Serogroup B Meningococcal Vaccines Booster Doses

Work Group interpretation, considerations for policy options, and next steps

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Agenda

- Work Group's interpretation of:
  - Persistence of immune response following a serogroup B meningococcal (MenB) primary series
  - Immunogenicity and persistence of MenB booster dose

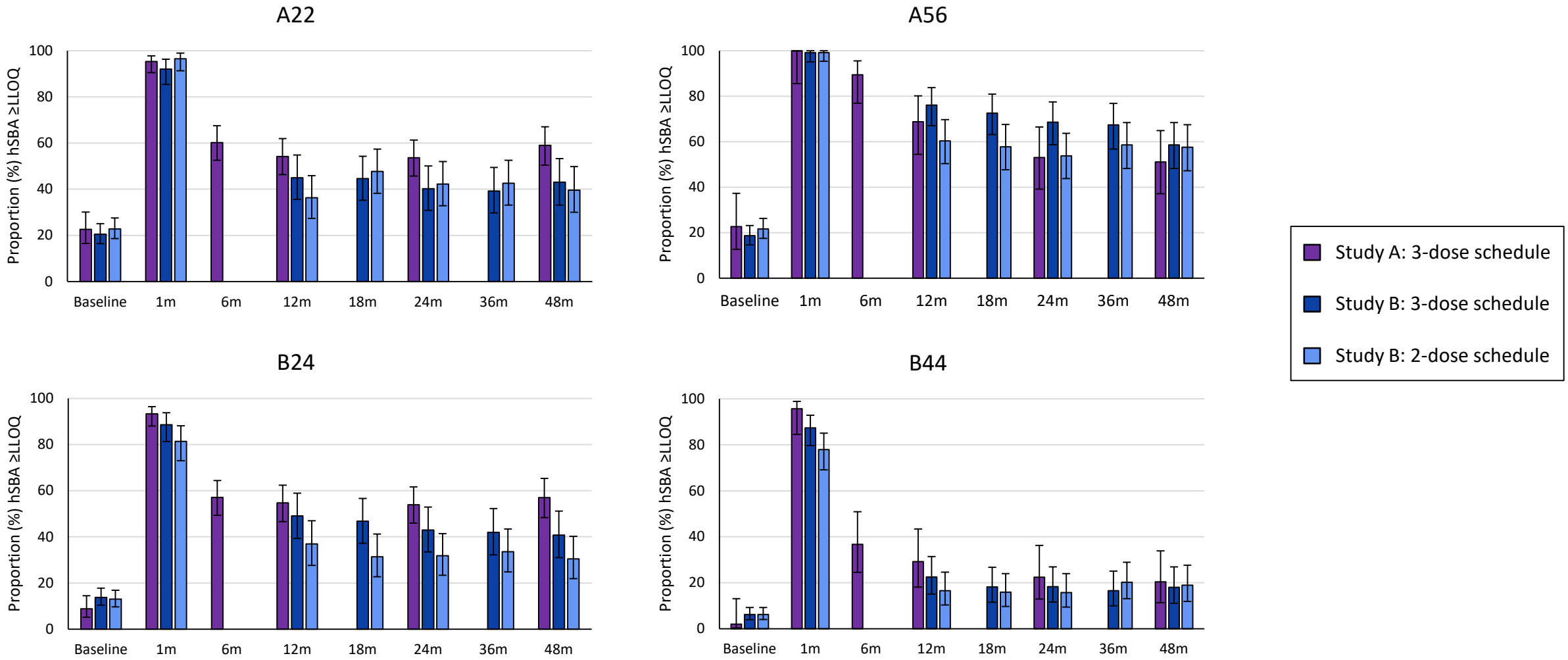
- Work Group considerations for MenB booster doses in persons at increased risk for serogroup B meningococcal disease

- Feedback from ACIP on potential policy options for MenB booster doses

Persistence of the immune response following a MenB primary series

MenB-FHbp

Immunogenicity and persistence of a MenB-FHbp primary series in healthy adolescents



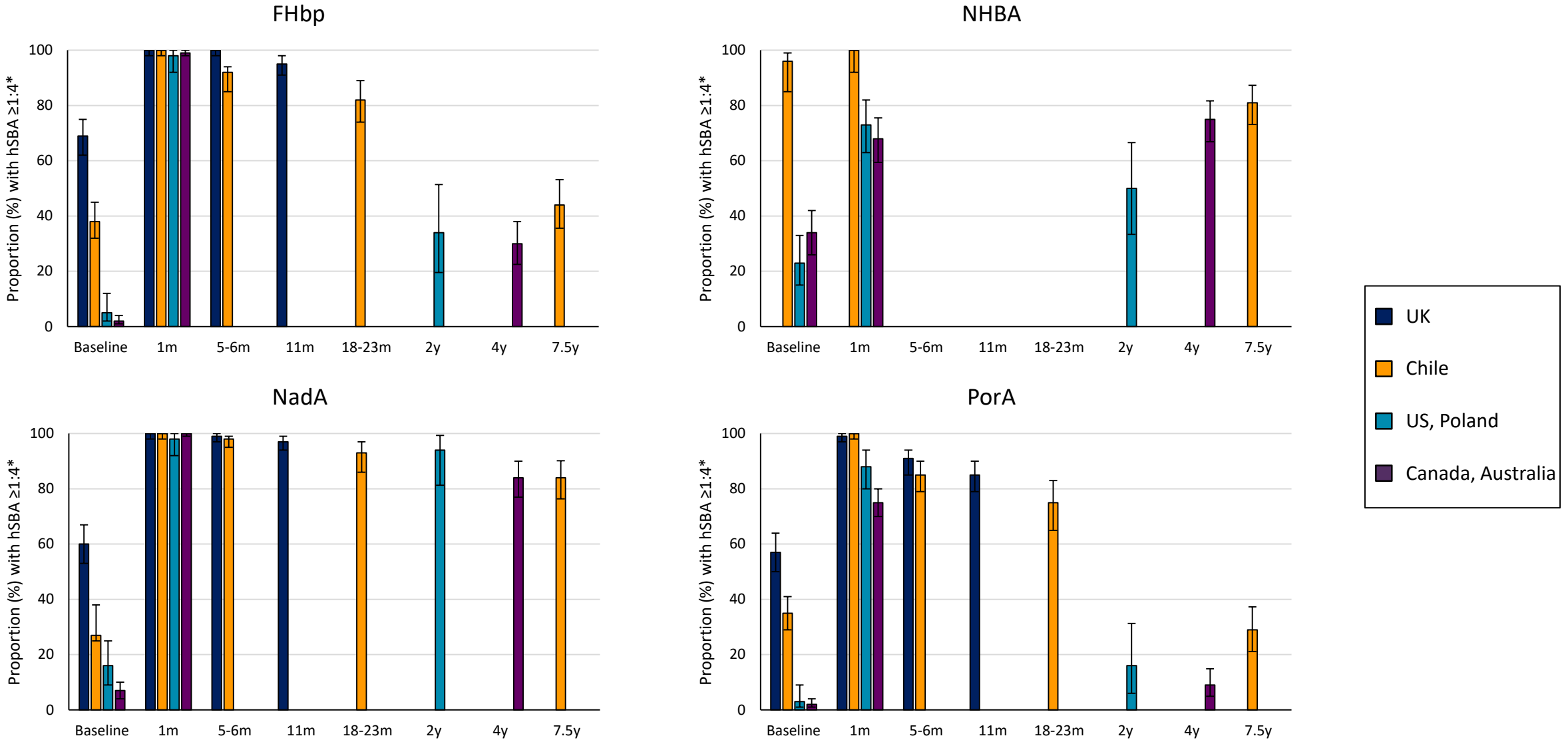
Adapted from Marshall H, Lancet Infectious Diseases 2017 and Vesikari, Vaccine 2019.
3-dose schedule: 0, 2, 6 months; 2-dose schedule: 0, 6 months; LLOQ=lower limit of quantification of the assay (1:8 for A56, B24, B44; 1:16 for

Work Group interpretation: Persistence of immune response following MenB-FHbp primary series

- **Work group interpretation: Antibodies wane by 12 months and then remain stable for up to 4 years in healthy adolescents.**

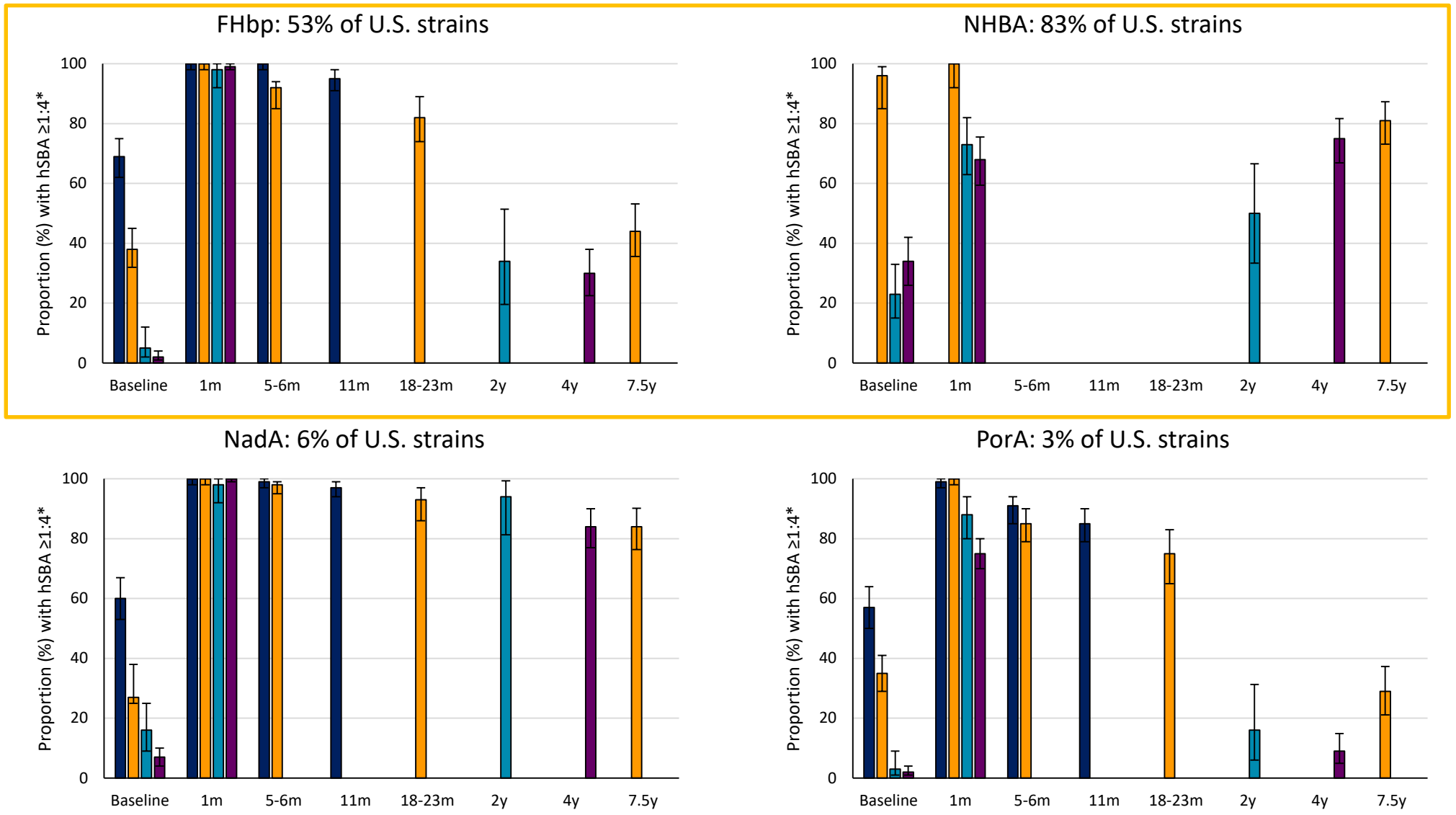
MenB-4C

Immunogenicity and persistence of MenB-4C primary series in healthy adolescents and adults



Adapted from Read RC, Vaccine 2017; Block SL, Vaccine 2015; Szenborn L, Pediatr Infect Dis J. 2018; Perrett KP, Vaccine 2015; Nolan T, Vaccine 2019; Santolaya ME, Lancet 2012; Watson PS, Expert Review of Vaccines 2019, and results on clinicaltrials.gov; * hSBA titer of 1:5 used in US/Poland study.

Immunogenicity and persistence of MenB-4C primary series in healthy adolescents and adults



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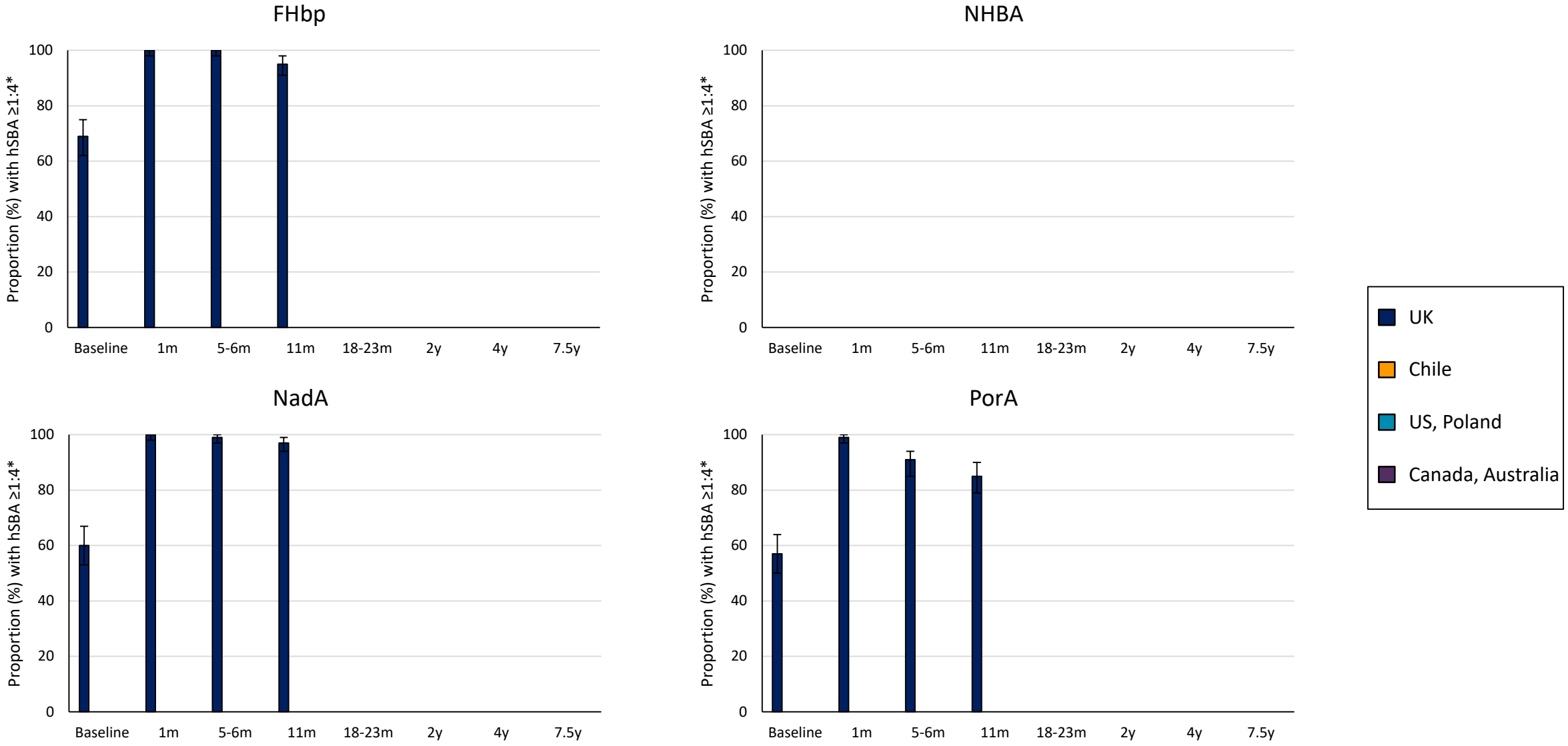
Immunogenicity and persistence of MenB-4C primary series in healthy adolescents and adults



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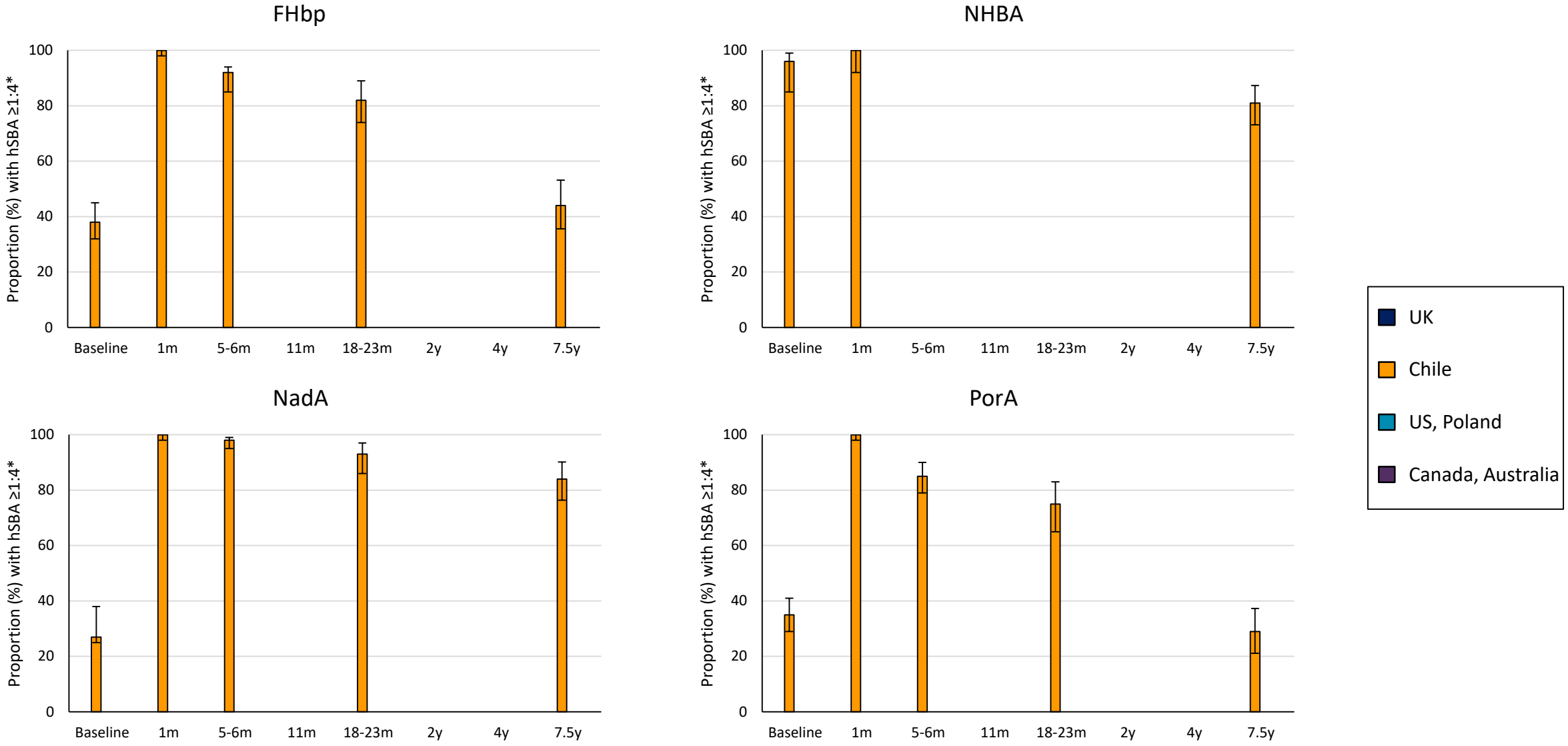
Immunogenicity and persistence of MenB-4C primary series in healthy adolescents and adults



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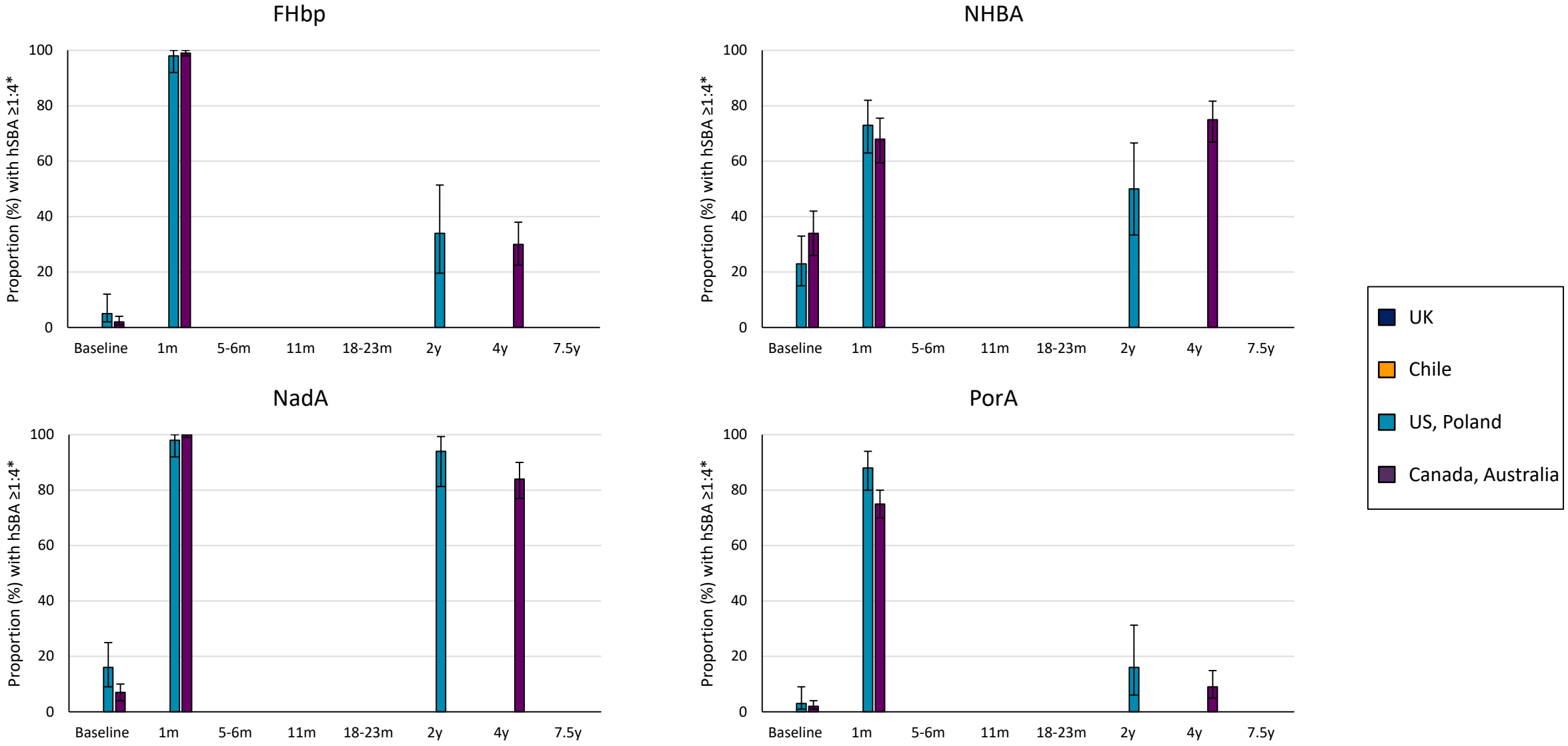
Immunogenicity and persistence of MenB-4C primary series in healthy adolescents and adults



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Work Group interpretation: Persistence of immune response following MenB-4C primary series

- Persistence difficult to generalize due to:
  - Heterogeneous results by vaccine antigen or between studies
  - Different time points assessed in different studies
  - Elevated baseline titers in two studies
  - Limited persistence data for NHBA

- **Work group interpretation: Antibodies wane by 2 years following the primary series in healthy adolescents and adults.**
  - Given limitations in data, cannot rule out earlier antibody waning.

Summary of Work Group interpretation for persistence of immune response following a MenB primary series

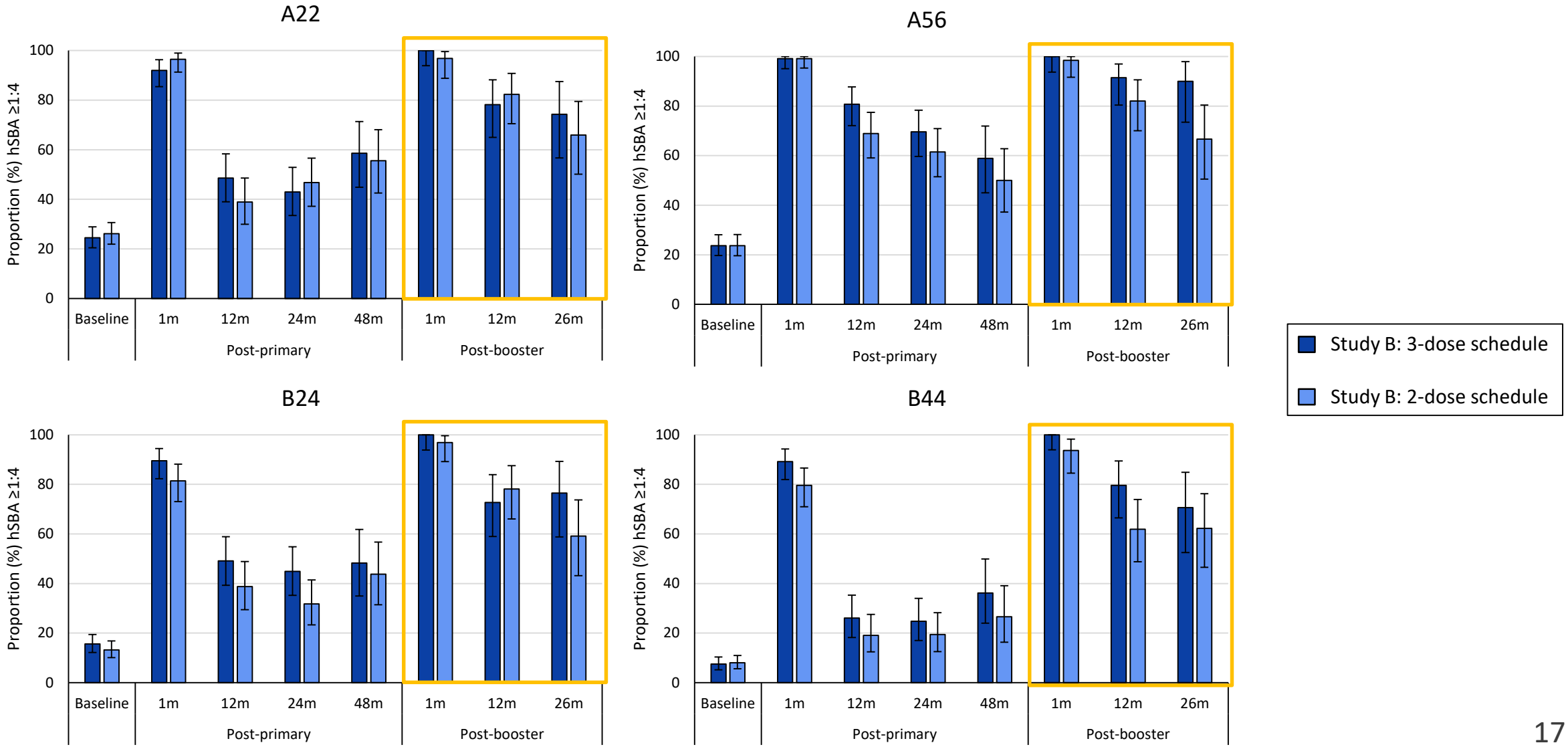
- Given the variable rate of waning between vaccines types and between studies, no generalization of antibody persistence following MenB primary vaccination.
  - Results from clinical trials cannot be directly compared between vaccine types.

- **Work group interpretation: By 1-2 years following primary MenB vaccination, booster vaccination is indicated in persons who remain at increased risk.**

Immunogenicity and persistence of a MenB booster dose

MenB-FHbp

Immunogenicity and persistence of a MenB-FHbp booster dose in healthy adolescents



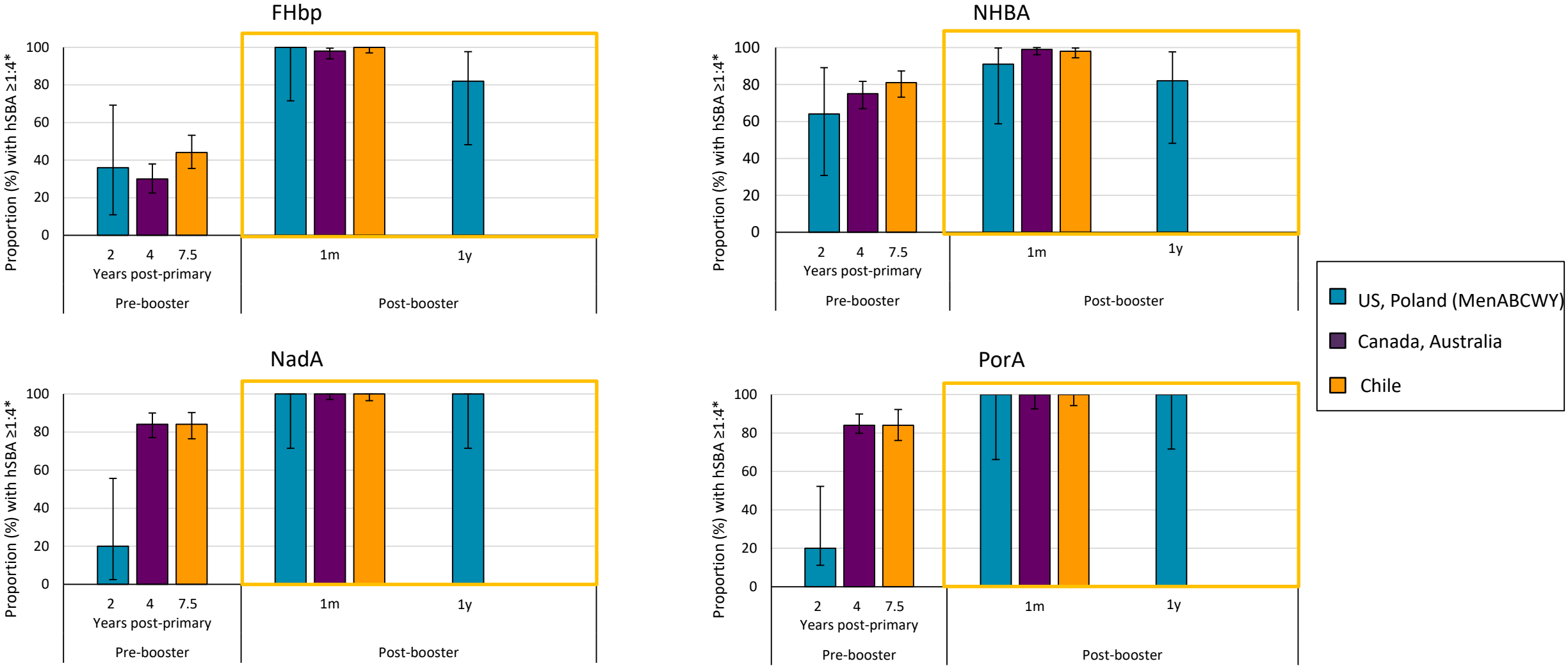
Adapted from Pfizer data presented to ACIP meningococcal work group. 3-dose schedule: 0, 2, 6 months; 2-dose schedule: 0, 6 months

Work Group interpretation: Immunogenicity and persistence of a MenB-FHbp booster dose

- **Work group interpretation: Immune response to a MenB-FHbp booster dose persists for at least 2 years in healthy adolescents.**

MenB-4C

Immunogenicity and persistence of a MenB-4C/MenABCWY booster dose in healthy adolescents and adults



Adapted from Szenborn L, Pediatr Infect Dis J. 2018; Nolan T, Vaccine 2019; Watson PS, Expert Review of Vaccines 2019;
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Work Group interpretation: Immunogenicity and persistence of a MenB-4C booster dose

- **Work group interpretation: Immune response to a MenB-4C booster likely persists for several years in healthy adolescents and adults.**
  - No further precision in estimate due to lack of observed data; modeled data suggests persistence through several years post-booster.

Summary of Work Group interpretation for persistence of immune response following a MenB booster dose

- MenB booster elicits robust immune response; persistence appears to exceed that of a MenB primary series.

- **Work group interpretation: Antibody persistence of a MenB booster dose is likely at least 2-3 years in healthy adolescents and adults.**

Summary of Work Group deliberations for MenB booster dose in persons at increased risk for serogroup B meningococcal disease

MenB Booster Doses – Why now?

- ACIP recommended a MenB primary series for persons at increased risk for serogroup B meningococcal disease 4 years ago.

- Starting in late 2018, several cases of serogroup B meningococcal disease reported in fully vaccinated persons (strain coverage analysis ongoing).

- Serogroup B outbreaks among college students continue to occur.
  - As MenB vaccination coverage in healthy adolescents increases, an increasing number of vaccinated college students will be exposed during an outbreak.

- No further data expected from manufacturers.
  - Additional data on MenB effectiveness and duration of protection in adolescents/adults or U.S. populations may take years to generate.

Summary of Work Group deliberations for MenB booster doses

- The Work Group reviewed data on:
  - Persistence of the immune response following a MenB primary series
  - Immunogenicity, persistence, and safety of a MenB booster dose

- The Work Group did not reach consensus on need for and timing of MenB booster doses.
  - A minority of Work Group members felt there was insufficient evidence on safety and efficacy of MenB booster doses to inform policy options.

- The following slides represent the views of the majority of work group members.

Work Group Interpretation: Need for MenB booster doses

- Meningococcal disease is a devastating infection and groups at increased risk represent small, targeted populations.

- Available evidence suggests waning of the primary series; a booster dose elicits a robust immune response.
  - Based on hSBA titers (serologic correlate of protection).

- **Work group interpretation: MenB booster vaccination is necessary to sustain protection against serogroup B meningococcal disease in persons who remain at increased risk.**

Work Group interpretation: Timing of MenB booster doses

- Studies indicate antibody waning 1-2 years following the primary series, and persistence of a booster dose for at least 2 years.

- Immunogenicity and persistence of MenB vaccination may be limited in persons with underlying conditions, especially complement deficiency/inhibitor use.

- **Work Group interpretation: MenB booster dose is indicated 1 year following completion of the primary series. Greater persistence expected after the booster dose; thus, a longer interval for repeat boosters may be considered.**

Work Group interpretation: Safety of MenB booster doses

- Clinical trials and other studies have demonstrated the safety of the MenB primary series.
  - Limited data available on booster doses; no serious adverse events reported.

- No data on safety in persons with underlying medical conditions.

- No data on repeat booster doses.

- **Work Group interpretation: Given the serious nature of meningococcal disease, potential benefits of MenB booster vaccination outweigh risks in persons at increased risk.**

Work Group interpretation: Programmatic considerations for MenB booster doses

- While harmonization with MenACWY booster doses desired, data do not support a 5-year interval for MenB booster doses.

- Booster dose recommendations for MenB-FHbp and MenB-4C should be harmonized to minimize unnecessary complexity.

- In outbreak situations, booster dose eligibility may be difficult to rapidly determine (e.g., completion of a primary series, vaccine type, and date of completion).
  - Additional clinical guidance will be necessary to facilitate booster dose implementation.

MenB booster policy options for persons at increased risk for serogroup B meningococcal disease

Policy considerations: Persons at increased risk due to complement deficiency/inhibitor use, asplenia, or microbiologists

Interval	Pros	Cons
Initial 1 year booster, followed by repeat boosters every 2-3 years	• Work Group felt this schedule best supported by available data. • Maximize protection in persons in whom immunogenicity/persistence may be reduced, or those with increased exposure. • Flexibility allows providers to harmonize MenACWY boosters with MenB booster every other time.	• More complicated than a standard interval. • May be more conservative than necessary.

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Standard interval every: • 2 years • 3 years	• More straightforward and prescriptive.	• May leave persons with insufficient protection for greater periods of time.

Policy considerations: Persons at increased risk due to a serogroup B outbreak

Interval	Pros	Cons
6 months	• Boost immunity prior to antibody waning, thus maximizing individual protection during a short-term period of increased exposure.	• More conservative management than other persons at increased risk, without substantial supportive evidence. • May send inaccurate message on duration of protection of MenB vaccines, leading to reduced vaccine confidence.

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1 year	• Most people expected to have protective antibodies at 1 year following primary series. • Consistent recommendation with other groups at increased risk.	• Because of variable rates of waning, some people may not have protective antibodies at 1 year to a particular strain.

Policy options for ACIP feedback

Group	Policy option
Persons with complement deficiency, complement inhibitor use, asplenia, or microbiologists	• MenB booster dose 1 year following completion of a MenB primary series, followed by MenB booster doses every 2-3 years thereafter, for as long as increased risk remains.
Persons at increased risk during an outbreak	• One-time MenB booster dose is recommended if it has been ≥1 year since completion of a MenB primary series. • A booster dose interval of ≥6 months may be considered by public health officials depending on the specific outbreak, vaccination strategy, and projected duration of elevated risk.

Discussion

- Does ACIP agree with the Work Group's interpretation on:
  - Need for booster doses?
  - Timing of booster doses (and should it be the same for both vaccines)?

- Are there any additional data that ACIP would like to see?

- Next steps: depending on ACIP feedback today, present policy options for a vote at an upcoming ACIP meeting.

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