Evidence to Recommendations Framework: Pfizer's MenABCWY Vaccine

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June 23, 2023

Outline

- Overview of policy questions and PICOs
- Evidence to Recommendations framework
- Summary of findings
- WG proposed options

Pfizer MenABCWY Vaccine

- Comprised of Trumenba (serogroup B) and Nimenrix (serogroups ACWY)
  - Trumenba
    - Consists of two purified recombinant lipidated FHbp antigens, one from each FHbp subfamily (A and B)
    - Currently licensed and available in US (10–25 years)
  - Nimenrix
    - Meningococcal group A, C, W, and Y polysaccharide tetanus toxoid conjugate vaccine
    - Not licensed in US but used extensively in Europe and elsewhere for over a decade

- Clinical trial data
  - Assessed
    - Two doses (0,6 m and 0,12 m apart)
  - Studied 10 through 25 years of age
  - Both MenACWY primed and naïve subjects
  - Longer interval studies underway (not available in time for initial product licensure)

Policy Questions for 3 PICOs

- Should the pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines? (PICO 1)

- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only? (PICO 2)

- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only? (PICO 3)

GRADE Table 1: Combined Policy Question and PICO

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 or older 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 (as appropriate by PICO) • Short-term immunity • Persistent immunity • Interference with other recommended vaccines administered concurrently • Serious adverse events • Non-serious adverse events

Routine Schedule and Increased Risk Populations

- Routine schedule
  - One MenACWY dose at 11–12 years and a booster at 16 years
  - Two MenB doses at 16–18 years (shared clinical decision-making recommendation)

- Increased risk, MenACWY (vaccines are interchangeable)
  - Recommended for certain medical conditions
    - Asplenia, complement deficiency, complement inhibitor use, and HIV infection
  - Some microbiologists
  - Exposure during an outbreak
  - Travel to hyperendemic areas
  - First-year college students
  - Military recruits

- Increased risk, MenB (vaccines are <u>not</u> interchangeable)
  - Recommended for certain medical conditions
    - Asplenia, complement deficiency, and complement inhibitor use
  - Some microbiologists
  - Exposure during an outbreak

How PICOs Translate into Schedule Options for Healthy Adolescents

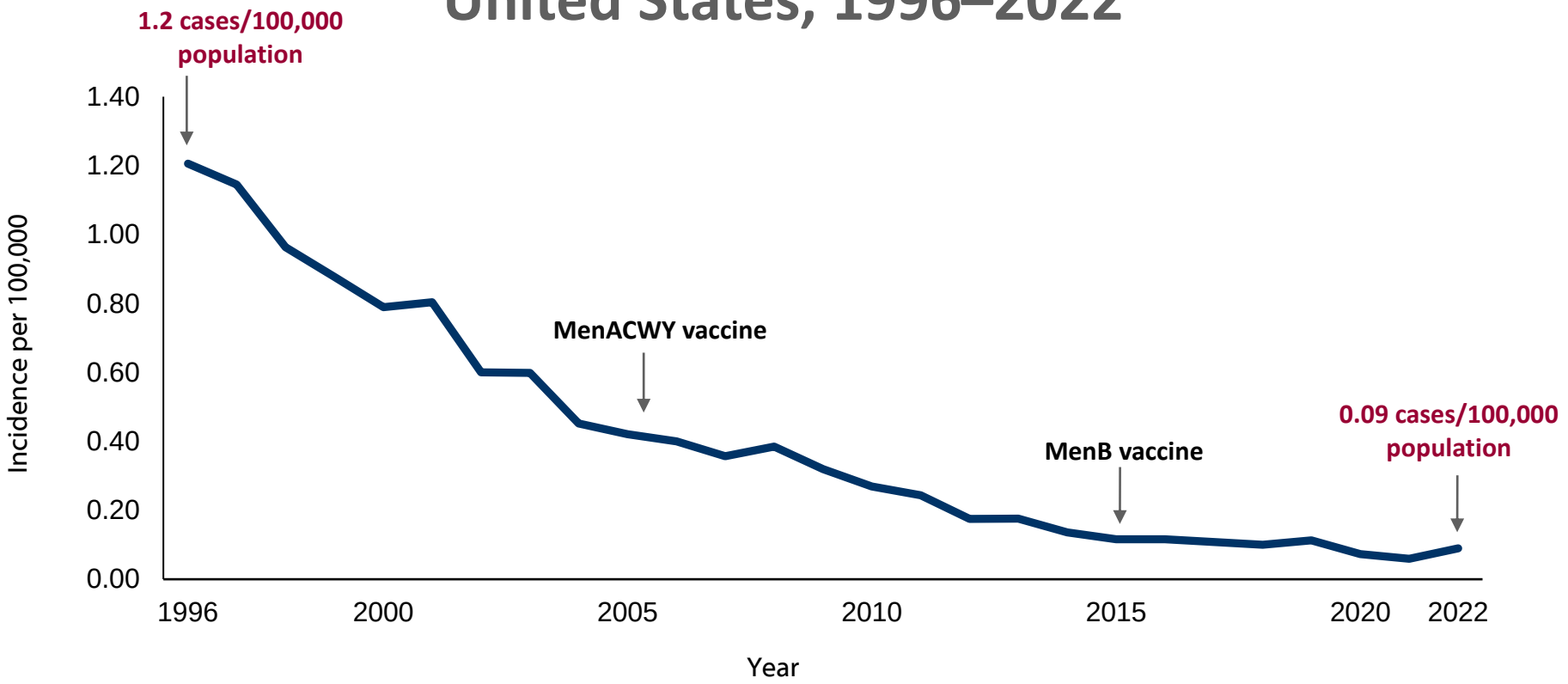
Options	11–12 year old dose	16 year old dose #1	16 year old dose #2
Standard of care (MenACWY only)	Q	Q	–
Standard of care (MenACWY + MenB)	Q	Q+B	B
PICO 1 (MenABCWY as option for MenACWY + MenB)	Q	P	B
PICO 2 (MenABCWY as option for MenACWY)	P	P	B
PICO 3 (MenABCWY as option for MenB)	Q	P	P
Combination of all 3 PICOs	P	P	P

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

Public Health Problem

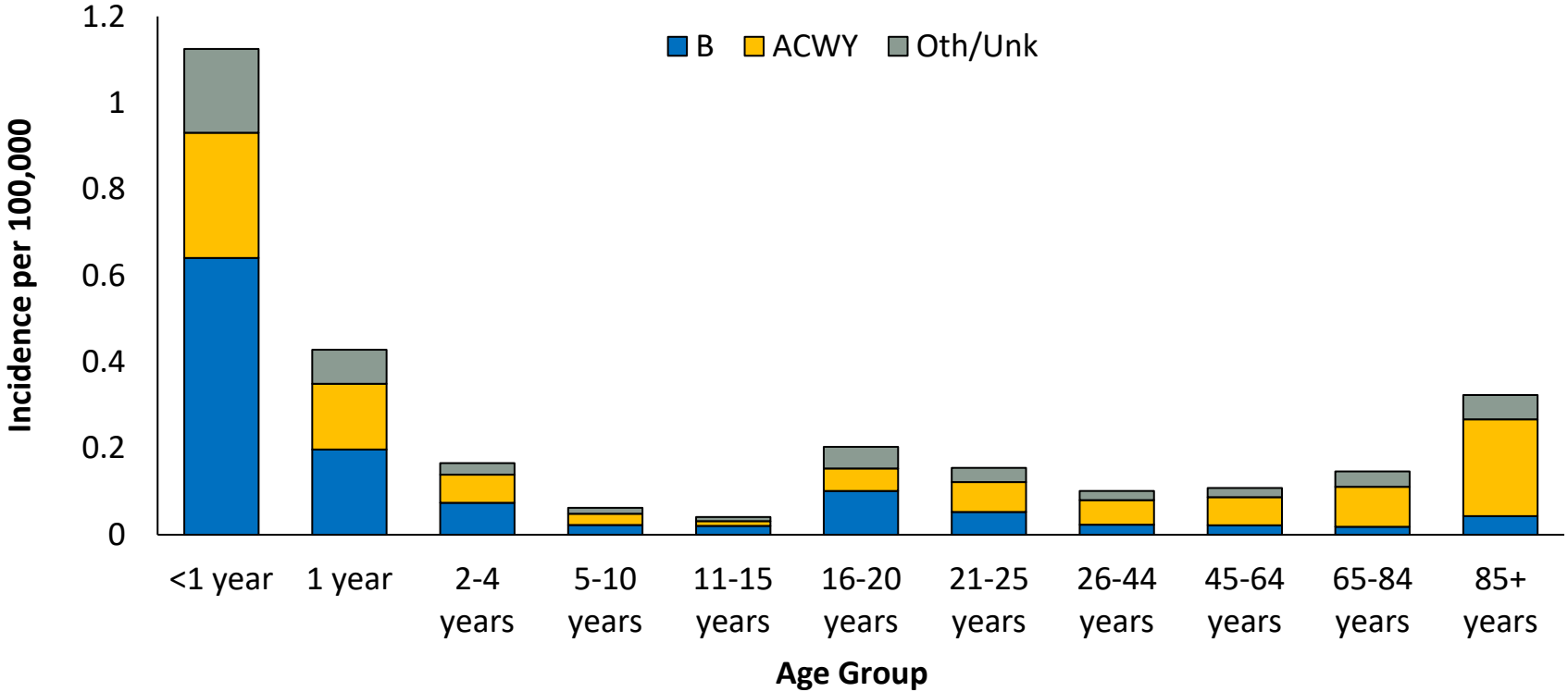
Is meningococcal disease a problem of public health importance?

Meningococcal Disease Incidence — United States, 1996–2022*



Source : 1996–2022 NNDSS Data. *2021–2022 NNDSS data are preliminary.

Average Annual Meningococcal Disease Incidence by Age Group and Serogroup — United States, 2010–2022*



Source: NNDSS data with additional serogroup data from the Active Bacterial Core Surveillance System and state health departments
*2022 data are preliminary

Even with treatment, morbidity and mortality are high

~10–15%

of cases are fatal

Even with treatment, mortality and morbidity are high

~10–15%

of cases are fatal

10–20% of survivors have permanent sequelae

Summary of the Public Health Problem

- Incidence of meningococcal disease
  - Low
  - Decreasing for some time
- Causes very severe disease
- Poor outcomes even with treatment

Public Health Problem — Work Group Interpretation

- Is meningococcal disease a problem of public health importance?

No	Probably No	Probably Yes	Yes	Varies	Don’t Know

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?

GRADE 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	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	RCT	US, Czech R., Finland, Poland	10–25 years	1600	543	1057	
Pfizer (NCT04440176), 2020	RCT	US	11–14 years	294	294	N/A	

GRADE 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

Complexity of Review

- Four outcomes of interest in evidence profile
  - Short-term immunity
  - Persistent immunity
  - Serious adverse events
  - Non-serious adverse events
- Three PICO questions
  - PICO 1: MenABCWY as an option for MenACWY+MenB
  - PICO 2: MenABCWY as an option for MenACWY
  - PICO 3: MenABCWY as an option for MenB
- Two populations
  - Healthy individuals 10 years old or older
  - People with medical conditions that put them at increased risk for invasive disease aged 10 years old or older (i.e., asplenia, complement deficiency, and HIV infection)

GRADE Table 4: Short-Term Immunity 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[1]	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: 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)				⊕⊕⊕◯ Moderate	CRITICAL
Short-term immunity for MenB (follow-up: 1 month)												
1	randomized trials	not serious	not serious	serious[1]	not serious	none	591/755 (78.3%)[2]	263/419 (62.8%)[2]	RR 1.25 (1.15 to 1.36)	15,692 more per 100,000 (from 9,415 more to 22,597 more)	⊕⊕⊕◯ Moderate	CRITICAL

[1] 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.

[2] Calculated based on serogroup B composite data.

GRADE Table 4: Short-Term Immunity for Persons at Increased Risk — 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[1,2]	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: 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)				⨁⨁◯◯ Low	CRITICAL
Short-term immunity for MenB (follow-up: 1 month)												
1	randomized trials	not serious	not serious	very serious[1,2]	not serious	none	591/755 (78.3%)[3]	263/419 (62.8%)[3]	RR 1.25 (1.15 to 1.36)	15,692 more per 100,000 (from 9,415 more to 22,597 more)	⨁⨁◯◯ Low	CRITICAL

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

[2] 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.

[3] Calculated based on serogroup B composite data.

GRADE Table 4: Persistent Immunity 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)		
Persistent immunity for MenACWY (follow-up: 48 months)												
1	randomized trials	not serious	not serious	very serious[1,2]	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	serious[2]	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

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

[2] 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.

GRADE Table 4: Persistent Immunity for Persons at Increased Risk — 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)		
Persistent immunity for MenACWY (follow-up: 48 months)												
1	randomized trials	not serious	not serious	very serious[1,2,3]	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[2,3]	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

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

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

[3] 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.

GRADE Table 4: Serious Adverse Events for Healthy and Increased Risk — PICOs 1, 2, and 3

Healthy Persons

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)		
2	randomized trials	not serious	not serious	serious[1]	serious[2]	none	13/2306 (0.6%)	8/1706 (0.5%)	RR 1.94 (0.72 to 5.22)	441 more per 100,000 (from 131 fewer to 1979 more)	⨁⨁◯◯ Low	CRITICAL

Persons at Increased Risk

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)		
2	randomized trials	not serious	not serious	very serious[1,3]	Serious[2]	none	13/2306 (0.6%)	8/1706 (0.5%)	RR 1.94 (0.72 to 5.22)	441 more per 100,000 (from 131 fewer to 1979 more)	⨁◯◯◯ Very low	CRITICAL

[1] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM plus 2 doses of MenB-FHbp.
[2] Downgraded because relative effect confidence intervals are wide.
[3] Clinical trials did not include patients at increased risk for invasive disease.

GRADE Table 4: Non-Serious Adverse Events Healthy and Increased Risk — PICOs 1, 2, and 3

Healthy Persons

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)		
Non-serious adverse events (assessed with: All adverse events through 1 month after 2nd vaccination)												
2	randomized trials	not serious	not serious	serious[1]	serious[2]	none	581/2306 (25.2%)	387/1706 (22.7%)	RR 1.31 (1.17 to 1.47)	7,032 more per 100,000 (from 3,856 more to 10,662 more)	⨁⨁◯◯ Low	IMPORTANT

Persons at Increased Risk

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)		
Non-serious adverse events (assessed with: All adverse events through 1 month after 2nd vaccination)												
2	randomized trials	not serious	not serious	Serious[1,3]	serious[2]	none	581/2306 (25.2%)	387/1706 (22.7%)	RR 1.31 (1.17 to 1.47)	7,032 more per 100,000 (from 3,856 more to 10,662 more)	⨁◯◯◯ Very low	IMPORTANT

[1] Comparisons were between 2 doses of MenABCWY and 1 dose of MenACWY-CRM plus 2 doses of MenB-FHbp.
[2] Downgraded because absolute effect confidence intervals are wide.
[3] Clinical trials did not include patients at increased risk for invasive disease.

Benefits and Harms — Work Group Interpretation

- How substantial are the desirable anticipated effects?

PICO 1 (MenABCWY as an option for MenACWY+MenB)

Minimal	**Small**	Moderate	Large	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

Minimal	**Small**	**Moderate**	Large	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

Minimal	Small	Moderate	Large	Varies	Don't Know

Benefits and Harms — Work Group Interpretation

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

PICO 1 (MenABCWY as an option for MenACWY+MenB)

Minimal	**Small**	Moderate	Large	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

Minimal	**Small**	Moderate	Large	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

Minimal	**Small**	Moderate	Large	Varies	Don't Know

Benefits and Harms — Work Group Interpretation

- Do the desirable effects outweigh the undesirable effects?

PICO 1 (MenABCWY as an option for MenACWY+MenB)

Favors intervention	Favors comparison	Favors both	Favors neither	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

Favors intervention	Favors comparison	Favors both	Favors neither	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

Favors intervention	Favors comparison	Favors both	Favors neither	Varies	Don't Know

Values

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

Perspective of the Target Population

- Limited data are available on values of the target population toward inclusion of the pentavalent vaccine

- In 2021, vaccination coverage of at least 1 dose was 89% for MenACWY and 31% for MenB among adolescents

- Limited data are available on vaccine uptake in other individuals recommended to receive MenACWY or MenB vaccine

Reduced Doses

- “Use of combination vaccines can reduce the number of injections patients receive and alleviate concern associated with the number of injections… The use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines. Considerations should include provider assessment, patient preference, and the potential for adverse events.”[1]

- “Combination vaccines represent one solution to the issue of increased numbers of injections during single clinic visits and generally are preferred over separate injections of equivalent component vaccines.”[2]

1 General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf

2 American Academy of Pediatrics. Red Book 2018. Report of the Committee on Infectious Diseases. 31st Ed. https://seciss.facmed.unam.mx/wp-content/uploads/2021/02/Red-Book-31th-Edition.pdf

Values — Work Group Interpretation

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

PICO 1 (MenABCWY as an option for MenACWY+MenB)

No	Probably No	**Probably Yes**	Yes	Varies	Don’t Know

PICO 2 (MenABCWY as an option for MenACWY)

No	Probably No	**Probably Yes**	Yes	Varies	Don’t Know

PICO 3 (MenABCWY as an option for MenB)

No	Probably No	**Probably Yes**	Yes	Varies	**Don’t Know**

Uncertainty in How People Value the Outcomes

- Limited data available on how much people value the main outcomes
- Vaccination rates for MenACWY, a routine recommendation, are high among the target population
- Vaccination rates for MenB are considerably lower, but decisions to vaccinate are based on shared clinical decision-making
  - Cause for lower rates unclear: lack of interest in vaccination, lack of awareness of option?

Values — Work Group Interpretation

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

PICO 1 (MenABCWY as an option for MenACWY+MenB)

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 2 (MenABCWY as an option for MenACWY)

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 3 (MenABCWY as an option for MenB)

Important uncertainty or variability	**Probably important uncertainty or variability**	Probably not important uncertainty or variability	No important uncertainty or variability	No known undesirable outcomes

Acceptability

- Is the intervention acceptable to key stakeholders?

Stakeholder Acceptability

- Limited data are available on the acceptance among key stakeholders of including MenABCWY as an option in the current vaccination schedule

- Proponents for increasing MenB vaccination likely would be supportive
  - Pentavalent vaccine combines MenB (a shared clinical decision-making recommendation) with MenACWY (a standard recommendation)
  - Could increase vaccination rates against serogroup B

- Patients who seek vaccination against all 5 serogroups also might be supportive due to the reduced number of doses needed (4 versus 3)

- Health care providers might be supportive, particularly if they could stock fewer vaccines[1,2]

[1] CDC. Timing and Spacing of Immunobiologics: General Best Practice Guidelines for Immunization. ACIP Timing and Spacing Guidelines for Immunization | CDC.

[2] Hall E, Odafe S, Madden J, Schillie S. Qualitative Conceptual Content Analysis of COVID-19 Vaccine Administration Error Inquiries. *Vaccines*. 2023; 11(2):254.

Acceptability — Work Group Interpretation

- Is the intervention acceptable to key stakeholders?

PICO 1 (MenABCWY as an option for MenACWY+MenB)

No	Probably	Probably Yes	Yes	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

Resource Use

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

CDC Cost Effectiveness Model Summary

- Weighted cost per dose + administration
  - MenACWY: $163 ($128–$191)
  - MenB: $210 ($155–$250)
  - MenABCWY: $278 ($255–$290)

- Most MenABCWY strategies would save more or the same number of cases as the standard of care, but they would do so at a much higher cost per QALY saved

- The exception is the Q-P-B, which could be incrementally cost saving (ICER QALY <0) relative to the standard of care

Resource Use — Work Group Interpretation

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

PICO 1 (MenABCWY as an option for MenACWY+MenB)

No	Probably No	**Probably Yes**	Yes	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

No	Probably No	**Probably Yes**	Yes	Varies	Don't Know

Equity

- What would be the impact on health equity?

Equity Considerations

- Limited data are available on the impact of the pentavalent vaccine on health equity

- It is not expected that the vaccine will negatively impact equity

- It could potentially reduce disparities among those who might be interested in being vaccinated against serogroup B but who might not receive clinical care that includes discussion of the MenB vaccine

Equity — Work Group Interpretation

- What would be the impact on health equity?

PICO 1 (MenABCWY as an option for MenACWY+MenB)

Reduced	Probably Reduced	**Probably No Impact**	Probably Increased	Increased	**Varies**	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

Reduced	Probably Reduced	Probably No Impact	**Probably Increased**	Increased	**Varies**	**Don't Know**

PICO 3 (MenABCWY as an option for MenB)

Reduced	Probably Reduced	Probably No Impact	Probably Increased	Increased	Varies	**Don't Know**

Feasibility

- Is the intervention feasible to implement?

Feasibility Considerations

- Challenges with insurance coverage specific to the pentavalent vaccine not expected
- Substantial financial burdens for providers or health systems not expected
- Pentavalent vaccine likely would be easily integrated into providers' practices
  - Would provide additional option in current schedule
  - Administration of the pentavalent vaccine is of equal complexity as currently available vaccines
  - Barriers to stocking the pentavalent vaccine not expected
  - Unclear, however, whether providers are willing to stock three different vaccine types
- Providers who routinely vaccinate persons aged 16–18 years might have an incentive to stock the vaccine to reduce the number of doses given to patients who prefer vaccination against all 5 serogroups

Feasibility — Work Group Interpretation

- Is the intervention feasible to implement?

PICO 1 (MenABCWY as an option for MenACWY+MenB)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

PICO 2 (MenABCWY as an option for MenACWY)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

PICO 3 (MenABCWY as an option for MenB)

No	Probably No	Probably Yes	Yes	Varies	Don't Know

Summary

EtR Summary for PICO 1 (MenABCWY as an option for MenACWY+MenB)

Domain	Question	Work Group Judgment
Public health problem	Is meningococcal disease a public health problem?	Yes
Benefits and harms	How substantial are the desirable anticipated effects?	Small
	How substantial are the undesirable anticipated effects?	Small
	Do the desirable effects outweigh the undesirable effects?	Favors intervention
	What is the overall certainty of the evidence profile?	Varies by group
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably yes
	Is there important uncertainty about or variability in how much people value the main outcomes?	Probably not important uncertainty or variability
Acceptability	Is the intervention acceptable to key stakeholders?	Probably yes or yes
Resource use	Is the intervention a reasonable and efficient allocation of resources?	Probably yes or yes
Equity	What would be the impact on health equity?	Probably no impact or varies
Feasibility	Is the intervention feasible to implement?	Probably yes or yes

Balance of Consequences — PICO 1 (MenABCWY as an option for MenACWY+MenB)

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

Is there sufficient information to move forward with a recommendation?

Yes	No

EtR Summary for PICO 2 (MenABCWY as an option for MenACWY)

Domain	Question	Work Group Judgment
Public health problem	Is meningococcal disease a public health problem?	Yes
Benefits and harms	How substantial are the desirable anticipated effects?	Minimal, small, or moderate
	How substantial are the undesirable anticipated effects?	Minimal or small
	Do the desirable effects outweigh the undesirable effects?	Favors intervention, comparison, or both
	What is the overall certainty of the evidence profile?	Varies by group
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably yes
	Is there important uncertainty about or variability in how much people value the main outcomes?	Probably important uncertainty or variability
Acceptability	Is the intervention acceptable to key stakeholders?	Probably yes or yes
Resource use	Is the intervention a reasonable and efficient allocation of resources?	Probably no or no
Equity	What would be the impact on health equity?	Probably increased, varies, or don't know
Feasibility	Is the intervention feasible to implement?	Probably yes or yes

Balance of Consequences — PICO 2 (MenABCWY as an option for MenACWY)

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

Is there sufficient information to move forward with a recommendation?

Yes	No

EtR Summary for PICO 3 (MenABCWY as an option for MenB)

Domain	Question	Work Group Judgment
Public health problem	Is meningococcal disease a public health problem?	Yes
Benefits and harms	How substantial are the desirable anticipated effects?	Minimal
	How substantial are the undesirable anticipated effects?	Minimal to small
	Do the desirable effects outweigh the undesirable effects?	Favors intervention or comparison
	What is the overall certainty of the evidence profile?	Varies by group
Values	Does the target population feel the desirable effects are large relative to the undesirable effects?	Probably yes or don't know
	Is there important uncertainty about or variability in how much people value the main outcomes?	Important or probably important
Acceptability	Is the intervention acceptable to key stakeholders?	Don't know
Resource use	Is the intervention a reasonable and efficient allocation of resources?	Probably yes or yes
Equity	What would be the impact on health equity?	Don't know
Feasibility	Is the intervention feasible to implement?	Probably yes or yes

Balance of Consequences — PICO 3 (MenABCWY as an option for MenB)

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

Is there sufficient information to move forward with a recommendation?

Yes	No

Proposed Options

Work Group Interpretation, PICO 1

- Should the pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines?

We do not recommend the intervention, but it may be used within FDA licensed indications
We recommend the intervention for individuals based on shared clinical decision-making
We recommend the intervention

Work Group Interpretation, PICO 2

- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?

We do not recommend the intervention, but it may be used within FDA licensed indications
We recommend the intervention for individuals based on shared clinical decision-making
We recommend the intervention

Work Group Interpretation, PICO 3

- Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only?

We do not recommend the intervention, but it may be used within FDA licensed indications
We recommend the intervention for individuals based on shared clinical decision-making
We recommend the intervention

- WG was divided on this option, but a small majority were in favor of not proposing
- WG agreed to have ACIP consider the strengths and weaknesses of this option

Schedule Options

Options	11–12 year old dose	16 year old dose #1	16 year old dose #2	WG Decision
Standard of care (MenACWY only)	Q	Q	–	N/A
Standard of care (MenACWY + MenB)	Q	Q+B	B	N/A
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)

Draft Proposal to the ACIP

- For individuals aged 10 years or older, Pfizer's MenABCWY vaccine may be used as an alternative to MenACWY and MenB vaccines only when both vaccines are indicated to be given at the same time. This proposal applies to healthy individuals (routine schedule) and those at increased risk for meningococcal disease.

Draft Proposal to the ACIP

- For individuals aged 10 years or older, Pfizer's MenABCWY vaccine may be used as an alternative to MenACWY and MenB vaccines only when both vaccines are indicated to be given at the same time. This proposal applies to healthy individuals (routine schedule) and those at increased risk for meningococcal disease.

  - Remarks:
    - This proposal is not intended to supersede or negate the shared clinical decision-making recommendation for MenB.
    - The licensed MenB vaccines are not interchangeable, so use of the Pfizer pentavalent vaccine for the first MenB dose would require subsequent doses to be a Pfizer MenB-FHbp vaccine or pentavalent Pfizer MenB-FHbp-containing vaccine.
    - The minimum interval for the Pfizer pentavalent vaccine is 6 months. Individuals at increased risk of meningococcal disease who are recommended to receive additional doses of MenACWY and MenB less than 6 months after a dose of pentavalent meningococcal vaccine should instead receive separate MenACWY and MenB-FHbp vaccines.
    - The workgroup will review extended interval data when available in anticipation that this may provide support for updated schedules that provide protection for all 5 serogroups.

Strengths and Weaknesses of Q-P-B (PICO 1)

- Strengths
  - Reduces doses from 4 to 3
  - Cost savings
    - ~$95 per person for the routine schedule
    - Q-Q-B-B (~$746) vs. Q-P-B (~$651)
  - Cost per QALY saved less than standard of care
  - Relatively straightforward proposal
- Weaknesses
  - Does not match dosing used in clinical trials (2 doses at 0,6m)
  - Would require stocking 3 vaccine types (MenACWY, MenABCWY, MenB), which might not be acceptable to some clinicians
  - Some clinics might not have funds available to stock multiple formulations, which could increase inequities
  - Could be challenging for some recipients to complete MenB series if provider does not carry MenB-FHbp
  - If ACIP does not recommend second dose of MenABCWY, insurance companies might not cover it in lieu of MenB
  - Potentially could increases risk of provider vaccine administration error[1,2]

[1] CDC. Timing and Spacing of Immunobiologics: General Best Practice Guidelines for Immunization. ACIP Timing and Spacing Guidelines for Immunization | CDC.
[2] Hall E, Odafe S, Madden J, Schillie S. Qualitative Conceptual Content Analysis of COVID-19 Vaccine Administration Error Inquiries. *Vaccines*. 2023; 11(2):254.

Strengths and Weaknesses of Q-P-P (PICO 3)

- Strengths
  - Reduces doses from 4 to 3
  - Small cost savings
    - ~$27 per person for the routine schedule
    - Q-Q-B-B (~$746) vs. Q-P-P (~$719)
  - Relatively straightforward proposal
  - Potentially allows stocking two vaccines for most patients
  - Matches dosing used in clinical trials (2 doses at 0,6m)

- Weaknesses
  - Persons needing 3 doses of MenB would still need Trumenba because of 6m minimum interval
  - Less cost savings than Q-P-B
  - Higher cost per QALY saved compared to standard of care
  - Concerns from WG that this option could lead to MenB vaccine being discontinued (but need for Trumenba for persons at increased risk might reduce likelihood)

Comparison of Q-P-B and Q-P-P

Criteria	Q-P-B	Q-P-P
Number of doses saved	1	1
Cost savings per person compared to standard of care	$95	$27
Less cost per QALY saved than standard of care	Yes	No
Number of vaccine types required for the routine schedule	3	2
Number of vaccines types required for the increased-risk schedule	3	3
Matches dosing used in clinical trials	No	Yes
Unnecessary doses of one or more serogroups	No	Yes

Acknowledgments

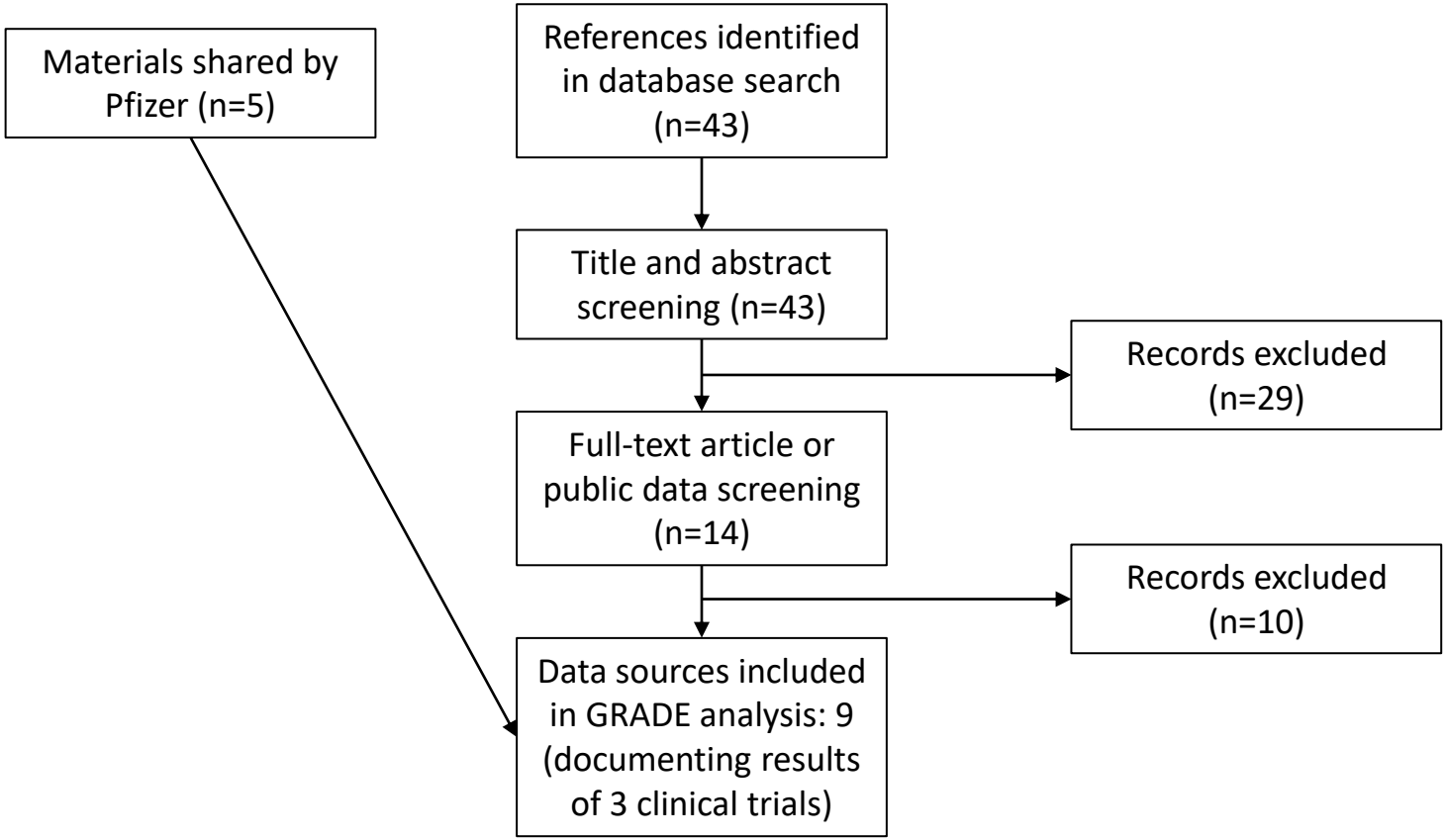
- ACIP Members on the WG
  - Kathy Poehling (Chair)
  - Lynn Bahta
  - Jamie Loehr
- Ex Officio WG Members
  - Margaret Bash (FDA)
  - Mark Connelly (FDA)
  - Francisco Leyva (NIH)
- WG Liaisons and Consultants
  - Amra Resic (AAFP)
  - Samir Shah (AAP)
  - Sharon McMullen (ACHA)
  - Cacky Tate (AIM)
  - Paul Cieslak (CSTE)
  - Kathy Hsu (IDSA)
  - Joseline Zafack (NACI)
  - Jeff Goad (NFID)
  - Jessica Cataldi (PIDS)
  - Amy Middleman (SAHM)
  - David Stephens (Emory)
- CDC Contributors
  - Jenn Collins (DBD/NCIRD)
  - Lucy McNamara (DBD/NCIRD)
  - LeAnne Fox (DBD/NCIRD)
  - Susan Hariri (DBD/NCIRD)
  - Amy Rubis (DBD/NCIRD)
  - Noele Nelson (DBD/NCIRD)
  - Alison Albert (DBD/NCIRD)
  - Angela Jiles (DBD/NCIRD)
  - Jonathan Duffy (DHQP/NCEZID)
  - Tanya Myers (DHQP/NCEZID)
  - Ismael Ortega-Sanchez (DVD/NCIRD)
  - Liz Velazquez (ISD/NCIRD)
  - Jessica MacNeil (ACIP Secretariat)
- GRADE/EtR Support
  - Doug Campos-Outcalt (Arizona)
  - Rebecca Morgan (Case Western Reserve)

Backup Slides

Evidence Retrieval

- Systematic review of studies in any language from Medline, Embase, Global Health, CINAHL, Cochrane, Scopus, and clinicaltrials.gov databases using search string:
  - 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*"
- Efforts made to obtain unpublished or other relevant data
- Included results that presented primary data on Pfizer's MenABCWY vaccine

Evidence Screening Steps



GRADE Certainty of Evidence Categories

Evidence Type	Study Design
High	Randomized controlled trials (RCTs) or overwhelming evidence from observational studies
Moderate	RCTs with important limitations, or exceptionally strong evidence from observational studies
Low	Observational studies, or RCTs with notable limitations
Very low	Clinical experience and observations, observational studies with important limitations, or RCTs with several major limitations

Short-Term Immunity Key Findings (Table 3a)

Author, Pub year	Age	Serogroup (Test strain)	n/N ABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	% (95% CI) for intervention	% (95% CI) for comparator	Effect estimate — RR (95% CI)
Seroresponse based on hSBA titer[1] 1 month after 1 intervention dose									
Pfizer CT (NCT04440163), 2020	10–25 years; ACWY naïve	A	484/499	242/254	MenABCWY (1 dose)	MenACWY-CRM (1 dose) + MenB-FHbp (1 dose)	97.0% (95.1–98.3)	95.3% (91.9–97.5)	1.02 (0.99–1.05)
		C	315/501	132/252			62.9% (58.5–67.1)	52.4% (46.0–58.7)	1.2 (1.05–1.37)
		W	390/492	178/244			79.3% (75.4–82.8)	73.0% (66.9–78.4)	1.09 (0.99–1.19)
		Y	405/494	175/248			82.0% (78.3–85.3)	70.6% (64.5–76.2)	1.16 (1.06–1.27)
	10–25 years; ACWY primed	A	416/439	220/227			94.8% (92.2–96.7)	96.9% (93.7–98.8)	0.98 (0.95–1.01)
		C	410/439	214/226			93.4% (90.7–95.5)	94.7% (90.9–97.2)	0.99 (0.95–1.03)
		W	417/428	214/222			97.4% (95.4–98.7)	96.4% (93.0–98.4)	1.01 (0.98–1.04)
		Y	417/442	209/223			94.3% (91.8–96.3)	93.7% (89.7–96.5)	1.01 (0.97–1.05)
Seroresponse based on hSBA titer 1 month after 2 intervention doses									
Pfizer CT (NCT04440163), 2020	10–25 years; B naïve[2]	B (A22)	646/778	313/396	MenABCWY (2 doses 6 months apart)	MenACWY-CRM (1 dose) + MenB-FHbp (2 doses 6 months apart)	83% (80.2–85.6)	79.0% (74.7–82.9)	1.05 (0.99–1.12)
		B (A56)	774/807	378/400			95.9% (94.3–97.2)	94.5% (91.8–96.5)	1.01 (0.99–1.04)
		B (B24)	567/833	239/418			68.1% (64.8–71.2)	57.2% (52.3–62.0)	1.19 (1.08–1.31)
		B (B44)	731/845	332/419			86.5% (84.0–88.7)	79.2% (75.0–83.0)	1.09 (1.03–1.15)
		B (composite)	591/755	263/419			78.3% (75.2–81.2)	68.7% (63.8–73.3)	1.25 (1.15–1.35)

[1] hSBA = 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.

[2] Serogroup B primed not assessed.

Persistent Immunity Key Findings (Table 3b)

Author, pub year	Age	Serogroup (Test strain)	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	% (95% CI) for intervention	% (95% CI) for comparator	Effect estimate — RR (95% CI)
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)	81.7% (70.7–89.9)	63.4% (46.9–77.9)	1.29 (1.00–1.67)
		C	44/71	16/42			62.0% (49.7–73.2)	38.1 % (23.6–54.4)	1.63 (1.06–2.49)
		W	64/70	29/41			91.4% (82.3–96.8)	70.7% (54.5–83.9)	1.29 (1.05–1.59)
		Y	71/71	40/42			100.0% (94.9–100.0)	95.2% (83.8–99.4)	1.05 (0.98–1.12)
	10–25 years; B naïve	B (A22)	39/139	30/94			28.1% (20.8–36.3)	31.9% (22.7–42.3)	0.88 (0.59–1.31)
		B (A56)	50/145	29/98			34.5% (26.8–42.8)	29.6% (20.8–39.7)	1.17 (0.80–1.70)
		B (B24)	53/145	26/98			36.6% (28.7–44.9)	26.5% (18.1–36.4)	1.38 (0.93–2.04)
		B (B44)	27/148	16/99			18.2% (12.4–25.4)	16.2% (9.5–24.9)	1.13 (0.64–1.98)
	10–25 years; ACWY primed	A	40/40	23/23			100.0% (91.2–100.0)	100.0% (85.2–100.0)	1.00 (1.00–1.00)
		C	75/76	52/58			98.7% (92.9–100.0)	89.7% (78.8–96.1)	1.10 (1.01–1.21)
		W	40/40	21/23			100.0% (91.2–100.0)	91.3% (72.0–98.9)	1.10 (0.97–1.24)
		Y	40/40	22/22			100.0% (91.2–100.0)	100.0% (84.6–100.0)	1.00 (1.00–1.00)

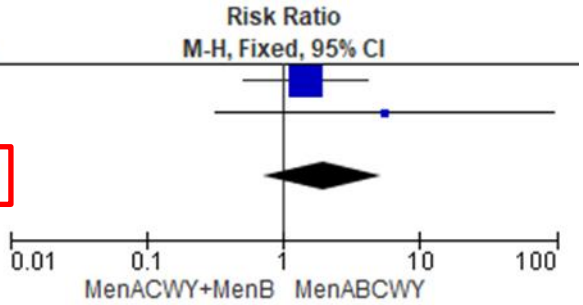
Persistent Immunity Key Findings, Continued

Author, pub year	Age	Serogroup	n/N MenABCWY	n/N comparison	Intervention vaccine	Comparator vaccine	% (95% CI) for intervention	% (95% CI) for comparator	Effect estimate — RR (95% CI)
Seroprotection (defined as hSBA titer ≥1:8) at 13 months (12 months for MenACWY-CRM) after last dose									
Pfizer CT (NCT04440176), 2020, and Pfizer CT (NCT03135834), 2017	11–14 years for NCT04440176 and 10–25 years for NCT03135834; both groups ACWY naive	A	102/126	42/59	1 dose of MenABCWY	1 dose of MenACWY-CRM	81.0% (73.0–87.4)	71.2% (57.9–82.2)	1.14 (0.95–1.37)
		C	92/127	32/62			72.4% (63.8–80.0)	51.6% (38.6–64.5)	1.40 (1.08–1.83)
		W	125/128	52/62			97.7% (93.3–99.5)	83.9% (72.3–92.0)	1.16 (1.04–1.30)
		Y	122/126	61/62			96.8% (92.1–99.1)	98.4% (91.3–100.0)	0.98 (0.94–1.03)

Serious Adverse Event Findings

Study or Subgroup	MenABCWY Events	MenABCWY Total	MenACWY+MenB Events	MenACWY+MenB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
NCT03135834	6[1]	543	8	1057	88.1%	1.46 [0.51, 4.19]
NCT04440163	7[2]	1763	0	649	11.9%	5.53 [0.32, 96.64]
Total (95% CI)		**2306**		**1706**	**100.0%**	**1.94 [0.72, 5.22]**
Total events	13		8			

Heterogeneity: Chi² = 0.80, df = 1 (P = 0.37); I² = 0%
Test for overall effect: Z = 1.32 (P = 0.19)



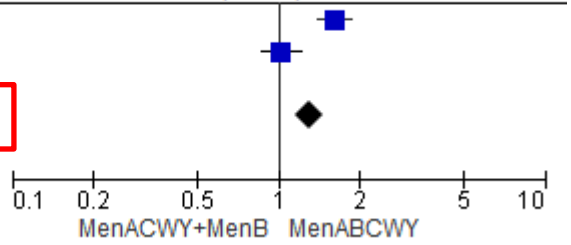
[1] Nine SAEs occurred in 7 patients: *Salmonella* gastroenteritis (1 patient), depression (1 patient), anxiety (1 patient), suicide attempt (1 patient), postural orthostatic tachycardia syndrome (1 patient), dyspnea (1 patient), head injury due to motor vehicle accident (1 patient), traumatic spinal cord injury (1 patient), depression with suicidal ideation (1 patient). **None of the SAEs were deemed related to the vaccine by the study investigators.**

[2] 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), suicidal ideation (2 patients). **None of the SAEs were deemed related to the vaccine by the study investigators.**

Non-Serious Adverse Event Findings

Study or Subgroup	MenABCWY Events	MenABCWY Total	MenACWY+MenB Events	MenACWY+MenB Total	Weight	Risk Ratio M-H, Fixed, 95% CI
NCT03135834	213	543	255	1057	47.3%	1.63 [1.40, 1.89]
NCT04440163	368	1763	132	649	52.7%	1.03 [0.86, 1.23]
Total (95% CI)		**2306**		**1706**	**100.0%**	**1.31 [1.17, 1.47]**
Total events	581		387			

Heterogeneity: Chi² = 15.29, df = 1 (P < 0.0001); I² = 93%
Test for overall effect: Z = 4.63 (P < 0.00001)



- Additional findings related to non-serious adverse events
  - NCT04440163: Attention-deficit/hyperactivity disorder (ADHD) was reported by 6 participants in the MenABCWY group as newly diagnosed chronic medical conditions (NDCMC). Five had an onset of ADHD-related symptoms that occurred prior to study enrollment and the remaining participant had a history of one or more conditions prior to enrollment that commonly co-occur with ADHD, including anxiety, depression, and substance use. **Overall, none of the NDCMCs reported were considered related to vaccine by the investigators.**
  - **No other non-serious adverse events that we are aware of were disproportionately overrepresented in the MenABCWY group from any of the trials.**

Nimenrix Background

- Nimenrix is not approved in the United States, but has been available in other parts of the world for about a decade

- The next few slides provide some background on the vaccine's safety, immunogenicity, and potential interference with other routinely administered vaccines

Nimenrix Safety

- First licensed in the European Union in April 2012
- Currently licensed in more than 80 countries worldwide
- More than 20 thousand people participated in Nimenrix clinical trials
- Over a decade of post-marketing safety data available
  - More than 30 million doses given worldwide
  - Safety consistent between CTs and post-marketing experience
  - Most common adverse events — fever, headache, injection site pain, nausea/vomiting, fatigue
  - Serious adverse events rare relative to doses given
  - Safety also consistent with other licensed meningococcal vaccines

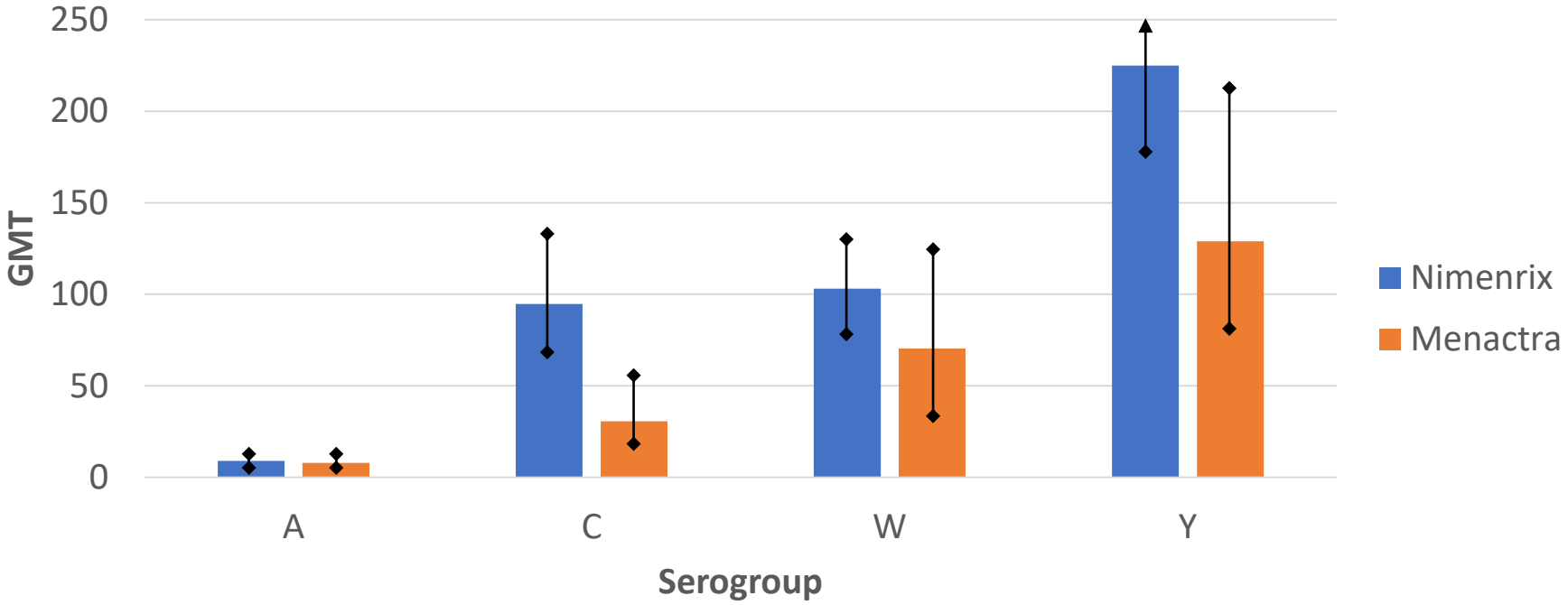
[1] Serra et al. Clinical trial and postmarketing safety experience with MenACWY-TT, a meningococcal group A, C, W, and Y tetanus conjugate vaccine. *Vaccine*. 2022; 40:7014–7021.

Nimenrix Safety, Continued

- One clinical trial on MenACWY-TT and asplenia[1]
  - Phase III, non-randomized study
  - 1 to 17 year olds with impaired splenic activity with age-matched healthy controls
- Results
  - Both study groups had high and comparable hSBA vaccine response rates across serogroups
    - First dose: 55.6–77.1% vs. 60.6–76.3%
    - Second dose: 73.0–100% vs. 73.0–85.3%
  - SAEs were comparable (4/43 vs. 1/43) and none were deemed vaccine related
    - Cystitis due to *Escherichia coli*, pneumococcal bacteremia, salmonellosis, and sickle-cell anemia with crisis

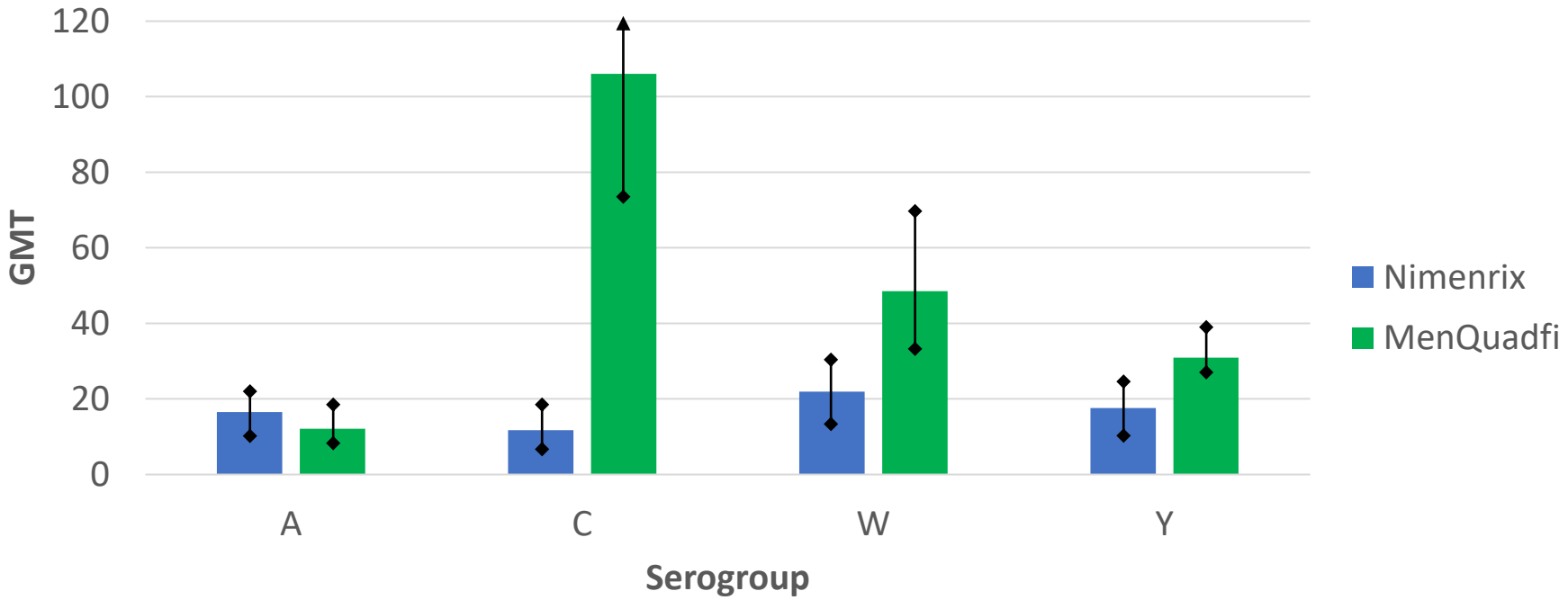
[1] Klein et al. Immunogenicity and safety of the quadrivalent meningococcal ACWY-tetanus toxoid conjugate vaccine (MenACWY-TT) in splenectomized orhyposplenic children and adolescents: Results of a phase III, open, non-randomized study. *Vaccine*. 2018. 36;2356–2363.

Nimenrix Persistence Compared to Menactra — 5 Years After Primary Vaccination in Young Adults Aged 11–25 Years[1]



[1] Pfizer. Nimenrix Product Label. ShowLabeling.aspx (pfizer.com).

Nimenrix Persistence Compared to MenQuadfi — 3 Years After Primary Vaccination in Children Aged 4–5 Years[1]



[1] Sanofi Pasteur. Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine Administered as a Booster Dose in Children Vaccinated 3 Years Earlier as Toddlers. EU Clinical Trials Registry. https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-001993-40/results.

Overall Certainty of Evidence — PICO 1 (Table 5)

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

Overall Certainty of Evidence — PICO 2 (Table 5)

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

Overall Certainty of Evidence — PICO 3 (Table 5)

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

Equity Considerations

Among 17yos in NIS-Teen 2021:

	HISPANIC	NON-HISPANIC WHITE ONLY	NON-HISPANIC BLACK ONLY	NON-HISPANIC OTHER + MULTIPLE RACE
% 1+ dose MenB	31.83	30.88	39.67	24.73

Equity Considerations, Continued

There is a higher disparity of MenB vaccine stocking by county SES, compared to MenACWY

- The total doses of MenACWY was higher per 100 children aged between 10 and 19 across all areas compared to MenB vaccines.
- The spatial regression analysis showed that, for both MenACWY and MenB, lower SES was associated with a shift towards stocking doses on the public vs private markets.

Vaccine	Socioeconomic Status	Total doses/100 children 10-19yo
Men B	High	28
	Medium	26
	Low	20
MenACWY	High	80
	Medium	84
	Low	75

Equity Considerations, Continued

- Potential equity issues exist involving meningococcal vaccination more generally[1]
  - "Among adolescents aged 17 years, coverage with ≥2 MenACWY doses was 11.8 percentage points lower for those living in non-MSAs than for those in MSA principal cities. Disparities between non-MSAs and MSA principal cities were statistically significant for adolescents living at or above the poverty level, but not for those living below the poverty level."
  - "Hispanic or Latino (Hispanic) adolescents had lower coverage with ≥2 MenACWY doses (−10.8 percentage points)."
  - "Adolescents who were uninsured had lower coverage with ≥1 MenACWY dose."

1 Pingali et al. National Vaccination Coverage Among Adolescents Aged 13–17 Years — National Immunization Survey-Teen, United States, 2021. *MMWR*. 2022. 71; 1101–1108.

Demographic Information for NCT04440163

Study C3511001 | Safety Population

10-25 years

Phase 3 study safety population demographics

	MenABCWY (N=1763)	MenB-fHbp + MenACWY-CRM (N=649)	Total* (N=2412)
Characteristic	%	%	%
Sex, male	48.0	50.8	48.8
Race			
White	77.1	80.4	78.0
Black or African American	10.4	9.4	10.2
Asian	2.6	1.8	2.4
American Indian or Alaska Native	0.6	0.9	0.7
Native Hawaiian or other Pacific Islander	0.2	0	0.2
Multiracial	1.7	1.2	1.6
Not reported	7.4	6.2	7.1
Ethnicity			
Hispanic/Latino	24.8	28.2	25.7
Not reported	0.6	0.8	0.7
Age group			
≥10 years to <18 years	67.4	63.0	66.2
≥18 years to <26 years	32.6	37.0	33.8
Mean age at first vaccination (SD), years	15.9 (4.57)	16.6 (4.48)	16.1 (4.55)
Geographic Location, US	71.5	75.0	72.5

*One participant who received MenB-fHbp+saline at Vaccination 1 was excluded. One participant who received MenABCWY+MenACWY-CRM at Vaccination 1 and MenB-fHbp at Vaccination 2 was included in the MenABCWY group.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

Routine and Increased Risk Vaccine Schedules for ≥10 Years Old

- Routine
  - One MenACWY dose at 11–12 years and a booster at 16 years
  - Two MenB doses at 16–18 years

- Increased risk, MenACWY (vaccines are interchangeable)
  - Recommended for certain medical conditions (asplenia, complement deficiency, complement inhibitor use, and HIV infection), some microbiologists, exposure during an outbreak, travel to hyperendemic areas, first-year college students, and military recruits
  - 2 doses ≥8 weeks apart for primary vaccination (only 1 dose for microbiologists, travelers, military) and single booster dose every 5 years thereafter for as long as person remains at increased risk
  - Only 1 dose during outbreaks if ≥5 years since MenACWY primary vaccination
  - Only 1 dose for first year college students within 5 years before starting college

- Increased risk, MenB (vaccines are not interchangeable)
  - Recommended for certain medical conditions (asplenia, complement deficiency, and complement inhibitor use), some microbiologists, and exposure during an outbreak
  - Bexsero: 2 doses ≥1 month apart followed by single dose 1 year later and every 2–3 years thereafter for as long as person remains at increased risk
  - Trumenba: 3 doses at 0, 1–2, and 6 months followed by single dose 1 year later and every 2–3 years thereafter for period of increased risk
  - Only 1 dose during outbreaks if ≥1 year after MenB primary series