GSK Pentavalent (MenABCWY) Vaccine: Review of Updated EtR and Work Group Considerations

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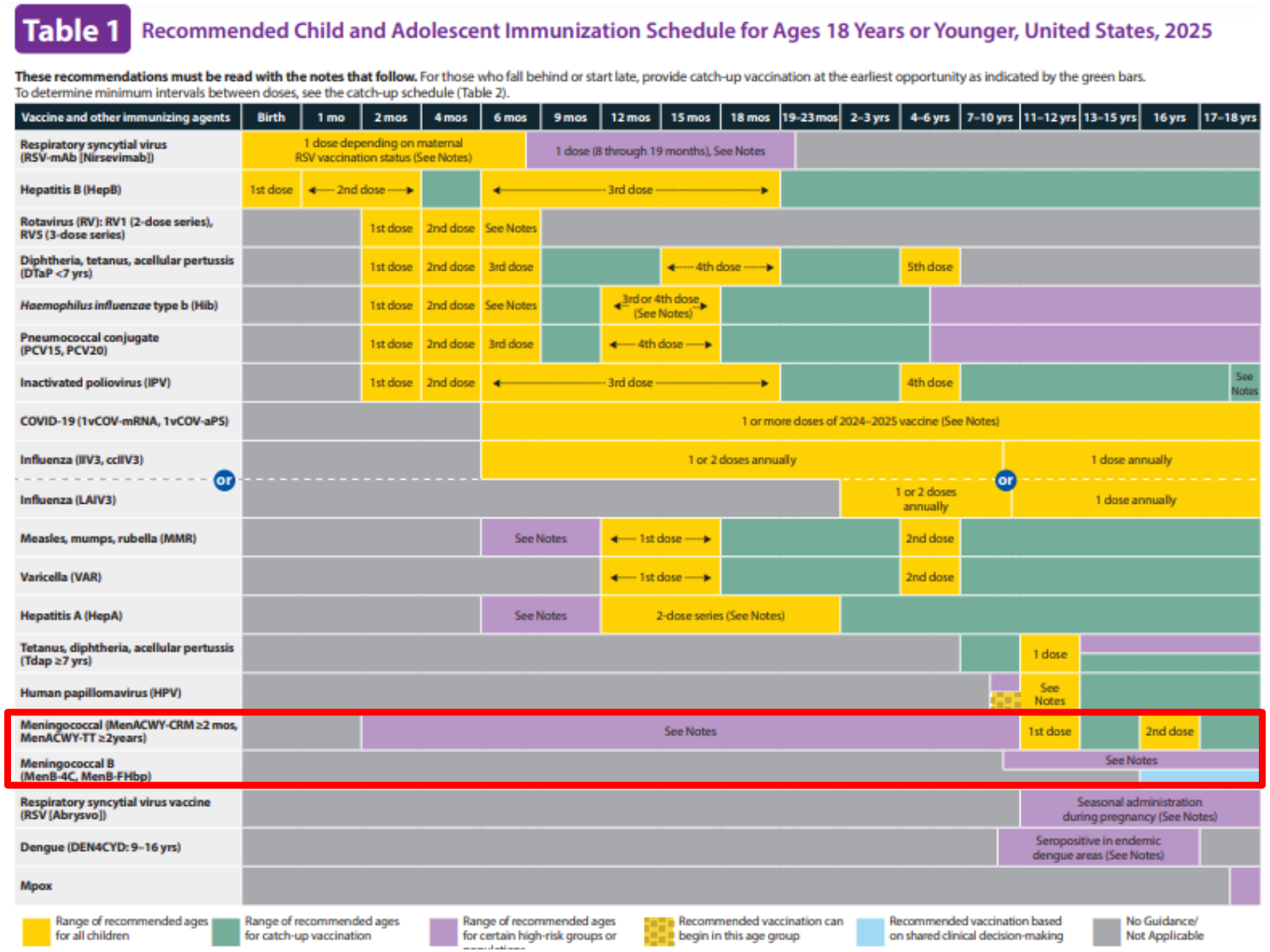
Advisory Committee on Immunization Practices

April 16, 2025

Meningococcal Vaccine Recommendations



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

Risk-Based Meningococcal Vaccine Recommendations

	MenACWY (≥2 months)	MenB (≥10 years)
Asplenia (functional or anatomic)	√	√
Complement deficiency/ complement inhibitor use	√	√
HIV infection	√	
Some microbiologists	√	√
Exposure during outbreak	√	√
Travel to hyperendemic areas	√	
First-year college students (if not previously vaccinated at ≥16 years)	√	

Interchangeability of Vaccine Products

- **MenACWY**
  - Brands are interchangeable
  - Same brand is preferred, but not required, for all doses in a series

- **MenB**
  - Brands are *not* interchangeable
  - Same brand must be used for all doses in a series (including booster doses)

Two Pentavalent MenABCWY Vaccines

	Pfizer (Penbraya)	GSK (Penmenvy)
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
Licensed	October 20, 2023	February 14, 2025
ACIP Vote	October 25, 2023	Today

Pfizer Pentavalent Vaccine

May be used when both MenACWY and MenB are indicated at the same visit for:

1) Healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine and

2) Persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia)

Use of the Pfizer Pentavalent Meningococcal Vaccine Among Persons Aged ≥10 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

Jennifer P. Collins, MD[1]; Samuel J. Crowe, PhD[1]; Ismael R. Ortega-Sanchez, PhD[2]; Lynn Bahta, MPH[3]; Doug Campos-Outcalt, MD[4]; Jamie Loehr, MD[5]; Rebecca L. Morgan, PhD[6]; Katherine A. Poehling, MD[7]; Lucy A. McNamara, PhD[1]

Abstract

Meningococcal disease is a life-threatening invasive infection caused by *Neisseria meningitidis*. Two quadrivalent (serogroups A, C, W, and Y) meningococcal conjugate vaccines (MenACWY) (MenACWY-CRM [Menveo, GSK] and MenACWY-TT [MenQuadfi, Sanofi Pasteur]) and two serogroup B meningococcal vaccines (MenB) (MenB-4C [Bexsero, GSK] and MenB-FHbp [Trumenba, Pfizer Inc.]), are licensed and available in the United States and have been recommended by CDC's Advisory Committee on Immunization Practices (ACIP). On October 20, 2023, the Food and Drug Administration approved the use of a pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya, Pfizer Inc.]) for prevention of invasive disease caused by *N. meningitidis* serogroups A, B, C, W, and Y among persons aged 10–25 years. On October 25, 2023, ACIP recommended that MenACWY-TT/MenB-FHbp may be used when both MenACWY and MenB are indicated at the same visit for the following groups: 1) healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine, and 2) persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia). Different manufacturers' serogroup B–containing vaccines are not interchangeable; therefore, when MenACWY-TT/MenB-FHbp is used, subsequent doses of MenB should be from the same manufacturer (Pfizer Inc.). This report summarizes evidence considered for these recommendations and provides clinical guidance for the use of MenACWY-TT/MenB-FHbp.

Introduction

Meningococcal disease is a life-threatening invasive infection caused by *Neisseria meningitidis*. CDC's Advisory Committee on Immunization Practices (ACIP) recommends routine administration of a single dose of quadrivalent (serogroups A, C, W, and Y) meningococcal conjugate vaccine (MenACWY) to persons at age 11 or 12 years, with a booster dose at age 16 years. ACIP recommends a 2-dose serogroup B meningococcal vaccine (MenB) series for persons aged 16–23 years, based on shared clinical decision-making, to provide short-term protection against meningococcal disease caused by most serogroup B strains (*1*). ACIP also recommends routine vaccination with MenACWY (for persons aged ≥2 months) and MenB (for persons aged ≥10 years) who are at increased risk for meningococcal disease caused by the serogroups covered by each vaccine (Box) (*1*).

In October 2023, a pentavalent meningococcal vaccine (MenACWY-TT/MenB-FHbp [Penbraya, Pfizer Inc.]) was licensed for use in persons aged 10–25 years (*2*). MenACWY-TT/MenB-FHbp contains the same components as those in two existing meningococcal vaccines: 1) *N. meningitidis* polysaccharide groups A, C, W, and Y conjugated to tetanus toxoid carrier protein (MenACWY-TT* [Nimenrix, Pfizer Inc.], a non–U.S.-licensed vaccine), and 2) two recombinant lipidated factor H–binding protein (FHbp) variants from *N. meningitidis* serogroup B (MenB-FHbp [Trumenba, Pfizer Inc.]). This report summarizes evidence considered for these recommendations and provides clinical guidance for the use of MenACWY-TT/MenB-FHbp.

Methods

During June 2022–October 2023, the ACIP Meningococcal Vaccines Work Group held monthly conference calls to review meningococcal disease epidemiology and evidence regarding use of MenACWY-TT/MenB-FHbp in persons currently recommended to receive MenACWY and MenB (policy question 1), MenACWY only (policy question 2), or MenB only (policy question 3). To guide deliberations, ACIP used the Evidence to Recommendations framework and considered the importance of meningococcal disease as a public health problem, benefits, and harms of MenACWY-TT/MenB-FHbp, values of the target population, acceptability, resource use, equity, and feasibility.† ACIP evaluated the available evidence on the following prespecified benefits and harms (each with ranked importance), using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (*3*): disease caused by serogroups A, B, C, W, and Y (critical); short-term immunity (critical); persistent immunity (important); serious

* Nimenrix and MenQuadfi (both abbreviated MenACWY-TT) are different vaccines containing different amounts of tetanus toxoid conjugate.
† https://www.cdc.gov/vaccines/acip/recs/grade/mening-MenACWY-TT-MenB-FHbp-etr.html

Considerations

- Each pentavalent vaccine assessed separately by Work Group
  - Lack of data directly comparing the two vaccines
- The MenACWY and MenB vaccine indications have not changed with the availability of pentavalent vaccine
- ACIP previously voiced preference to harmonize recommendations between the Pfizer and GSK pentavalent vaccines
  - Unless a vaccine-specific reason to have a different recommendation exists

Assessing Immunogenicity

- Exogenous complement ("traditional" hSBA assays)
  - Seroprotection
  - Seroresponse*
  - GMTs
- Endogenous complement
  - Immunologic Vaccine Effectiveness: Immune response against diverse serogroup B strains
- Serologic correlate of protection exists only for serogroup C

*E.g.: a post-vaccination hSBA titer at least 4-fold the LOD or ≥LLOQ, whichever is greater, for participants with pre-vaccination hSBA titer <LOD, a post-vaccination hSBA titer at least 4-fold the LLOQ for participants with pre-vaccination hSBA titer ≥LOD and <LLOQ, and a post-vaccination hSBA titer at least 4-fold the pre-vaccination hSBA titer for participants with pre-vaccination hSBA titer ≥ LLOQ

LOD, limit of detection; LLOQ, lower limit of quantitation

PICO Questions: GSK Pentavalent Vaccine

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 MenB vaccine based on shared clinical decision-making

Acronyms

Q=Quadrivalent (MenACWY vaccine)

B=MenB vaccine

P=Pentavalent (MenABCWY vaccine)

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Current Recommendation: Q-QB-B or Q-Q

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? **Q-P-B**

PICO 2:

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

PICO 3:

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

Acronyms

Q=Quadrivalent (MenACWY vaccine)

B=MenB vaccine

P=Pentavalent (MenABCWY vaccine)

Current Recommendation: Q-QB-B or Q-Q

PICO 1: "Yes" for Pfizer pentavalent vaccine

- 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? **Q-P-B**

PICO 2: "No" for Pfizer pentavalent vaccine

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

PICO 3: "No" for Pfizer pentavalent vaccine

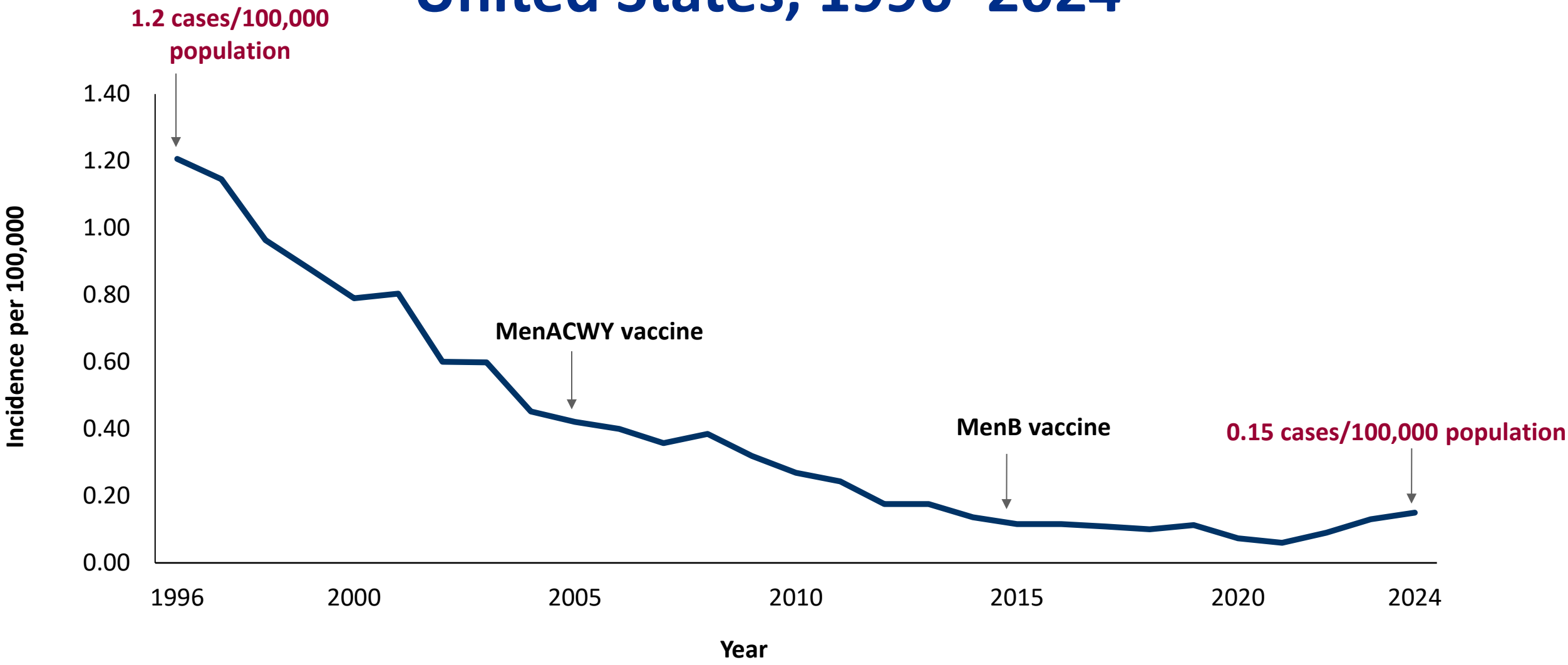
- Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenB only? **Q-P-P**

Updated Evidence-to-Recommendations Framework: GSK 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 comparison	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
Health 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

Public health problem

Meningococcal Disease Incidence – United States, 1996–2024*



Abbreviations: MenACWY vaccine = quadrivalent (serogroups A, C, W, and Y) meningococcal conjugate vaccine; MenB vaccine = serogroup B meningococcal vaccine
Source: 1996–2024 NNDSS Data. *2024 NNDSS data are preliminary.

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

Serogroup B Immunogenicity Lower than Previously Shared with ACIP

- Comparator of Bexsero at 0, 2 month interval
  - August 2024: Bexsero label changed from 0, ≥1 month to 0, 6 months
- Longer intervals between vaccine doses associated with higher immunogenicity
- Additionally, some data points in label have been updated

Work Group Assessment

- Clinical significance of comparatively lower immunogenicity uncertain
  - Serologic correlate of protection lacking for serogroup B disease
- The Work Group's recommendation for the GSK pentavalent vaccine remains unchanged
  - ACIP to weigh the change in immunogenicity in their deliberations

Previous Synthesis to ACIP (Remains Unchanged from June 2024):

- For “traditional” exogenous hSBA titers against 4 vaccine indicator strains, MenABCWY was:
  - Non-inferior to **MenB 0, 2** months for 3 strains
  - Non-inferior to **MenB 0, 6** months for 2 strains
- Endogenous complement hSBA assay against a broad range of strains (Immunologic Vaccine Effectiveness): Success criteria met
  - Although MenABCWY had lower point estimates (especially compared to MenB 0,6)

Previous Synthesis Unchanged Regarding: ACWY Immunogenicity and Safety

- MenABCWY non-inferior to MenACWY in most study groups
  - Except serogroup A for 1 dose MenABCWY vs. 1 dose MenACWY in naïve recipients
    - Serogroup A disease very rare in the United States

- MenABCWY safety profile similar to MenB, except slightly more unsolicited adverse events with MenABCWY
  - More adverse events than with MenACWY

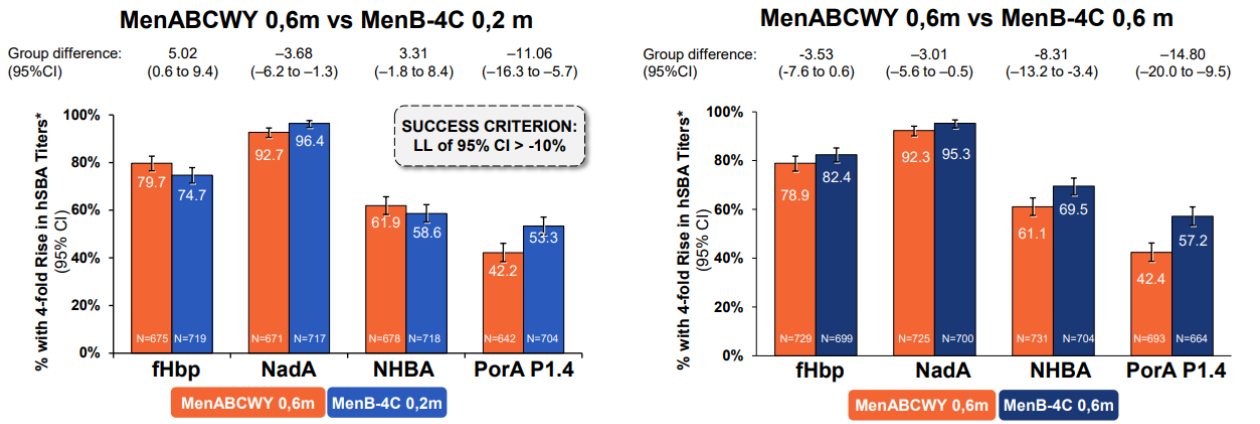
Composite response=hSBA ≥LLOQ for all 4 indicator strains

- **Poorer immunogenicity when comparing to 0,6 month schedule**
- **Success criterion not met for all strains (unchanged since June ACIP)**
- **Some change in numbers**

Presentation to ACIP, Jun 2024

Package Insert, Feb 2025

hSBA: MenABCWY Immune Response Against Serogroup B Reference Strains



- Secondary endpoint not met because success criterion not met for all 4 strains
- MenABCWY elicited comparable immune responses for 3 reference strains vs MenB-4C 0,2 and 2 reference strains vs MenB-4C 0,6m.

*At 1 month after 2nd MenABCWY or 2nd MenB-4C vaccination, relative to baseline. 4-fold rise in hSBA titer for each strain was defined as a post-vaccination titer ≥4-fold the LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. LOD – limit of detection; LLOQ – lower limit of quantitation; LOD: fHbp: 3; NadA: 6; NHBA: 4; PorA P1.4: 4. LLOQ: fHbp: 5; NadA: 15; NHBA: 4; PorA P1.4: 6. fHbp, factor H binding protein; hSBA, human serum bactericidal assay; LL, lower limit; LOD – limit of detection; LLOQ – lower limit of quantitation; NadA, *Neisseria* adhesin A; NHBA, Neisserial heparin-binding antigen; Por A P1.4, porin A

Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

Presentation by GSK at ACIP, June 2024

Table 5. Percentages of Participants With hSBA Seroresponse and Composite Response Against Meningococcal Serogroup B Indicator Strains Following PENMENVY and BEXSERO, Study 1[a]

	% Seroresponse (95% CI)[b,c,d,e]		
Antigen (Indicator Strain)	**PENMENVY**	**BEXSERO (0, 6 Months)**	**Percent Difference PENMENVY – BEXSERO**
fHbp (M14459)	N = 675 73.2 (69.7, 76.5)	N = 654 78.1 (74.8, 81.2)	-5.0 (-9.6[f], -0.3)
NadA (96217)	N = 671 92.7 (90.5, 94.5)	N = 655 95.9 (94.1, 97.3)	-3.2 (-5.8[f], -0.7)
NHBA (M13520)	N = 678 61.8 (58.0, 65.5)	N = 659 69.7 (66.0, 73.1)	-7.9 (-12.9[g], -2.8)
OMV (NZ98/254)	N = 642 42.2 (38.4, 46.1)	N = 624 58.3 (54.4, 62.2)	-16.1 (-21.5[g], -10.6)

Presentation to ACIP, Jun 2024

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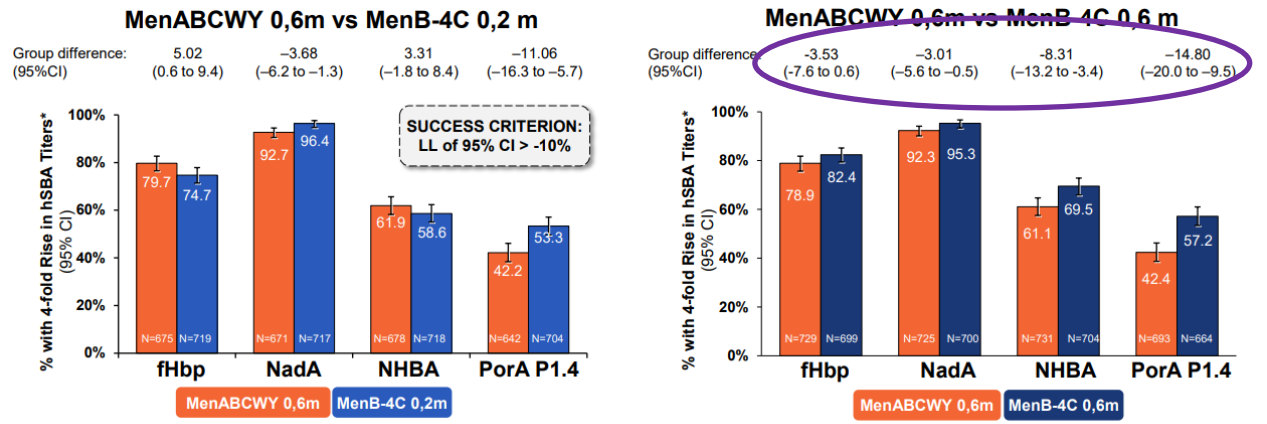
Package Insert, Feb 2025

hSBA: MenABCWY Immune Response Against Serogroup B Reference Strains



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PorA

- Non-inferiority not demonstrated for PorA strain for 0, 2 or 0, 6 month comparison
  - PorA indicator strain is important because it represents the outer membrane vesicle (OMV) component of the vaccine and has bearing on cross-protection

Penmenvy (GSK) Package Insert

Composite response=hSBA ≥LLOQ for all 4 indicator strains

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% Composite Response (95% CI)[d,e,h,i,j]			
Timepoint	**PENMENVY**	**BEXSERO (0, 6 Months)**	-
Baseline (pre-vaccination)	N = 747 1.1 (0.5, 2.1)	N = 708 0.6 (0.2, 1.4)	-
1 Month post-dose 2	N = 707 70.0 (66.5, 73.4)	N = 683 80.1 (76.9, 83.0)	-

Study 1: NCT04502693.

Penmenvy (GSK) Package Insert

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Study 1: NCT04502693.

Penbraya (Pfizer) Package Insert

	PENBRAYA %	**Trumenba + MenACWY-CRM %**	**PENBRAYA – Trumenba Difference**
Serogroup B Variant	**N=755-845**	**N=383-419**	**Difference % (95% CI)**
Composite[d]			
Pre-Dose 1	1.2	2.0	-
Post-Dose 2	78.3	68.7	9.6 (4.2, 15.2)

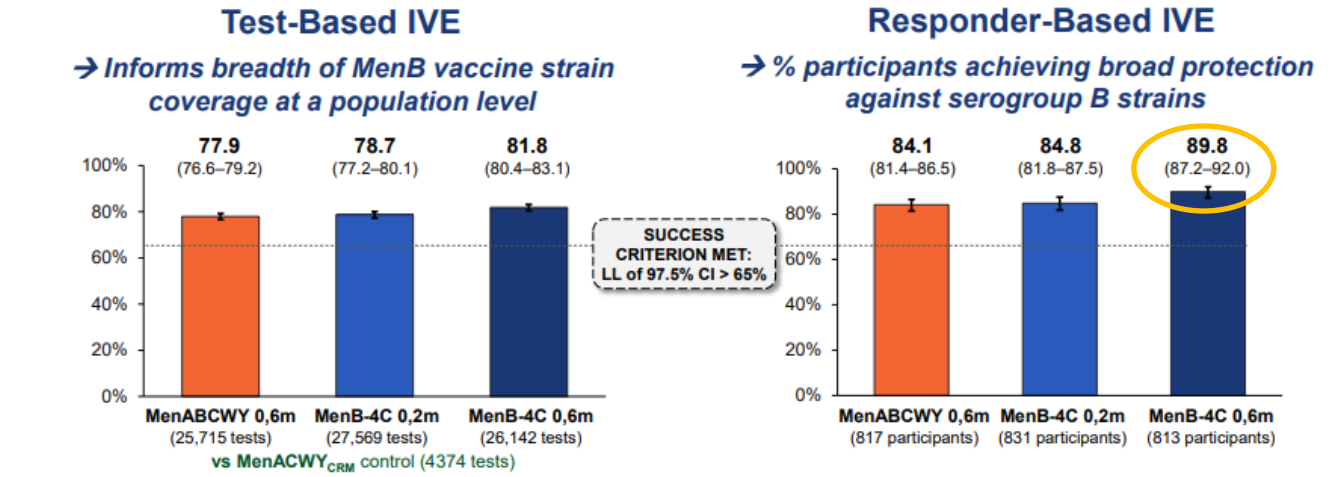
Abbreviations: CI = confidence interval; hSBA = serum bactericidal assay using human complement; LLOQ = lower limit of quantitation; LOD = limit of detection; MenACWY-CRM = meningococcal (serogroups A, C, W and Y) oligosaccharide diphtheria CRM_{197} conjugate vaccine; Trumenba= meningococcal serogroup B factor H binding protein.
Note: The LLOQ is an hSBA titer = 1:16 for A22 and 1:8 for A56, B24, and B44 and serogroups A, C, W, and Y.
Note: Seroresponse is defined as the 4-fold increase as follows: (1) For participants with a baseline hSBA titer <1:4 (LOD), a 4-fold response was defined as an hSBA titer ≥1:16. (2) For participants with a baseline hSBA titer ≥ LOD and < LLOQ, a response is defined as an hSBA titer ≥4 times the LLOQ. (3) For participants with a baseline hSBA titer ≥ LLOQ, a response is defined as an hSBA titer ≥4 times the baseline titer.

a. Evaluable immunogenicity populations.
b. NCT04440163
c. Non-inferiority was demonstrated (using 10% margin) post-vaccination by assessing the difference between vaccination serogroups.
d. Composite response = hSBA ≥ LLOQ for all 4 primary meningococcal B strains.

Presentation to ACIP, Jun 2024

- **Poorer immunogenicity when comparing to 0,6 month schedule**
- **Success criterion met**
- **Minimal change in numbers**

enc-hSBA: Immune Response against Diverse Serogroup B Strains after 2 doses of MenABCWY or MenB-4C



MenABCWY achieved breadth of bactericidal effect against a diverse and broad panel of serogroup B strains, similar to MenB-4C 2-dose administered 2 or 6 months apart

The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-6m→MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (**LL of 95% CI > 65%**) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit; IVE: immunological vaccine effectiveness
Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

Presentation by GSK at ACIP, June 2024

Package Insert, Feb 2025

Table 3. Percentage of Participants Whose Sera Killed ≥70% of Meningococcal Serogroup B Strains Tested[a] (Responder-Based) Following PENMENVY and BEXSERO, Study 1[b]

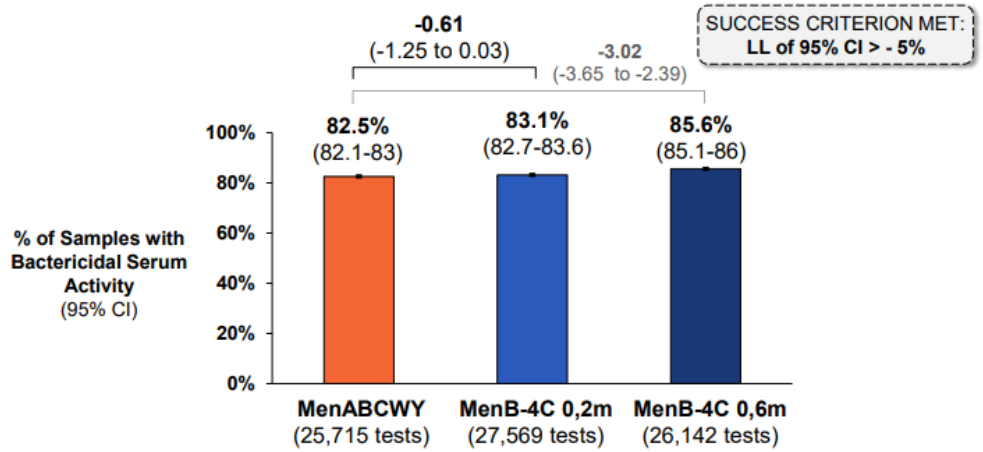
Group[c]	N	% Responders[d] (95% CI)
PENMENVY	817	84.1 (81.4[e], 86.5)
BEXSERO (0, 6 Months)	813	89.8 (87.5, 91.8)
BEXSERO (0, 2, 6 Months)	790	93.4 (91.5, 95.0)

Study 1: NCT04502693.

GSK presentation to ACIP, Jun 2024

- **Poorer immunogenicity when comparing to 0,6 month schedule**
- **Success criterion met**
- **No change in numbers**

enc-hSBA: Noninferiority of Immune Response against Diverse Serogroup B Strains in MenABCWY vs MenB-4C



MenABCWY was noninferior to MenB-4C, based on bactericidal effects against diverse strains assessed by enc-hSBA assay

*The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-6m→MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 97.5% CI > 65%) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit
Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

Presentation by GSK at ACIP, June 2024

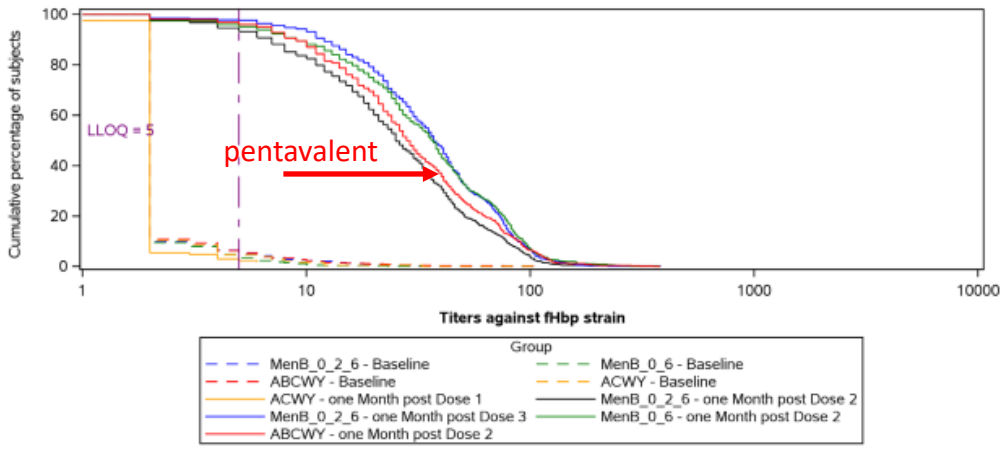
Integrated FDA Review, Mar 2025

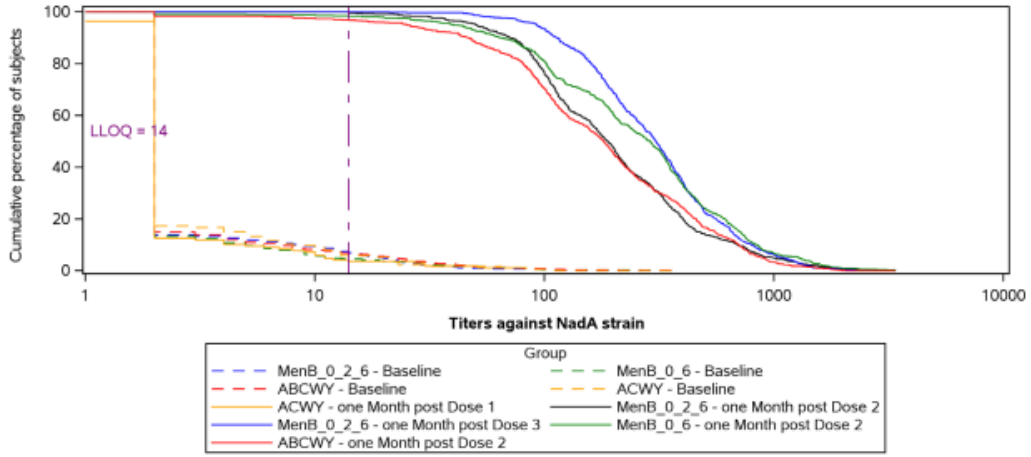
Table 22. Percentages of Tests[a] with Bactericidal Activity Against Meningococcal Serogroup B Strains (Test-Based) Following MenABCWY, Bexsero, and Menveo, Per Protocol Set[b], Study V72_72

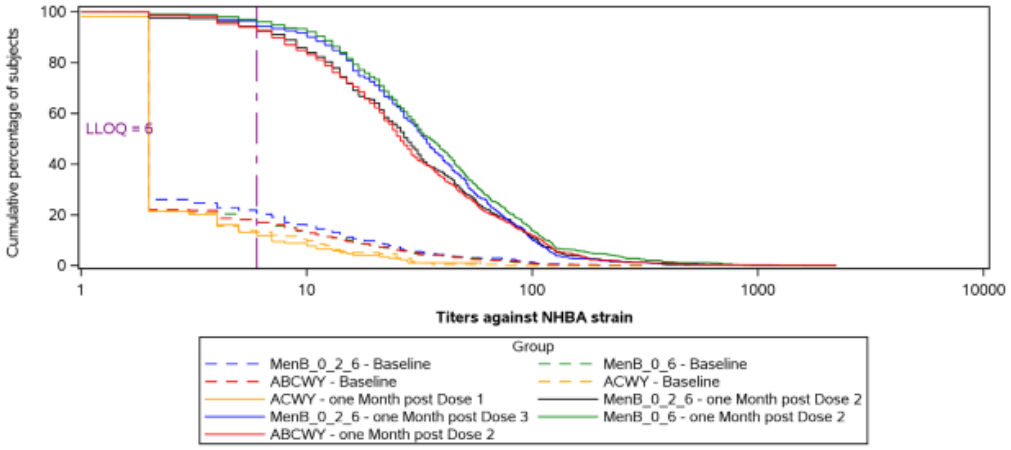
Group[c]	Number of Participants	% of Tests with Bactericidal Activity (n/N)
MenABCWY	754	82.5 (21,222 / 25,715)
Bexsero (0, 6 months)	764	85.6 (22,365 / 26,142)
Bexsero (0, 2, 6 months)	747	86.7 (22,184 / 25,596)
Menveo	133	21.0 (918 / 4,374)

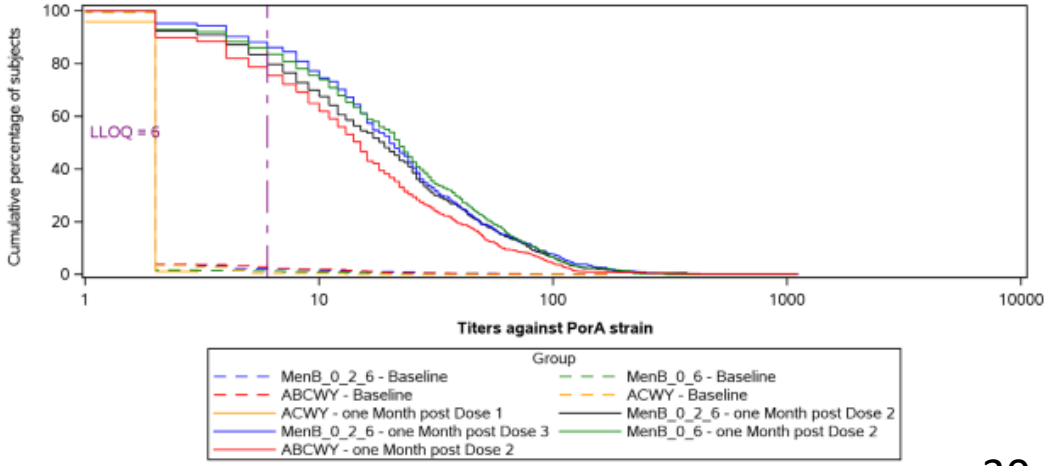
Source: PENMENVY (Meningococcal Groups A, B, C, W and Y Vaccine) package insert. GlaxoSmithKline Biologics SA.
n=Number of tests with bactericidal activity, N=Total number of tests.
[a] Each test qualitatively assessed (yes/no) the bactericidal activity of one participant's serum using the enc-hSBA assay against one of the 110 U.S. meningococcal serogroup B strains. Each participant's serum was tested against a maximum of 35 strains randomly selected from the 110strain panel.
[b] Per Protocol Set includes all participants in the Full Analysis Set minus participants with protocol deviations that lead to exclusion from the Per Protocol Set.

Reverse Cumulative Distribution of hSBA Against Indicator Strains

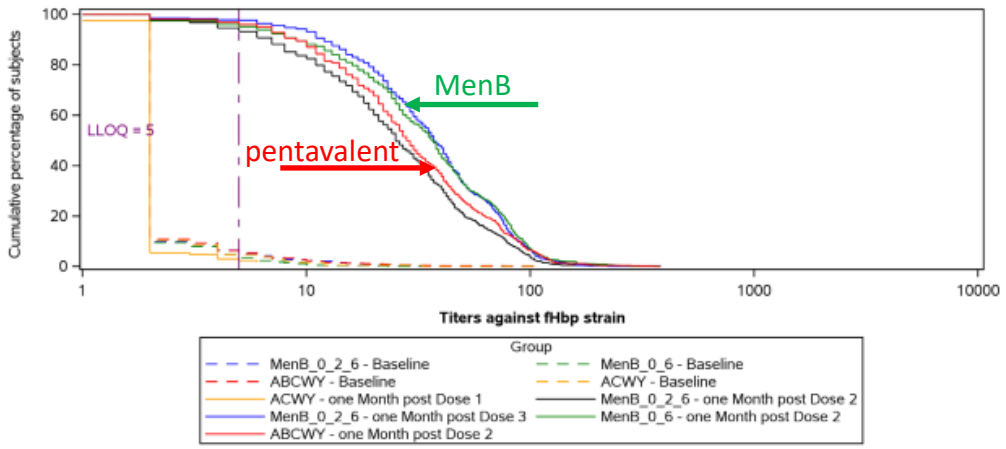


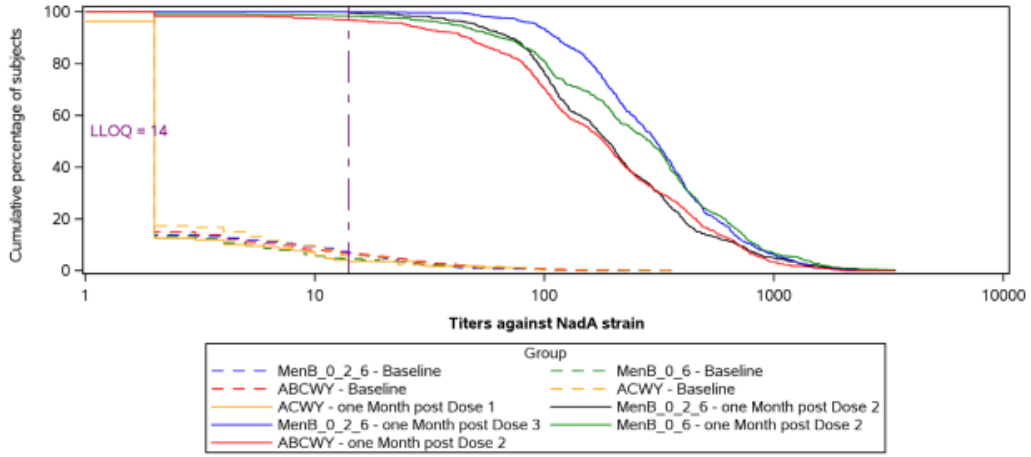


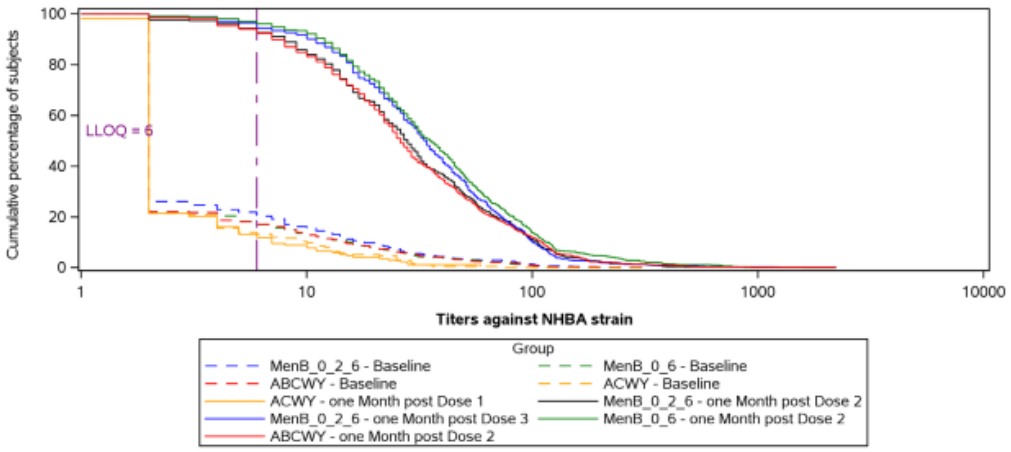


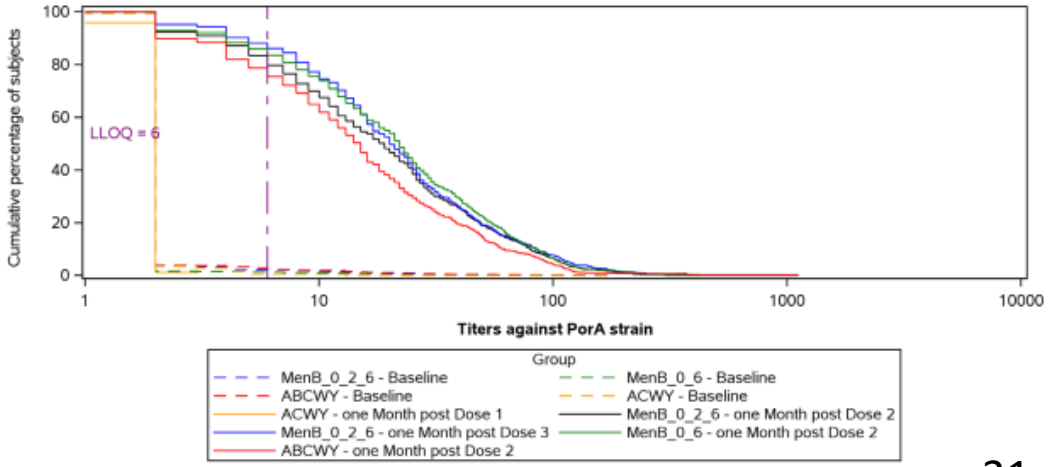


Reverse Cumulative Distribution of hSBA Against Indicator Strains







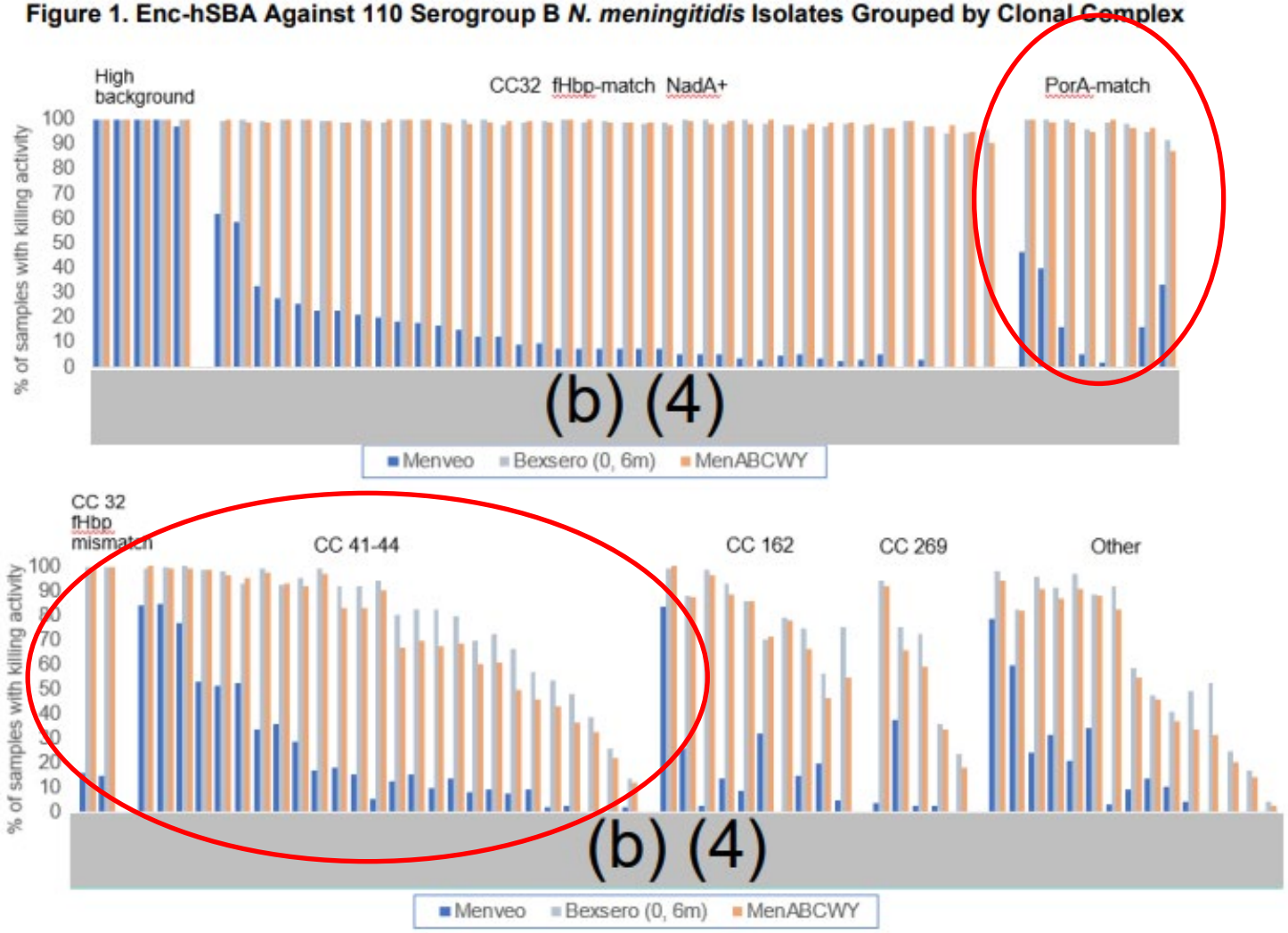


Enc-hSBA against 110 Isolates by Clonal Complex

For PorA/OMV: enc-hSBA likely most reflective of U.S. strains and exogenous assay likely most reflective of New Zealand strain

CC 41/44 represents 72/179 (40.2%) of U.S. isolates from 2020-2024

Figure 1. Enc-hSBA Against 110 Serogroup B *N. meningitidis* Isolates Grouped by Clonal Complex



MenABCWY Non-Inferior to MenACWY$_{CRM}$ in MenACWY-Naïve and MenACWY-Primed Participants

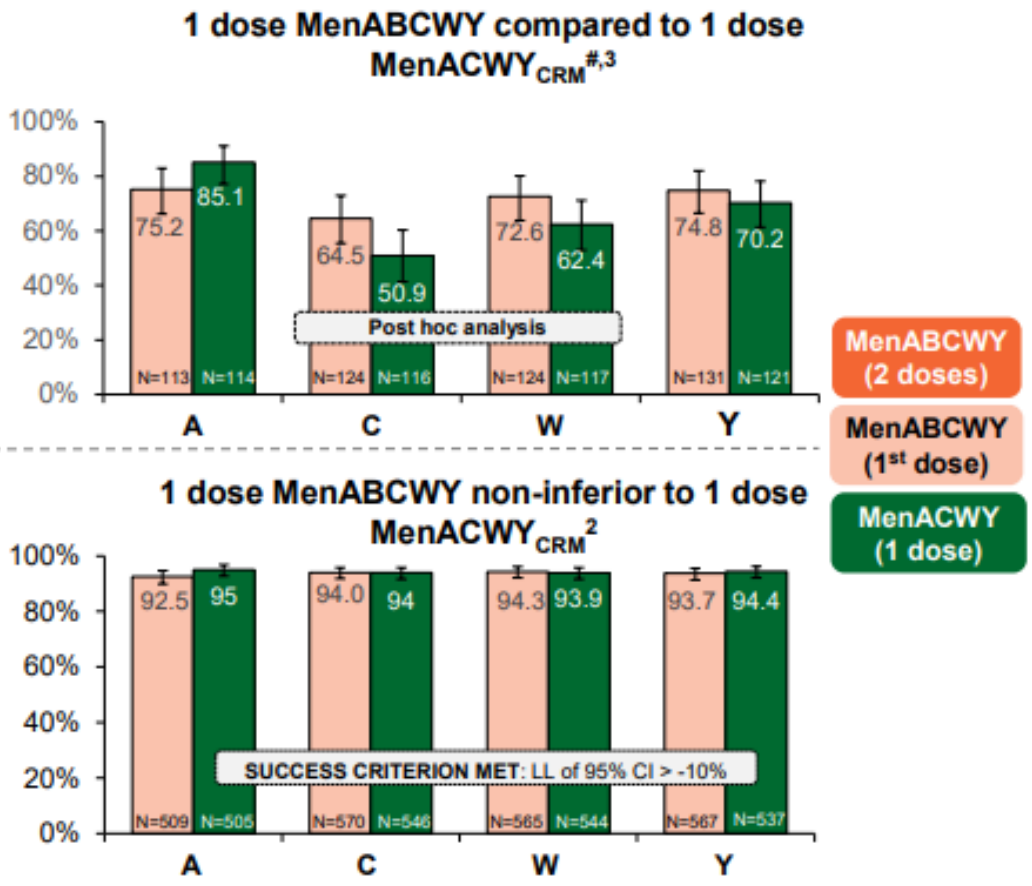
V72_72: MenACWY-Naïve

% with 4-fold Rise in hSBA Titers*† (95% CI)

MenABCWY-019: MenACWY-Primed**

% with 4-fold Rise in hSBA Titers*† (95% CI)

- For serogroups CWY, 1 dose pentavalent immunogenicity greater than 1 dose Menveo for naïve recipients
- For serogroup A, 1 dose pentavalent immunogenicity lower than 1 dose Menveo for naïve recipients (Serogroup A does not circulate in U.S.)
- For primed recipients, 1-dose immunogenicity similar for serogroups A, C, W, and Y



*At 1 month after 1 or 2 doses of MenABCWY or after single MenACWY vaccination; †Defined as a post-vaccination titer ≥4-fold the LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the LLOQ if pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer if pre-vaccination titer ≥LLOQ. LOD: 4 for MenA, MenC, MenW, and MenY. LLOQ = 12 for MenA; 8 for MenC; 8 for MenW; 10 for MenY, except for the post-hoc analysis for which LLOQs were 8 for MenA and 11 for MenC; ‡Licensure criteria agreed with CBER; #full set analysis; **Primed participants had received a dose of MenACWY vaccine at least 4 years prior. CI – confidence interval, hSBA - human serum bactericidal assay, LOD – limit of detection; LLOQ – lower limit of quantitation

1. Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024; 2. Clinicaltrials.gov identifier NCT04707391, accessed May 31st, 2024; 3. GSK, Data on File 2024N555056.

Serious Adverse Events Assessed as Possibly Related to Vaccination

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

Serogroup B Immunogenicity Summary

- MenABCWY immunogenicity slightly lower than MenB
  - Clinical significance uncertain as serologic correlate of protection is lacking
- For “traditional” exogenous hSBA titers against 4 vaccine indicator strains, MenABCWY was:
  - Non-inferior to **MenB 0, 2** months for 3 strains
  - Non-inferior to **MenB 0, 6** months for 2 strains
- Endogenous complement hSBA assay against a broad range of strains (Immunologic Vaccine Effectiveness): Success criteria met
- Work Group’s interpretation has not changed
- ACIP to consider the magnitude of the difference in immunogenicity in their deliberations

Benefits and Harms

- How substantial are the desirable 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	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

*Represents minority opinion added since last presented to ACIP

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

Resource use

Pediatric Price Per Dose

		Public	Private
MenACWY	**Menveo**	$119.986*	$166.747
	MenQuadfi	$114.36*	$171.972
MenB	**Trumenba**	$142.73*	$207.32*
	Bexsero	$154.504*	$237.126
MenABCWY	**Penbraya**	$189.35	$230.75
	Penmenvy*	$181.00* (final price: pending negotiation)	$241.00** (final price: $230-255)

*Updated contract price **Value used in CDC cost-effectiveness model

https://www.cdc.gov/vaccines-for-children/php/awardees/current-cdc-vaccine-price-list.html

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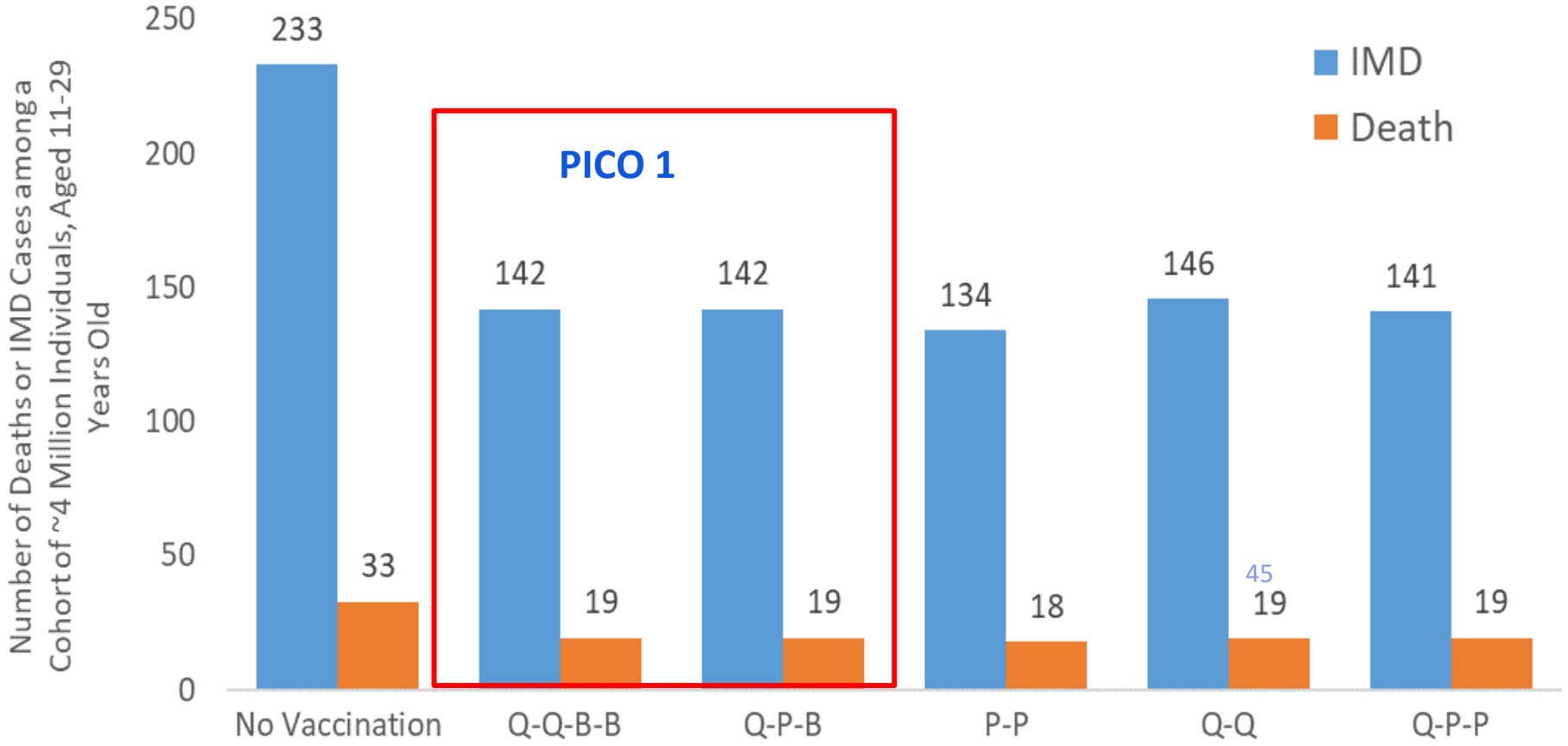
Health Outcomes*: Cumulative Number of IMD Cases and Deaths for a Single Birth Cohort from Ages 11 through 29 Years



Q=Quadrivalent (MenACWY) vaccine; B=MenB vaccine; P=Pentavalent (MenABCWY) vaccine; IMD=Invasive meningococcal disease.

*All numbers are cumulative over the analytical horizon of the model for a single cohort of 11-year-olds. For example, in the "No Vaccination" strategy, there were a total of 233 undiscounted episodes of IMD among about 4 million individuals, who started in the model at 11 years old and aged to 29 years old.

Cost-Effectiveness

PICO	Intervention	Comparator	Diff. in QALYs*	Diff. in Cost*	ICER ($/QALY)
1	Q-P-B	Q-QB-B	0	-$175 million	**Cost-saving****
2	P-P	Q-Q	33	$373 million	$11,332,778
3	Q-P-P	Q-QB-B	2	-$166 million	**Cost-saving**
		Q-P-B	2	$9 million	$4,510,830

- **In a sensitivity analysis, with the updated price assumptions, PICO #1 (Q-P-B) remained cost-saving (when compared to Q-QB-B).**

Q=Quadrivalent (MenACWY) vaccine; B=MenB vaccine; P=Pentavalent (MenABCWY) vaccine; QALY=Quality-adjusted life year.
*Annual discount is 3%; 2024$; **In this comparison, costs are reduced, but health outcomes remain the same when comparing Q-P-B to Q-QB-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

Evidence-to-Recommendations Framework

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 comparison*	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
Health 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

*Added since last presented to ACIP

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*	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

*Added since last presented to ACIP

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

Comments Regarding Proposed Recommendation

- PICO 1 would typically involve 1 dose of pentavalent vaccine (and 1 dose of MenB vaccine)
  - –Studies evaluated 2 doses of pentavalent vaccine
- Recommendations for use of both pentavalent vaccines could be revisited as part of future adolescent schedule deliberations if desired

Vote Language

PICO 1 (QPB)	√
PICO 2 (PP)	X
PICO 3 (QPP)	X

ACIP recommends GSK's MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit*

*1) healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine and 2) persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia)

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- Jennifer Collins
- Amy Rubis

Thank you!

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