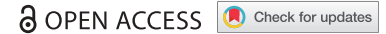


REVIEW



## A physician's guide to the 2-dose schedule of MenB-FHbp vaccine

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### ABSTRACT

Meningococcal serogroup B (MenB) is the predominant cause of invasive meningococcal disease in the United States, with older adolescents and young adults attending college at increased risk. Notably, MenB caused all meningococcal disease outbreaks at US colleges between 2011 and 2018. MenB disease is vaccine-preventable. The MenB-FHbp vaccine can be administered on a 2-dose (0 and 6 months) schedule to healthy adolescents and young adults or as a tailored 3-dose (0, 1–2, and 6 months) schedule for individuals at increased risk. This review focuses on the 2-dose schedule (0 and 6 months) of MenB-FHbp. Clinical evidence demonstrating strong and broadly protective immunogenicity in adolescents after primary vaccination, immune persistence up to 48 months post-primary vaccination (18–61% of subjects across schedules), and immune memory evidenced by robust response to a single booster dose are described. Implementation approaches to ensure adolescents and young adults are fully vaccinated against meningococcal disease are discussed.

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### Introduction



Invasive meningococcal disease (IMD) is a vaccine-preventable bacterial infection.<sup>1,2</sup> Meningococcal serogroup B (MenB) is currently the predominant IMD-causing serogroup among US adolescents and young adults, with college students at increased risk.<sup>3,4</sup> This review focuses on the more recently approved 2-dose schedule (administered at 0 and 6 months) of MenB-FHbp (Trumenba<sup>®</sup>; Pfizer Inc, Philadelphia, PA, USA), a MenB vaccine for healthy adolescents and young adults.<sup>5</sup> The clinical data supporting breadth of immune coverage of circulating pathogenic MenB strains, short- and long-term immunogenicity, and establishment of immune memory evidenced by booster responses are described. Implementation approaches to ensure that adolescents and young adults are fully vaccinated against meningococcal disease are also discussed.

### Meningococcal disease epidemiology

IMD, caused by the Gram-negative bacterium *Neisseria meningitidis*, is an uncommon but serious infection that progresses rapidly such that within 24 h, the clinical manifestations can progress from flu-like symptoms to septicemia and/or meningitis.<sup>1,6,7</sup> The nonspecific nature of early symptoms can often result in misdiagnosis or delay in treatment.<sup>7</sup> Even with appropriate medical care, meningococcal disease is fatal in approximately 8–15% of cases and up to 20% of survivors experience debilitating long-term physical and/or neurologic effects, such as limb amputation, hearing loss/impairment, and pain.<sup>6–8</sup>

Of the six serogroups known to cause meningococcal disease globally (A, B, C, W, X, and Y),<sup>8,9</sup> MenB is the leading cause of meningococcal disease in the United States.<sup>3</sup> According to data from the Centers for Disease Control and Prevention (CDC) Enhanced Meningococcal Disease Surveillance (EMDS), the incidence of meningococcal disease is highest in infants younger than 1 y (0.63 per 100,000 individuals), with a secondary peak occurring among 16- to 23-y-olds (0.20 per 100,000 individuals). In both groups, MenB is the leading cause of disease, accounting for 60% and 69% of cases, respectively.<sup>10</sup> MenB also has been the predominant cause of death due to meningococcal disease across all ages in the United States in 2015 and 2016 and the second leading cause of death in 2017 (deaths per year for 2015, 2016, and 2017 were 17, 14, and 16 for serogroup B; 8, 12, and 18 for serogroup C; 5, 6, and 3 for serogroup W; 10, 9, and 2 for serogroup Y; and 11, 7, and 6 for ungroupable/unknown, respectively).<sup>3,10,11</sup>

Meningococcal carriage peaks at approximately 19 y of age<sup>12</sup> and is a precondition for transmission and invasive disease.<sup>8,12</sup> In this epidemiologic context of heightened carriage and IMD among older adolescents, although the incidence is low, US college students are demonstrably at increased risk for MenB disease. Specifically, EMDS data from 2014 to 2016 revealed that 18- to 24-y-olds attending college have a threefold higher risk for MenB disease compared with those not attending college (relative risk [RR], 3.54 [95% confidence interval (CI), 2.21–5.41]); in contrast, there was no difference in the combined risk of disease caused by serogroups C, W, and Y between college students and those

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Personal classification: Infectious disease

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not attending college (RR, 0.56 [95% CI, 0.27–1.14]).<sup>13</sup> MenB has caused all US college outbreaks of meningococcal disease from 2011 to 2018.<sup>14–17</sup> Even after excluding campus outbreak cases, college students' risk of disease remains elevated (RR, 2.76 [95% CI, 1.73–4.44]),<sup>13</sup> although the majority (~68%) of MenB cases occur sporadically among 18- to 24-y-olds and are not associated with outbreaks.<sup>13</sup>

### Meningococcal vaccines and Advisory Committee on Immunization Practices recommendations

Two classes of vaccines help protect against meningococcal disease: quadrivalent conjugate MenACWY vaccines, which are based on capsular polysaccharide A, C, W, and Y antigens coupled to carrier proteins,<sup>18–20</sup> and MenB vaccines, which are based on subcapsular protein antigens.<sup>5,21</sup>

Quadrivalent MenACWY vaccines have been licensed in the United States since 2005<sup>1</sup> and are universally recommended (Category A<sup>22</sup>) by the US Advisory Committee on Immunization Practices (ACIP) for all 11- to 12-y-olds, with a booster dose at 16 y of age (Table 1).<sup>1</sup> Two available MenACWY vaccines are MenACWY-CRM (Menveo®, GSK Vaccines Srl, Sovicille, Italy) and MenACWY-D (Menactra®, Sanofi Pasteur Inc., Swiftwater, PA, USA).<sup>18,19</sup>

MenB vaccines were first licensed in the United States in 2014 under the US Food and Drug Administration (FDA) accelerated approval process in response to two US college-based MenB outbreaks in 2013.<sup>2</sup> Two products are currently approved for use in adolescents and young adults 10–25 y of age: MenB-FHbp and MenB-4C (Bexsero®; GlaxoSmithKline Vaccines, Srl, Siena, Italy).<sup>5,21</sup> MenB-FHbp is composed of two recombinant lipidated FHbp variants, one each from subfamily A and subfamily B.<sup>5</sup> MenB-FHbp is administered in either a 2-dose schedule (at 0 and 6 months) to healthy individuals who are not at increased disease risk or a tailored

3-dose schedule (at 0, 1–2, and 6 months) for those at increased risk of meningococcal disease and in response to MenB disease outbreaks, to provide earlier protection and maximize short-term immunogenicity (Figure 1).<sup>23</sup> MenB-4C is composed of recombinant proteins: neisserial adhesin A (NadA), neisserial heparin-binding antigen (NHBA), non-lipidated FHbp subfamily B, and outer membrane vesicles (OMVs) containing PorA P1.4 (VR2).<sup>21,24</sup> MenB-4C is administered in a 2-dose schedule with at least 1 month between doses.<sup>21</sup> Because the two MenB vaccines are compositionally distinct and have different immunization schedules, they are not interchangeable and ACIP does not state a preference; once a vaccination series is started, the same product must be used to complete the series.<sup>23</sup> MenB vaccines have an ACIP Category A recommendation for individuals ≥10 y of age who are at increased risk for MenB disease, such as those with asplenia, complement deficiency, or laboratory or outbreak exposure,<sup>2</sup> and a Category B recommendation (individual clinical decision-making in consultation with a health-care provider) for healthy individuals 16–23 y of age (16–18 y preferred)<sup>23,25</sup> (Table 1); currently, there are no recommendations regarding booster dosing with MenB vaccines.

### How was the breadth of MenB-FHbp coverage evaluated?

Vaccine-elicited protection against meningococcal infection is evaluated by the *in vitro* serum bactericidal assay using human complement (hSBA), which measures antibody and complement-mediated killing of meningococcal test strains.<sup>26</sup> An hSBA titer (i.e., the highest serum dilution that kills ≥50% of test bacteria<sup>26</sup>) of ≥1:4 is widely accepted by the US FDA and other regulators as a correlate of protection against IMD,<sup>27–30</sup> and has been used for licensure of MenACWY, MenB, and other meningococcal vaccines.<sup>5,18,19,21</sup> The hSBA titer for protein-

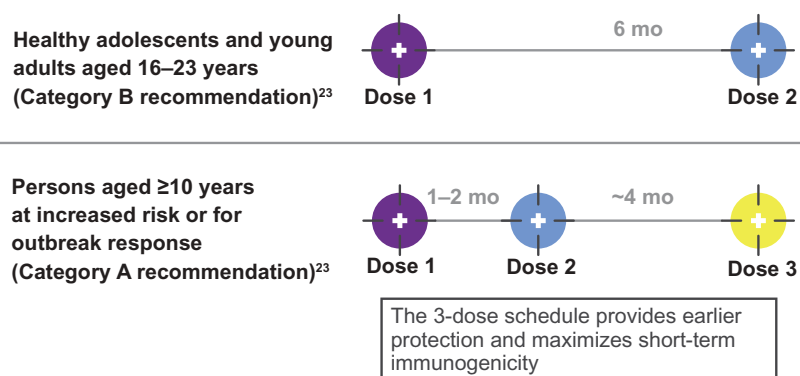
**Table 1.** Summary of ACIP recommendations for meningococcal vaccination and dosing of adolescents.

Vaccine	Target group	Primary dosing	Booster dose	Category <sup>a</sup>
MenB <sup>2,23,25</sup>	Healthy individuals aged 16–23 y (16–18 y preferred)	2 doses	–	B
	Individuals aged ≥10 y at risk due to <ul style="list-style-type: none"> <li>● Persistent complement component deficiencies</li> <li>● Anatomic or functional asplenia</li> <li>● Routine exposure as a microbiologist</li> <li>● Serogroup B meningococcal disease outbreak</li> </ul>	2 or 3 doses (vaccine-dependent)	–	A
MenACWY <sup>1</sup>	Healthy individuals aged 11–18 y (11–12 y preferred) <sup>b</sup>	1 dose	1 dose, if primary dosing given before age 16 y	A
	Individuals with <ul style="list-style-type: none"> <li>● Persistent complement deficiencies</li> <li>● Functional or anatomic asplenia</li> </ul>	2 doses	1 dose 5 y after primary dosing and repeated every 5 y thereafter	A
	Individuals who are <ul style="list-style-type: none"> <li>● First-year college students aged ≤21 y and living in residential housing</li> <li>● Traveling to or residents of countries where meningococcal disease is epidemic or hyper-endemic</li> <li>● At risk during an outbreak attributed to a vaccine serogroup</li> <li>● Are microbiologists routinely exposed to <i>Neisseria meningitidis</i></li> </ul>	1 dose	1 dose 5 y after primary dosing and repeated every 5 y thereafter <sup>b</sup>	A

ACIP = Advisory Committee on Immunization Practices; MenACWY = meningococcal serogroups A, C, W, and Y vaccine; MenB = meningococcal serogroup B vaccine.

<sup>a</sup>ACIP Category A represents a recommendation for all those in an age- or risk factor-based group; Category B is a recommendation for individual clinical decision-making.

<sup>b</sup>For individuals who remain at increased risk.



**Figure 1.** US Advisory Committee on Immunization Practices recommendations for MenB-FHbp 2-dose and 3-dose schedules.<sup>23</sup> For the 2-dose schedule: if dose 2 is administered <6 months after dose 1, a third dose should be given ≥4 months after dose 2. For the 3-dose schedule: if dose 2 is administered ≥6 months after dose 1, a third dose does not need to be administered.

based vaccines is influenced by antigen sequence variation and surface protein expression level in circulating meningococcal strains.<sup>26</sup> Therefore, choice of test strains for use in hSBAs to determine breadth of coverage is critical for MenB vaccines.

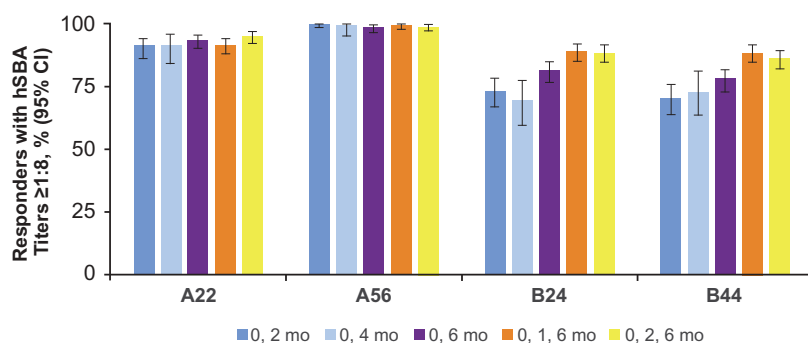
FHbp is a surface-exposed protein present on nearly all meningococcal strains that consists of two distinct subfamilies (A and B);<sup>31</sup> the bivalent MenB-FHbp vaccine contains both FHbp-A and B proteins.<sup>32</sup> Furthermore, >91% of invasive MenB strains express FHbp at sufficient levels to be susceptible to MenB-FHbp-elicited bactericidal antibodies.<sup>33</sup> MenB-FHbp-elicited protective responses were evaluated in clinical studies by measuring hSBA responses against a diverse panel of four primary MenB test strains (A22 and A56 from FHbp subfamily A and B24 and B44 from FHbp subfamily B) and ten additional strains. These 14 test strains differ from the vaccine antigens and collectively represent >83% epidemiologic coverage of circulating disease strains in the United States.<sup>34</sup> In pivotal phase 3 studies, responses to the four primary strains predicted responses to the ten additional strains.<sup>32</sup>

### What is the clinical evidence supporting the 2-dose series of MenB-FHbp?

The immunogenicity and safety of MenB-FHbp has thus far been evaluated in 11 published clinical studies wherein more than 15,000 adolescents and young adults received the vaccine.<sup>35</sup> These studies evaluated 2- and 3-dose schedules,

long-term immunogenicity, booster dose responses, and co-administration with vaccines commonly given to adolescents, including MenACWY-D, Tdap (Adacel<sup>®</sup>, Sanofi Pasteur Inc., Swiftwater, PA, USA), 4vHPV (Gardasil<sup>®</sup>, Merck & Co, Inc., Whitehouse Station, NJ, USA), and Tdap/IPV (Repevax<sup>®</sup>, Sanofi Pasteur, Lyon, France) vaccines.<sup>36–38</sup>

Clinical data supporting the MenB-FHbp 2-dose schedule were from a phase 2 randomized clinical study in healthy adolescents aged 11–18 y that evaluated multiple schedules: 2 doses (administered at 0 and 2 months, 0 and 4 months, or 0 and 6 months) or 3 doses (at 0, 1, and 6 months or 0, 2, and 6 months).<sup>39</sup> An hSBA titer ≥1:8, which is more stringent than the recognized correlate of protection of ≥1:4,<sup>27–29</sup> was used as the primary end point of the study.<sup>39</sup> Before vaccination, 4.4–28.1% of subjects had hSBA titers ≥1:8.<sup>40</sup> Upon completion of a 2-dose MenB-FHbp series, broadly protective responses were elicited in 70.1–100% of subjects against the diverse panel of four primary strains (Figure 2).<sup>39</sup> In the same study, similar response rates (86.1–99.4%) were observed for both of the 3-dose series. For all assessed dosing regimens in this study, statistically significant increases in hSBA titers ≥1:8 were observed from before vaccination to 1 month following completion of the MenB-FHbp series. In addition, similar percentages of subjects achieved greater than or equal to fourfold increases in hSBA titers over baseline at 1 month after completion of the vaccination series: 64.5–90.1% for the 2-dose series and 74.1–93.8% for



**Figure 2.** Clinical data supporting MenB-FHbp 2- and 3-dose schedules to elicit protective responses against diverse primary strain panels.<sup>39</sup> Percentage of subjects demonstrating a protective hSBA titer of ≥1:8 against a diverse panel of test strains is shown from sera collected 1 month after the final dose (after the second dose for the 2-dose schedules [0 and 2 months, 0 and 4 months, or 0 and 6 months] and after the third dose for the 3-dose schedules [0, 1, and 6 months or 0, 2, and 6 months]). hSBA = serum bactericidal assay using human complement.

the 3-dose series.<sup>5</sup> Importantly, the composite response for all four primary strains combined was similar for the 2-dose schedule (0 and 6 months; 72.9% [95% CI, 65.9–79.1]) and 3-dose schedule (0, 1 and 6 months; 80.3% [95% CI, 73.7–85.9]; 0, 2 and 6 months; 81.8% [95% CI, 74.9–87.4]) at 1 month after completion of the primary vaccination series.<sup>5</sup> Reports of adverse events were similar across the dosing schedules tested, were mostly mild or moderate in severity, and did not potentiate with subsequent doses.<sup>39</sup> Notably, immunogenicity of the 2-dose series generally increased with the length of interval between the 2 doses and was highest in those receiving vaccine at 0 and 6 months (Figure 2).<sup>39</sup>

Vaccine-elicited immune responses peak after vaccination and then progressively wane with time.<sup>41</sup> Therefore, the long-term immunogenicity of MenB-FHbp was evaluated over a period of 4 y after primary vaccination with either the 2-dose or 3-dose schedule, followed by a single booster dose to evaluate immune memory; hSBA responses against the same diverse panel of four primary strains were measured.<sup>23</sup> Regardless of the dosing schedule used, the proportion of MenB-FHbp recipients with protective antibodies (hSBA titer  $\geq 1:4$ ) across primary test strains and dose schedules peaked 1 month after primary vaccination (78.9–99.1% of subjects<sup>23</sup>) then declined over the course of 12 months (16.5–76.1% of subjects achieved hSBA titers  $\geq 1:8$  or 1:16 at 12 months<sup>42</sup>) and subsequently remained stable for up to 48 months (18.0–61.3% of subjects achieved hSBA titers  $\geq 1:8$  or 1:16 at 48 months<sup>42</sup>) (Figure 3).<sup>23</sup> After administration of a single MenB-FHbp booster dose approximately 48 months after the primary series, hSBA response rates met or exceeded those at 1 month after the primary series, exemplifying a strong and broadly protective anamnestic response.<sup>23</sup> Data on the long-term persistence of the antibody response to the MenB-FHbp booster dose are not yet published.

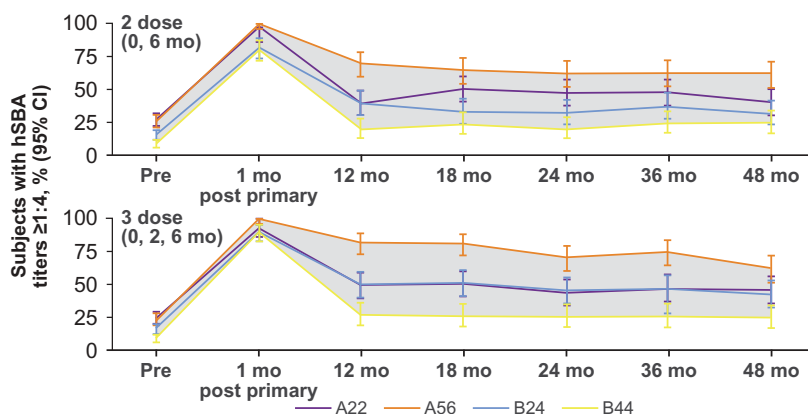
### What is the clinical evidence for the protective response of MenB-FHbp and MenB-4c against antigenically diverse circulating strains?

Antibody response to MenB vaccines is affected by the degree of match between the vaccine antigens and circulating pathogenic strains, immunogenicity of vaccine antigen(s), and immune

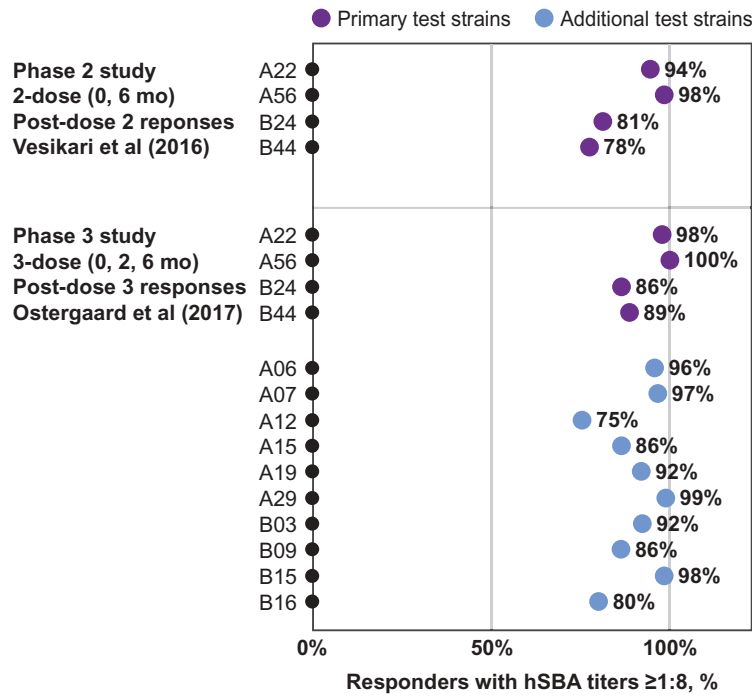
responses of the vaccinated individual. The sub-capsular proteins in MenB vaccines have multiple sequence variants and have differing surface expression levels on circulating pathogenic strains,<sup>26</sup> both of which affect the bactericidal activity of vaccine-elicited antibodies. Therefore, to demonstrate broad protective coverage while targeting an antigen that has variability, it is essential to evaluate each MenB vaccine by hSBA against a panel of diverse strains that differ from the vaccine antigen and are epidemiologically representative (i.e., outbreak and non-outbreak/endemic strains).

MenB-FHbp demonstrated consistent responses against diverse panels of test strains with 2-dose and 3-dose schedules as seen in the phase 2 and phase 3 studies of the clinical development program (Figure 4).<sup>32,39</sup> Among adolescents immunized with a 3-dose MenB-FHbp series, additional clinical studies have reported similar protective responses after 2 or 3 doses, including a larger panel of 27 diverse MenB strains containing isolates from two US college outbreaks, as well as a panel of six French outbreak strains.<sup>43–46</sup> An independent clinical study of 17 laboratory and health-care workers immunized with a 3-dose MenB-FHbp series evaluated hSBA activity (titer  $\geq 1:4$ ) against a large and diverse panel of endemic and hyper-endemic MenB disease-causing strains and strains from six US college outbreaks; this study found protective responses consistent with those seen within the MenB-FHbp clinical program (Figure 5 shows a subset of these strains, including four from US college outbreaks).<sup>46</sup> Taken together, these data provide continued confidence that the MenB-FHbp vaccine 2-dose regimen provides sufficient broad and sustained protective coverage against the diversity of circulating MenB strains in comparison with the 3-dose regimen.

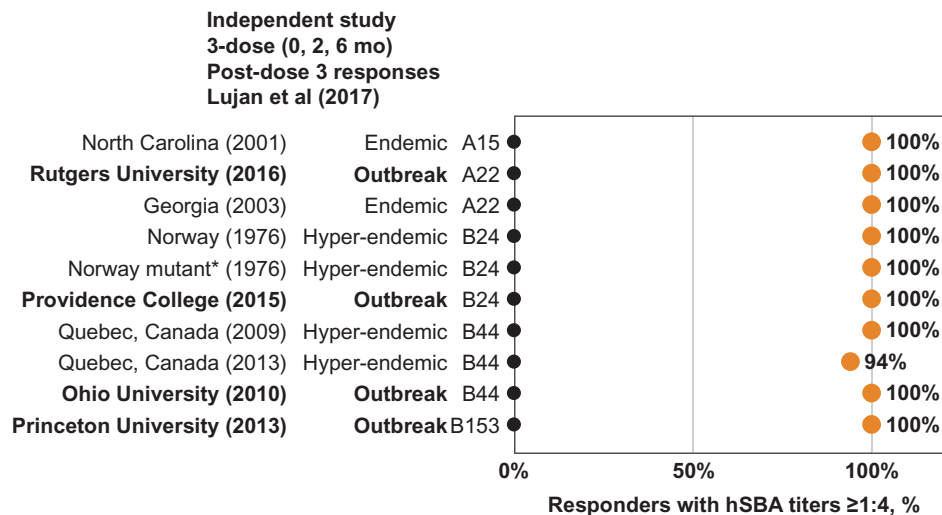
The MenB-4C vaccine contains NHBA, FHbp-subfamily B, NadA, and OMV (containing PorA P1.4 [VR2]).<sup>21,24</sup> These protein antigens are present in approximately 98%, 60%, 30%, and 5.3%, respectively, of disease-causing MenB strains in the United States based on evaluation of gene presence and protein expression in a panel of US invasive clinical isolates grown *in vitro* at the Bacterial Meningitis Laboratory of the CDC.<sup>47,48</sup> MenB-4C clinical studies for licensure evaluated hSBA responses with closely matched, antigen-specific (vaccine homologous) indicator strains rather than strain panels,



**Figure 3.** Persistence of hSBA responses up to 48 months after primary vaccination against the four primary test strains for the 2-dose (0 and 6 months) and 3-dose (0, 2, and 6 months) MenB-FHbp schedules.<sup>23</sup> Because the 4-strain test panel is epidemiologically representative of diverse, circulating disease-causing strains,<sup>34</sup> the shaded area between the curves represents the range of subjects with protective immune responses against most circulating MenB strains. hSBA = serum bactericidal assay using human complement.



**Figure 4.** MenB-FHbp shows consistent protective responses across diverse MenB strains – including FHbp subfamilies A and B. Point estimates from two clinical studies showing the percentage of MenB-FHbp recipients demonstrating a protective hSBA titer  $\geq 1:8$  against a diverse panels of test strains after vaccination with the MenB-FHbp 2-dose (0 and 6 months)<sup>39,40</sup> or 3-dose (0, 2, and 6 months) schedule.<sup>32</sup> The primary test panel of four strains (two from FHbp subfamily A and two from FHbp subfamily B) was evaluated in both phase 2 and phase 3 studies shown; a panel of ten additional test strains (six from FHbp subfamily A and four from FHbp subfamily B) was evaluated in the phase 3 study with the 3-dose schedule. For the phase 3 study, data in adolescents are shown.<sup>32</sup>



**Figure 5.** MenB-FHbp shows consistent protective responses across diverse MenB strains – including FHbp subfamilies A and B and outbreak strains. Point estimates from an independent clinical study showing the percentage of MenB-FHbp recipients demonstrating a protective hSBA titer of  $\geq 1:4$  against a diverse panel of test strains (three FHbp subfamily A and seven FHbp subfamily B strains) after vaccination with MenB-FHbp 3-dose (0, 2, and 6 months) series.<sup>46</sup> The full test panel (six FHbp subfamily A and eight FHbp subfamily B strains) included endemic and hyper-endemic MenB disease-causing strains, and strains from campus outbreaks in the United States; a subset of that test panel, for which percentages of subjects showing immune titers  $\geq 1:4$  were reported in the publication, is shown. \*Mutant Norway 1976 strain expresses 50% less FHbp subfamily B. FHbp = factor H binding protein; hSBA = serum bactericidal assay using human complement.

for three of the four antigens (no strain was evaluated for the NHBA antigen for US licensure).<sup>49</sup> Two clinical studies reported that after completing the 2-dose schedule, protective pre- and post-vaccination responses increased from 2–7% to 70–100% among 11- to 17-y-old subjects<sup>50</sup> and from 4–5% to 82–93% among 10- to 25-y-old subjects (an hSBA titer  $\geq 1:5$  was used, which is more stringent than the accepted immune

correlate of 1:4).<sup>51</sup> Two additional studies reported that after completing the 2-dose schedule, pre- and post-vaccination responses increased from 34–44% to >99% among 11- to 17-y-olds<sup>52</sup> and from 57–69% to 99–100% among 18- to 24-y-old subjects (hSBA titer  $\geq 1:4$ ).<sup>53</sup> An independent, real-world study examined pre- and post-vaccination immune responses to the MenB-4C 2-dose schedule (administered at 0 and

1 month) deployed in the 2013–2014 Princeton University MenB outbreak.<sup>54</sup> This study showed that 83–98% of those who received MenB-4C seroconverted against two antigen-specific indicator strains (greater than or equal to fourfold rise in hSBA titer) and 20% of MenB-4C recipients seroconverted against the actual MenB outbreak strain.<sup>55</sup> Lack of hSBA data against MenB strain panels makes it difficult to assess breadth of immune coverage by MenB-4C, though vaccine effectiveness data among infants (82.9%; 95% CI, 24.1–95.2) have been reported from the first 10 months of the United Kingdom's national immunization program.<sup>56</sup>

### What are known barriers to adolescent immunization delivery and what are potential solutions to these barriers?

The adolescent population is difficult to reach for immunization: they are generally healthy and tend to have fewer medical visits as they move through their teens, with a decline in number of visits at around 16 y of age.<sup>57</sup> According to the 2014 Medical Expenditure Panel Survey, only 54% of those aged 9–21 y saw a primary care physician,<sup>57</sup> which is likely the care provider from whom the majority of adolescents receive vaccines. Individuals in this age group are also transitioning between providers: pediatricians cared for the majority of 11- to 17-y-olds and family practitioners saw most 18- to 21-y-olds.<sup>57</sup> Parents expect their children's physicians to provide guidance on adolescent vaccinations,<sup>58</sup> but studies have shown that these physicians struggle to understand the reasons for different types of meningococcal vaccines and the ACIP meningococcal vaccine recommendations.<sup>59</sup> For MenB vaccines, the ACIP Category B recommendation requires individual clinical decision-making in the context of a patient-provider discussion,<sup>60</sup> and several studies have shown that this recommendation is especially confusing for health-care providers to implement.<sup>59,61–63</sup> However, it is noteworthy that the American Academy of Pediatrics states that not discussing MenB disease and the available licensed vaccines with families is not an option.<sup>60</sup> Taken together, these factors likely contribute to the disparate immunization rates for adolescent vaccines. According to the most recent (2017) National Immunization Survey–Teen data, the immunization rate for multidose MenB vaccines, collected 2 y after the initial (2015) recommendations for vaccinating healthy persons 16–23 y of age (16–18 y preferred), was approximately 14.5% for ≥1 dose among 17-y-olds.<sup>64</sup> For context, the vaccination rate for the primary MenACWY dose (at 11–12 y<sup>65</sup>) is 84% among 13-y-olds, but the rate for the booster dose (at 16 y<sup>65</sup>) is only 44% among 17-y-olds.<sup>64</sup> In addition, 48.6% of adolescents are now up-to-date with the human papilloma virus (HPV) 2-dose vaccination series (at 11–12 y of age).<sup>64</sup> Single-dose Tdap<sup>65</sup> remains the benchmark, with an 88.7% vaccination rate for ≥1 dose among adolescents 13–17 y of age. It is notable that MenB vaccines are comparatively newer, have a multidose regimen, and have a non-routine ACIP recommendation for a population that is known to be a challenge to vaccinate, all of which can affect immunization rates.

Age-based immunization platforms are catalysts for vaccination because they provide a forum for discussion and create an

expectation of vaccination during the medical visit. The CDC's nascent immunization platform for 16-y-olds is an essential tool for improving adolescent immunization delivery, akin to the successful immunization platform for 11-y-olds that was created in 1996 and has helped improve adolescent vaccination rates substantially.<sup>66</sup> An immunization platform for 16-y-olds is strongly supported by the Society for Adolescent Health and Medicine, the Immunization Action Coalition, and the Adolescent Immunization Initiative.<sup>66–68</sup> In addition, the 2017–2018 CDC Childhood Immunization Schedule newly highlights the immunization platform at 16 y of age as a shaded column to increase awareness among providers and parents that two meningococcal vaccines (MenACWY and MenB) are recommended for that age group.<sup>65,69</sup> The MenB-FHbp 0- and 6-month schedule is comparable to other vaccines such as HPV and hepatitis A that are also given on a 0- and 6-month schedule and are familiar to providers,<sup>65</sup> and a 2-dose series (rather than 3-dose) can potentially help improve adherence and series completion. Opportunities for improving adolescent vaccination rates include discussing vaccination at sports and camp physicals, during annual administration of flu vaccines, at acute care and follow-up visits, and during routine visits for chronic illness.<sup>67</sup> In addition, reminding parents and providers that all ACIP-recommended vaccinations (Category A or B) are covered currently under the Affordable Care Act would be helpful.<sup>60</sup>

### Conclusion

Vaccination remains the best means of preventing MenB disease, which is currently the predominant IMD-causing serogroup among US adolescents and young adults; college students are especially at increased risk. Vaccination with both MenACWY and MenB is needed for complete protection against the most common serogroups causing meningococcal disease. For healthy adolescents, the licensed MenB-FHbp 2-dose regimen (0 and 6 months) was deemed to provide sufficient protection in comparison with the 3-dose regimen, is recommended by ACIP, and can be conveniently administered as part of the CDC's 16-y-old immunization platform along with the MenACWY booster dose. For those at increased risk congenitally (e.g., due to asplenia or complement deficiency) or situationally (e.g., due to outbreaks), the tailored 3-dose regimen (0, 1–2, and 6 months) of MenB-FHbp provides rapid protection and maximizes short-term immunogenicity. As summarized herein, substantial clinical data are available on the breadth and duration of broad immunity elicited by the MenB-FHbp 2-dose series against genetically diverse MenB disease-causing strains and on the concomitant use of MenB-FHbp with other adolescent vaccines.

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## Disclosure of potential conflicts of interest

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