at Increased Risk

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
Long-term immunity after series completion vs MenACWY (follow-up: 2 years)												
0												
Long-term immunity after series completion vs MenB (follow-up: 2 years							fHbp				Very low	Important
1	Randomized trials	Not serious	None[3]	Very serious[4,5]	Serious[6]	GSK funded	70	119	1.46 (0.84, 2.54)	8,000 more (4,379 fewer to 20,379 more)		
							NadA					
							72	121	0.90 (0.77, 1.06)	8,000 fewer (20,228 fewer to 4,228 more)		
							NHBA					
							71	122	1.31 (0.86, 2.00)	9,000 more (4,770 fewer to 22,770 more)		
							PorA					
							71	121	1.17 (0.61, 2.22)	2,000 more (9,069 fewer to 13,069 more)		

*MenABCWY and MenB given on a 0,6 month schedule

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented.

[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.

[3]Only one study included, therefore results are consistent by default.

[4]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. Goldschneider et al. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med. 1969;129(6):1307–26.

[5]Studies did not include persons at increased risk

[6]Based on both the precision of the relative and absolute effects and the relatively small sample size

Adverse events

Serious
Non-serious after one dose
Non-serious after ≥2 doses

Serious Adverse Events Assessed as Possibly Related to Vaccination, Regardless of Dosing Schedule

Study	Number			
	Pentavalent	MenACWY	MenB	MenACWY/MenB
Saez-Llorens 2015[1]	0	0	--	--
Block 2015	0	0	0	--
Welsch 2018	0	0	--	--
Vesikari 2021	2 (seizure, connective tissue disorder)	--	0	--
Beran 2021	0	0	1 (syncope)	0
v72_72[2]	1 (neuromyelitis optica)	1 (pyrexia)	1 (ulcerative colitis)	--
MenABCWY_019	0	0	--	--

[1]One related event during extension study in a recipient of a MenABCWY that contained ¼ of the usual OMV component
[2]These were reported as related to vaccination by investigators; however, they were not considered adverse drug reactions related to vaccination after GSK and independent evaluation

Serious Adverse Events Assessed as Related to Vaccination for Healthy Persons and Those at Increased Risk

Healthy Persons

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
7	Randomized trials	Not serious	Not serious	Not serious	Serious[3]	GSK funded	4,016 (0-2 events per study)	3,921 (0-2 events per study)	1.03 (0.30, 3.60)	6 fewer (150 fewer to 138 more)	Moderate	Critical

Persons at Increased Risk

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect (95% CI)	Absolute effect RD (95% CI) per 100,000		
7	Randomized trials	Not serious	Not serious	Serious[4]	Serious[3]	GSK funded	4,016 (0-2 events per study)	3,921 (0-2 events per study)	1.03 (0.30, 3.60)	6 fewer (150 fewer to 138 more)	Low	Critical

[1]If >1 study included, effects and confidence intervals derived from a random-effects meta-analysis are presented; if one study included, traditional Wald confidence intervals are presented
[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.
[3]Based on the precision of the relative effect
[4]Studies did not include persons at increased risk.

The apparent directional discrepancy between RR and RD is due to a continuity correction for the RR to adjust zeros

Non-Serious Adverse Events for Healthy Persons

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
After one dose												
4	Randomized trials	Not serious	vs MenB									
			Not serious	Not serious	Not serious	GSK funded	2,766	2,315	1.00 (0.98, 1.02)	106 more (1,434 fewer to 1,647 more)	High	Important
1			vs MenB/MenACWY									
			None[3]	Not serious	Serious[4]	GSK funded	100	204	0.93 (0.86, 1.00)	6,588 fewer (13,337 fewer to 161 more)	Moderate	Important
6			vs MenACWY									
			Not serious	Not serious	Serious[5]	GSK funded	2,683	1,190	1.97 (1.65, 2.36)	42,626 more (36,291 to 48,962 more)	Moderate	Important
After two or more doses												
2	Randomized trials	Not serious	vs MenB									
			Not serious	Not serious	Not serious	GSK funded	1,680	2,660	1.00 (0.98, 1.02)	135 more (1,837 fewer to 2,107 more)	High	Important
2			vs MenACWY									
			Not serious	Not serious	Serious[5]	GSK funded	1,935	779	2.19 (1.89, 2.54)	43,148 more (38,813 to 47,484 more)	Moderate	Important

[1]f >1 study included, effects and confidence intervals were derived from a random-effects meta-analysis; if one study included, effect and confidence intervals were derived using the Wald method
[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.
[3]Only one study included, therefore results are consistent by default.
[4]Based on the imprecision of the absolute effect and the relatively small sample size
[5]Based on the imprecision of the relative and absolute effects, despite the relatively large sample size.

Non-Serious Adverse Events for Persons at Increased Risk

Certainty assessment							No. of patients		Effect[1]		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations[2]	GSK MenABCWY	Comparator	Relative effect RR (95% CI)	Absolute effect RD (95% CI) per 100,000		
After one dose												
4	Randomized trials	Not serious	vs MenB									
			Not serious	Serious[3]	Not serious	GSK funded	2,766	2,315	1.00 (0.98, 1.02)	106 more (1,434 fewer to 1,647 more)	Moderate	Important
1			vs MenB/MenACWY									
			None[4]	Serious[3]	Serious[5]	GSK funded	100	204	0.93 (0.86, 1.00)	6,588 fewer (13,337 fewer to 161 more)	Low	Important
6			vs MenACWY									
			Not serious	Serious[3]	Serious[6]	GSK funded	2,683	1,190	1.97 (1.65, 2.36)	42,626 more (36,291 to 48,962 more)	Low	Important
After two or more doses												
2	Randomized trials	Not serious	vs MenB									
			Not serious	Serious[3]	Not serious	GSK funded	1,680	2,660	1.00 (0.98, 1.02)	135 more (1,837 fewer to 2,107 more)	Moderate	Important
2			vs MenACWY									
			Not serious	Serious[3]	Serious[6]	GSK funded	1,935	779	2.19 (1.89, 2.54)	43,148 more (38,813 to 47,484 more)	Low	Important

[1]f >1 study included, effects and confidence intervals were derived from a random-effects meta-analysis; if one study included, effect and confidence intervals were derived using the Wald method
[2]Includes potential conflicts of interest that are not factored into the grading of the certainty of evidence.
[3]Studies did not include persons at increased risk.
[4]Only one study included, therefore results are consistent by default.
[5]Based on the imprecision of the absolute effect and the relatively small sample size
[6]Based on the imprecision of the relative and absolute effects, despite the relatively large sample size.

Summary of Evidence

	PICO 1: Certainty		PICO 2: Certainty		PICO 3: Certainty	
Outcome	Healthy	Increased Risk	Healthy	Increased Risk	Healthy	Increased Risk
Critical outcomes						
Meningococcal disease caused by serogroups A, B, C, W, and Y	--	--	--	--	--	--
Short-term immunity	Moderate	Low	Moderate	Low	Moderate	Low
Serious adverse events	Moderate	Low	Moderate	Low	Moderate	Low
Important outcomes						
Interference with other recommended vaccines administered concurrently	--	--	--	--	--	--
Non-serious adverse events	Moderate	Low	Moderate	Low	Moderate	Low
Persistent immunity	Low**	Very low**	--	--	Low	Very low

*Three options: critical, important but not critical, of limited importance for decision making; **MenB only

Benefits and Harms

- How substantial are the <u>desirable</u> anticipated effects?

	Minimal	Small	Moderate	Large	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB		X				
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X	X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X					
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB		X				
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X				
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X				

Grey area = previous determinations for Pfizer pentavalent vaccine

Benefits and Harms

- How substantial are the undesirable anticipated effects?

	Minimal	Small	Moderate	Large	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB		X				
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X				
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X	X				
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB	X					
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X				
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X					

Grey area = previous determinations for Pfizer pentavalent vaccine

Benefits and Harms

- Do the desirable effects outweigh the undesirable effects?

	Favors intervention	Favors comparison	Favors both	Favors neither	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB	X					
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X	X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X	X				
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB	X					
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X	X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X	X	X			

Grey area = previous determinations for Pfizer pentavalent vaccine

Benefits and Harms: Short-term Immunity

- What is the overall certainty of this evidence for the critical outcomes?

	No studies found	Very low	Low	Moderate	High
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X	
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X	

Grey area = previous determinations for Pfizer pentavalent vaccine

Benefits and Harms: Serious Adverse Events

- What is the overall certainty of this evidence for the critical outcomes?

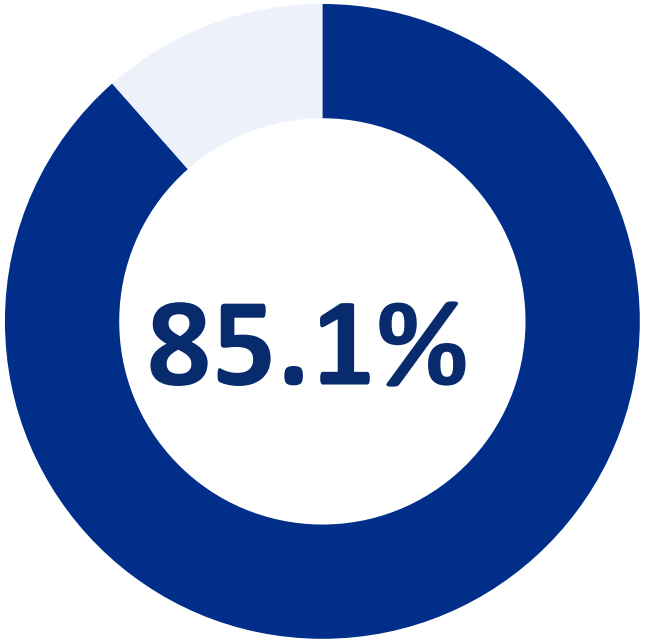
	No studies found	Very low	Low	Moderate	High
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB		X	X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X	X		
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X	

Grey area = previous determinations for Pfizer pentavalent vaccine

Values

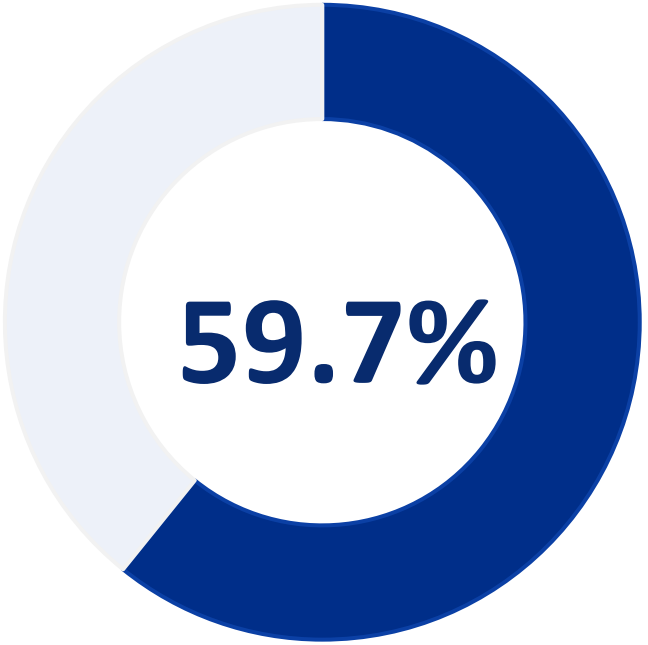
- Does the target population feel that the desirable effects are large relative to the undesirable effects?
- Is there important uncertainty about or variability in how much people value the main outcome?

MenACWY Coverage among Adolescents (2023)



≥ 1 dose

among 13 yr olds

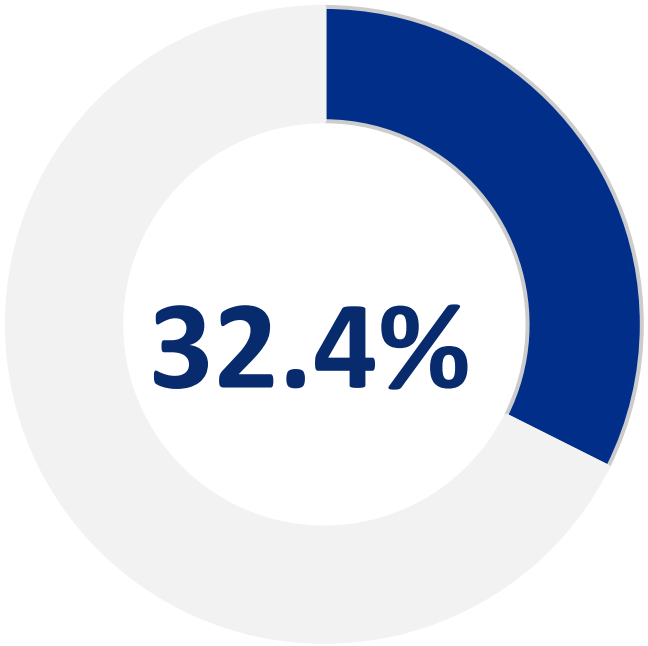


≥ 2 doses

among 17 yr olds

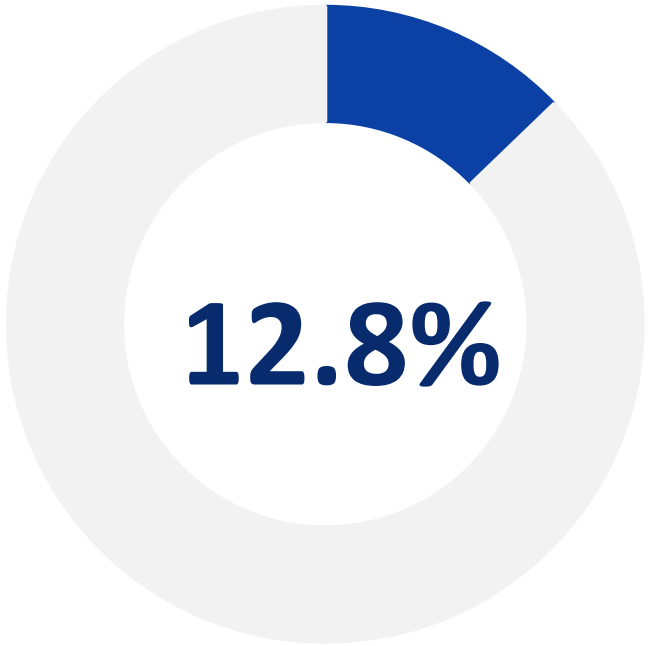
Pingali C et al. MMWR Morb Mortal Wkly Rep 2024.

MenB Coverage among Adolescents (2023)



≥ 1 dose

among 17 yr olds



≥ 2 doses

among 17 yr olds

Pingali C et al. MMWR Morb Mortal Wkly Rep 2024.

Values

- Most adolescents and parents prefer a simplified meningococcal vaccine schedule (with fewer injections and fewer visits):
  - 89.6% of 16–23 year-olds
  - 69.1% of parents

Begum S et al. Infect Dis Ther 2024 (note GSK affiliation)

Values

- Does the target population feel that the desirable effects are large relative to the undesirable effects?

	No	Probably no	Probably yes	Yes	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X			
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X			X
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X		X

Grey area = previous determinations for Pfizer pentavalent vaccine

Values

- Is there important uncertainty about or variability in how much people value the main outcome?

	Important uncertainty or variability	Probably important uncertainty or variability	Probably not important uncertainty or variability	No important uncertainty or variability	No known undesirable outcomes
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X			
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X	X		

Grey area = previous determinations for Pfizer pentavalent vaccine

Acceptability

- Is the intervention acceptable to key stakeholders?

Combination Vaccines

- CDC's **General Best Practice Guidance for Immunization** and **American Academy of Pediatrics Red Book** both state a general preference for combination vaccines over separate injections of equivalent component vaccines[1,2]

Potential advantages	Potential disadvantages
• Improved vaccine coverage rates • Timely catch-up immunizations • Reduced shipping and stocking costs • Reduced costs for extra health care visits necessitated by deferral of vaccination • Facilitation of additional new vaccines into vaccination programs	• Adverse events that might occur more frequently with combination vaccines than with individual components • Confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses • Extra doses of certain antigens in the combination product (MenB vaccine is more reactogenic than MenACWY vaccine)

[1]General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
[2]American Academy of Pediatrics. Red Book 2024-27 Report of the Committee on Infectious Diseases. 33rd Edition.

Preference for Fewer Injections

- Adolescents prefer fewer injections due to injection site discomfort
- Parents/caregivers prefer fewer injections to reduce number of physician visits
  - Parental work loss

Begum S., et al. OFID ppS515-6. IDWeek2023 (GSK affiliation).

Acceptability

- Is the intervention acceptable to key stakeholders?

	No	Probably no	Probably yes	Yes	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB						X
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X			
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X		

Grey area = previous determinations for Pfizer pentavalent vaccine

Resource use

- Is the intervention a reasonable and efficient allocation of resources?

Economic Analysis

- **PICO 1:** Q-P-B was found to be cost-saving relative to the current recommendation (vs. Q-Q-B-B).

- **PICO 2:** P-P-N could improve health outcomes, but costs $11.3 million per QALY saved (vs. Q-Q-N).

- **PICO 3:** Q-P-P is cost-saving compared to Q-Q-B-B.
Q-P-P is $4.5 million per QALY saved more than Q-P-B.

Resource Use

- Is the intervention a reasonable and efficient allocation of resources?

	No	Probably no	Probably yes	Yes	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X				
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X		
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY		X			X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB					X*	

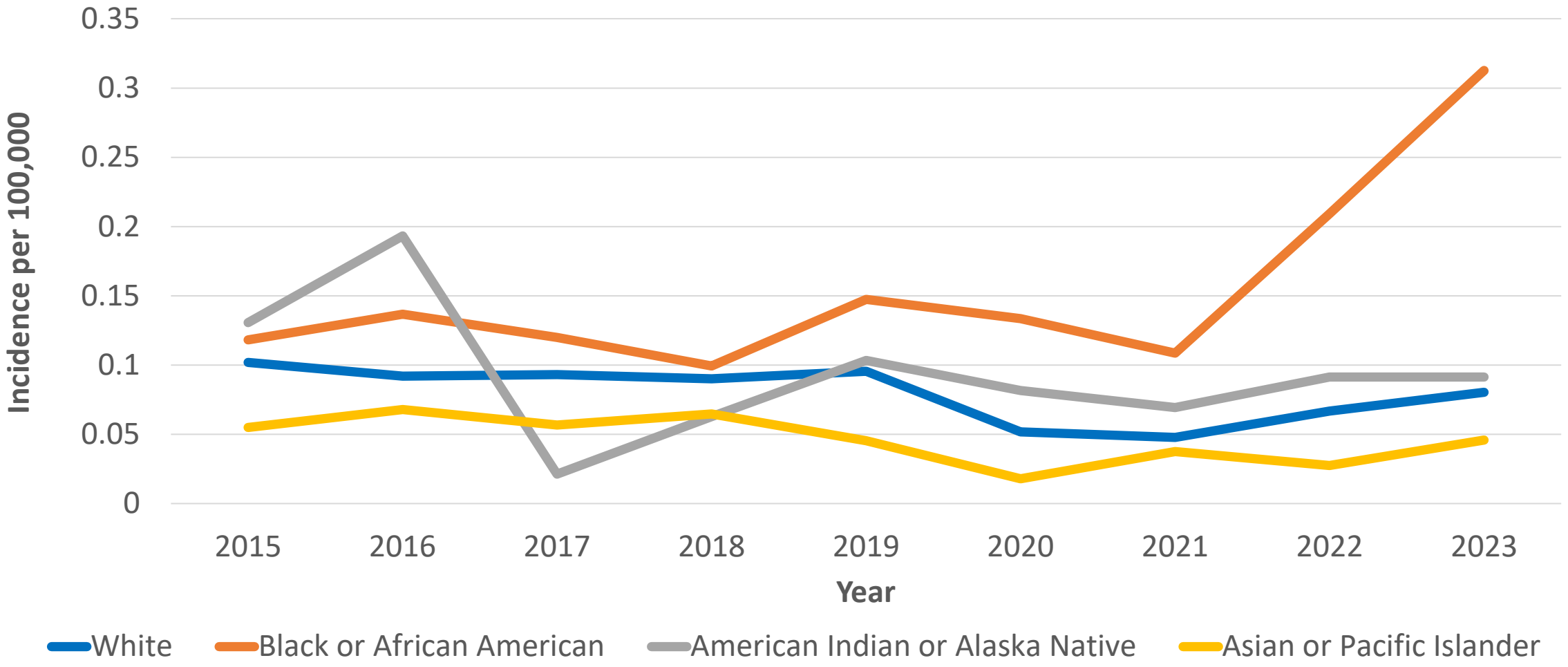
Grey area = previous determinations for Pfizer pentavalent vaccine

*WG sentiment varied from no to yes

Equity

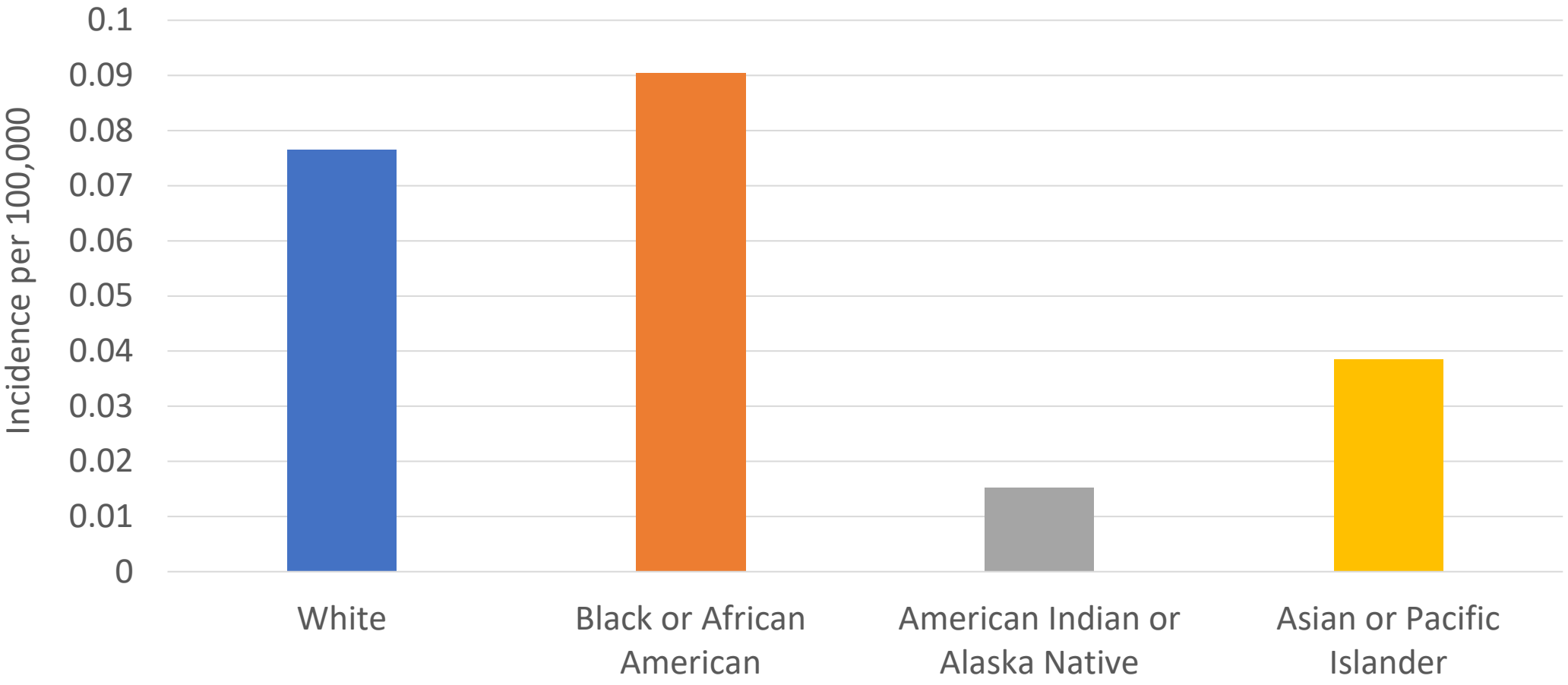
- What would be the impact on health equity?

Meningococcal Disease Incidence by Race—United States, 2015–2023*



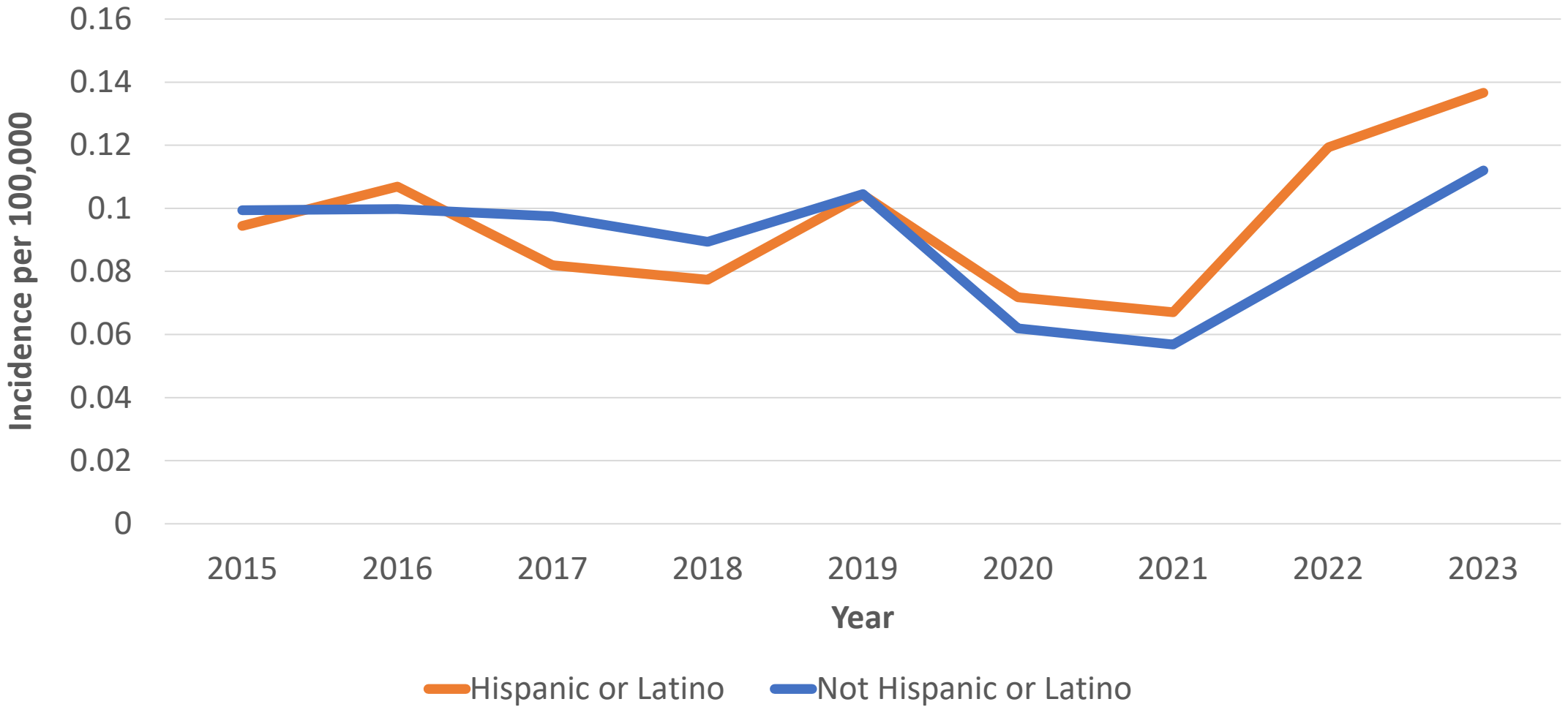
Source: NNDSS data with additional serogroup data from ABCs and state health departments. *2023 NNDSS data are preliminary.
Race is unknown for 5-12% of cases per year

Average Annual Meningococcal Disease Incidence by Race among 11–20 year olds—United States, 2015–2023*



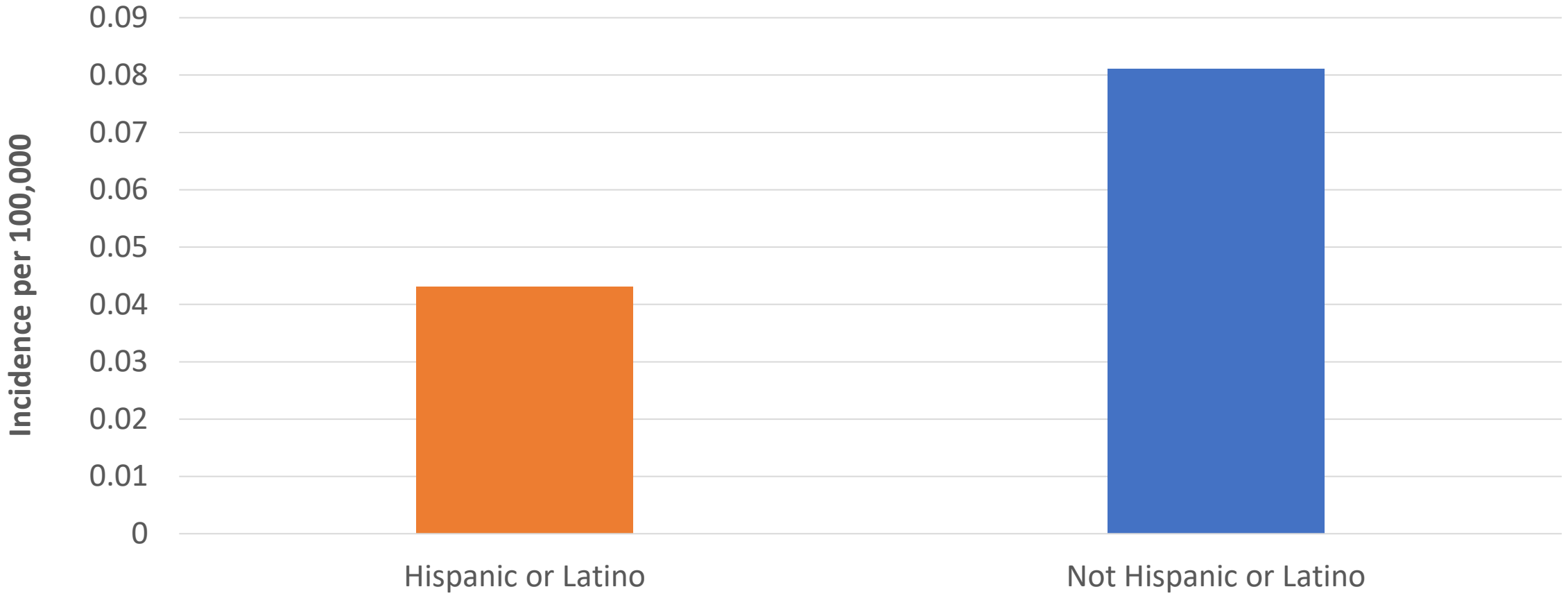
Source: NNDSS data with additional serogroup data from ABCs and state health departments. *2023 NNDSS data are preliminary.
Race is unknown for 6-15% of cases per year

Meningococcal Disease Incidence by Ethnicity — United States, 2015–2023*



Source: NNDSS data with additional serogroup data from ABCs and state health departments. *2023 NNDSS data are preliminary.
Ethnicity is unknown for 2-16% of cases per year

Average Annual Meningococcal Disease Incidence by Ethnicity among 11–20 year olds—United States, 2015–2023*



Source: NNDSS data with additional serogroup data from ABCs and state health departments. *2023 NNDSS data are preliminary.
Ethnicity is unknown for 3-27% of cases per year

MenB Vaccine Availability

- Counties with lower socioeconomic status (SES) had fewer MenB doses stocked

  - 20 doses/100 adolescents for low SES counties

    vs.

  - 28 doses/100 adolescents for high SES counties

Schley et al. BMC Publ Hlth 2024 (note: Pfizer affiliation)

Equity and Shared Clinical Decision-Making

- Provider or patient awareness of a SCDM recommendation is a pre-requisite for discussions with patients and could lead to health inequities
  - Only 51% of pediatricians and 31% of family physicians reported always or often discussing MenB vaccination
- Pentavalent vaccine could potentially reduce disparities among those who might be interested in MenB vaccination but who might not receive clinical care that includes discussion of MenB vaccine

Gidengil et al. Vaccine 2023; Kempe et al. Pediatrics 2018.

Lack of MenB Vaccine Interchangeability

- Lack of MenB vaccine interchangeability currently restricts existing MenABCWY vaccine use to patients of providers stocking Pfizer MenB vaccine products

Equity

- What would be the impact on health equity

	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X			X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY				X		X	X
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB							X
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X			
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY				X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB				X			

Grey area = previous determinations for Pfizer pentavalent vaccine

Feasibility

- Is the intervention feasible to implement?

Feasibility

- Challenges with insurance or financial burdens related to pentavalent vaccine not expected
- GSK pentavalent vaccine would provide additional option and may reduce number of doses for some people
- Lack of MenB vaccine interchangeability complicates stocking considerations

Feasibility

- Is the intervention feasible to implement?

	No	Probably no	Probably yes	Yes	Varies	Don't know
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB			X	X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB			X	X		
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB				X		
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY			X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB				X		

Grey area = previous determinations for Pfizer pentavalent vaccine

EtR Domain	Question	Work Group Determination – PICO 1	Work Group Determination – PICO 2	Work Group Determination – PICO 3
Public health problem	Is invasive meningococcal disease a problem of public health importance?	Yes	Yes	Yes
Benefits and harms	How substantial are the desirable anticipated effects?	Small	Small	Small
	How substantial are the undesirable anticipated effects?	Minimal	Small	Minimal
	Do the desirable anticipated effects outweigh the undesirable effects?	Favors intervention	Favors intervention/ comparison/both	Favors intervention/ comparison/both
	What is the overall certainty of evidence?	Low	Low	Low
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Yes	Probably yes	Probably yes/yes/ don't know
	Is there important variability in how patients value the outcome?	Probably not/no	Probably/probably not	Probably/probably not
Acceptability	Is the intervention acceptable to key stakeholders?	Yes	Probably yes	Probably yes/yes
Resource use	Is the intervention a reasonable and efficient allocation of resources?	Yes	Probably no/varies	Varies
Equity	What would be the impact of the intervention on health equity?	Probably increased	Probably increased/increased	Probably increased
Feasibility	Is the intervention feasible to implement?	Yes	Probably yes/yes	Yes

Balance of Consequences

	Undesirable consequences ***clearly outweigh*** desirable consequences in most settings	Undesirable consequences ***probably outweigh*** desirable consequences in most settings	The balance between desirable and undesirable consequences is ***closely balanced or uncertain***	Desirable consequences ***probably outweigh*** undesirable consequences in most settings	Desirable consequences ***clearly outweigh*** undesirable consequences in most settings	There is ***insufficient evidence*** to determine the balance of consequences
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB					X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	X				
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X	X	X		
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB					X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X		X	X		
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB		X	X	X	X	

Grey area = previous determinations for Pfizer pentavalent vaccine

Work Group Interpretation

- Is there sufficient information to move forward with a recommendation?

	Yes	No
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB	X	
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X	

Work Group Interpretation

	We ***do not*** recommend the intervention	We ***do*** recommend the intervention
PICO 1 (QPB vs. QQBB): MenABCWY vs. MenACWY + MenB		X
PICO 2 (PPB vs. QQBB or PP vs. QQ): MenABCWY vs. MenACWY	X	
PICO 3 (QPP vs. QQBB): MenABCWY vs. MenB	X	X

Comment Regarding Work Group Interpretation

- Several Work Group members noted that it would be important to harmonize recommendations between the GSK and Pfizer pentavalent vaccines
  - Unless there is a vaccine-specific reason to have a different recommendation

Next Steps

- An interim recommendation for the GSK vaccine could mirror the recommendation made for the Pfizer vaccine last year
  - Accept PICO 1, reject PICOs 2 and 3
- Recommendations for use of both pentavalent vaccines could then be revisited as part of future adolescent schedule deliberations if desired

Acknowledgements

- Avnika Amin
- Lucy McNamara
- Xiaoyu Dong
- Rebecca Morgan
- Doug Campos-Outcalt
- Noele Nelson
- Susan Hariri
- LeAnne Fox
- Jennifer Collins
- Amy Rubis

Thank you!

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