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REVIEW

Past, present, and future policy considerations regarding meningococcal vaccination in the United States

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ABSTRACT

Introduction: In 2005, the United States Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination against invasive meningococcal disease (IMD) caused by serogroups A, C, W, and Y (MenACWY) for all 11–12-year-olds, as well as 2–10-year-olds at high risk. In 2010, a booster dose was recommended for all 16-year-olds, as well as for high-risk patients every 3–5 years. In 2015, optional (as opposed to routine) vaccination against meningococcal serogroup B (MenB) at the preferred age of 16–18 years was recommended (Category B, later changed to shared clinical decision-making). In 2023, a vaccine (MenABCWY) against the five serogroups primarily responsible for IMD in the U.S. became available.

Areas covered: This review summarizes the evolution of public policy that led to each milestone vaccine recommendation, reviews epidemiologic data published following the recommendations, and discusses the current state of meningococcal immunization policy.

Expert opinion: The use of MenABCWY has the potential to consolidate policy, improve coverage rates for the five serogroups, address disparities in vaccination coverage, and simplify vaccine delivery.

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ACIP; invasive meningococcal disease; meningococcal vaccination; MenACWY; MenB; MenABCWY; public health policy; vaccination policy

1. Introduction

Vaccination against invasive meningococcal disease (IMD; a rapidly progressive, life-threatening illness caused by *Neisseria meningitidis* infection, principally causing fulminant sepsis and meningitis) [1] has been recommended in the United States (U.S.) for adolescents since 2005 [2]. While IMD is uncommon, the rationale for routine vaccination rests upon the unpredictable occurrence of the disease, its rapid progressive course, high fatality rate despite appropriate therapy, and severe sequelae in survivors [3–6].

IMD in the U.S. is typically caused by five serogroups (A, B, C, W, and Y) defined by their capsular polysaccharides [7]. The original 2005 policy for the prevention of IMD among adolescents, namely routine vaccination against serogroups A, C, W, and Y (MenACWY), was set when the incidence of disease was approximately 0.61 per 100,000 and only vaccines against serogroups A, C, W, and Y were available [8]. Over the ensuing 2 decades, there were four major developments: 1) the overall incidence of IMD plummeted, partially due to the MenACWY program [8]; 2) serogroup B emerged as the most common cause of IMD in adolescents and young adults [8,9]; 3) vaccines against serogroup B (MenB) became available and were recommended as an option [10]; and, recently, 4) a vaccine protecting against all five serogroups (MenABCWY) was licensed [11]. In light of these changes, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) has signaled that it is time to comprehensively reevaluate meningococcal vaccination recommendations for adolescents and young adults [12].

MenACWY has been recommended for all adolescents at 11–12 years of age since 2005, with a booster at 16 years of age recommended since 2010 [13–15]. MenB has been recommended for 16–23-year-olds (16–18 years of age preferred) since 2015 based on shared clinical decision-making (SCDM) [13,16]. The SCDM recommendations are individually based and are intended to be flexible, considering the characteristics, values, and preferences of patients, together with the clinical discretion of healthcare providers [17]. In addition, both MenACWY and MenB are routinely recommended for other individuals at increased risk for meningococcal disease (the minimum age is 2 months and 10 years, respectively) [13], but this review focuses on the recommendations for healthy adolescents and young adults.

In October 2023, the ACIP recommended MenABCWY as an option when both MenACWY and MenB would be given on the same day. In practice, this recommendation would be most commonly applicable to healthy 16-year-olds due for their MenACWY booster who have elected to initiate the MenB series under SCDM [11,13], as well as certain high-risk individuals when the timing of doses for MenACWY and MenB coincide [13].

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Article highlights

- Invasive meningococcal disease (IMD) in the United States (U.S.) is uncommon but serious.
- MenACWY is routinely recommended for adolescents and young adults and MenB is considered 'optional,' even though IMD caused by serogroup B is more prevalent in the U.S., compared with IMD caused by other serogroups.
- A combination MenABCWY vaccine is now available.
- Public policy regarding vaccine prevention of IMD is likely to evolve in the context of different recommendations for the existing vaccines, the availability of MenABCWY, emerging data on implementation, and changing epidemiology.

The current ACIP recommendations, which evolved over the past two decades through a stepwise approach, were punctuated by the milestone years of 2005, 2010, and 2015, and most recently, 2023. These changes were motivated by the prevailing epidemiology of IMD, the availability of new vaccines, new safety and immunogenicity data, cost-effectiveness models, the feasibility of various vaccination regimens, and the opinions of numerous stakeholders. It is important to underscore that these changes were incremental and contingent on the concurrent circumstances. For example, the 2015 recommendation for use of MenB was made in the context of the existing routine recommendation for MenACWY at 11–12 years of age and 16 years of age.

There are several reasons to reassess the current recommendations. The epidemiology of IMD continues to change, and it may have been affected by the COVID-19 pandemic [18]. New data have become available from clinical trial and real-world experiences; societal values and preferences have also evolved. In addition, the difference in recommendations (routine for MenACWY versus SCDM for MenB) implies that prevention of IMD caused by serogroups A, C, W, and Y is more important compared with serogroup B, which contradicts the current epidemiology. This, along with the confusion and barriers from SCDM [19–21], may be partially responsible for the low MenB immunization rates. Finally, the availability of MenABCWY represents an opportunity to consolidate recommendations, simplify practice, and improve coverage for all relevant serogroups.

This review summarizes the public policy considerations that influenced the milestone meningococcal vaccination recommendations, delineates the current state of meningococcal immunization, and explores how future policy recommendations may evolve in the U.S., particularly with the availability of MenABCWY. The timeline of meningococcal vaccine recommendations is presented in Figure 1, along with the corresponding IMD epidemiology over the years. Considerations for milestone recommendations for healthy individuals are summarized in Table 1 and for high-risk individuals in Table 2.

2. 2005 milestone: routine use of MenACWY at 11–12 years of age

2.1. Context and unmet need

Until 2005, the only vaccine against serogroups A, C, W, and Y available in the U.S. was Meningococcal Polysaccharide Vaccine (Quadrivalent; MPSV4), licensed in 1981 [43,47]. MPSV4 was recommended for certain high-risk groups, including persons with complement component deficiency, functional or anatomic asplenia, travelers to countries with epidemic or hyperendemic meningococcal disease, and military recruits. It was also considered for use during outbreaks and for laboratory workers who might be exposed to *Neisseria meningitidis* [43]. College students were recognized to be at increased risk, and the recommendation at the time was to educate them about the risk and vaccinate if they wanted protection [43]. MPSV4 provided only short-term protection [48].

As the awareness of IMD among adolescents and young adults was increasing, the first Meningococcal Conjugate Vaccine, Quadrivalent (MenACWY-D, containing serogroups A, C, W, and Y polysaccharides conjugated to diphtheria toxoid) was licensed [49], and the ACIP's meningococcal work group (WG) was tasked with reviewing policy for its use. The incidence of IMD prior to 2005 was 0.5 – 1.1 per 100,000 individuals [43].

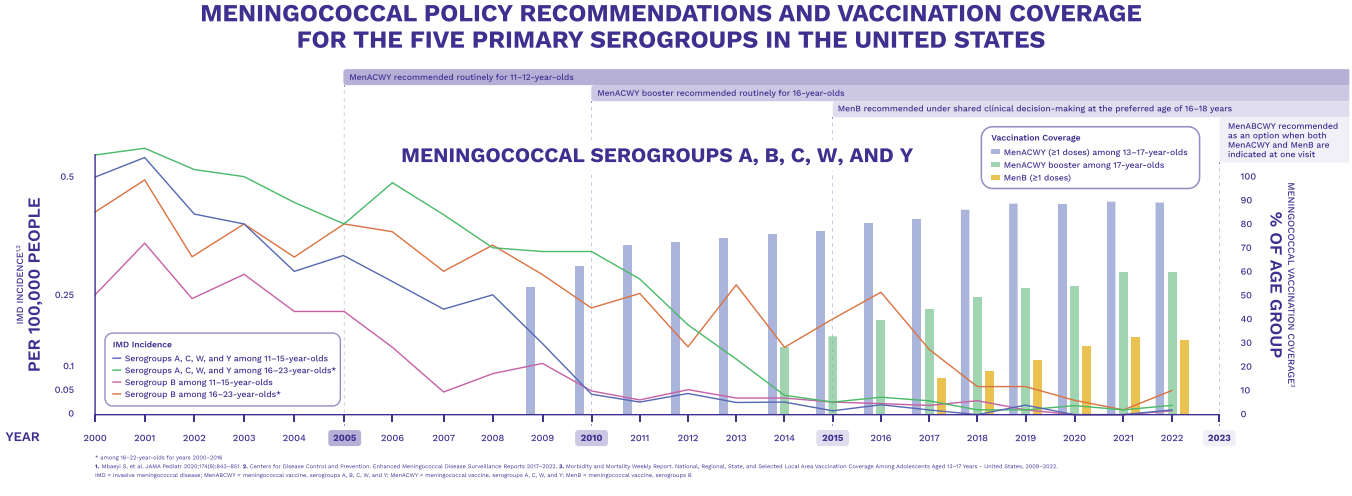

Figure 1. Timeline of ACIP milestone recommendations, meningococcal vaccine epidemiology, and meningococcal vaccine uptake in the U.S. [8,22–42].

Table 1. The ACIP milestone recommendations for meningococcal vaccines and indicated rationale: healthy individuals.

Recommendation	Date of the ACIP meeting	Rationale
MenACWY		
MenACWY routine recommendation for: • 11-12-year-olds at the adolescent visit, adolescents at high school entry • College freshmen living in dormitories and other high-risk groups • All other adolescents wishing to decrease their risk formeningococcal disease	February 2005 [14]	• Strengthened role of the ACIP-recommended routine adolescent visit and the wish to effect a rapid impact on disease incidence • Expected limited MenACWY-D vaccine supply in the first years after the approval
Addition of a booster recommendation to the MenACWY routine recommendation: • Vaccination of 11–12-year-olds at the adolescent vaccination visit, with a booster at 16 years of age • For adolescents vaccinated at 13–15 years of age, a booster 5 years after the first dose, through 21 years of age	October 2010 [15]	• Programmatical feasibility, as vaccination at this age platform would be least disruptive to the vaccine schedule and provide greatest reduction in disease burden • Continued protection of 11-13-year-olds • Robust immune response after booster administration
MenB		
MenB vaccine series Category B (individual clinical decision-making) recommendation for: • Adolescents and young adults 16–23 years of age (16–18 years of age preferred)	June 2015 [16]	• Low disease burden and need for additional data on vaccine effectiveness, duration of protection, and impact of carriage (considerations against a Category A recommendation) • Support of a policy option that included vaccinating all adolescents rather than only college students, since an important burden of disease occurred in 18–23-year-olds not attending college (consideration in support of a vaccination recommendation)
MenB recommendation change from Category B to shared clinical decision-making	June 2019 [44]	• Improved clarity of the ACIP's recommendations

Abbreviations: ACIP, Advisory Committee on Immunization Practices; MenACWY, meningococcal serogroups A, C, W, and Y vaccine; MenACWY-D, meningococcal conjugate vaccine (quadrivalent); MenB, meningococcal serogroup B vaccine.

2.2. WG and ACIP discussions

In 2004, the WG considered several key factors. Epidemiologic data indicated that IMD incidence was higher among 11–18-year-olds versus other age groups, highlighting the unmet need in this population [50]. The safety and immunogenicity clinical trial data positioned MenACWYD as a well tolerated and effective option for immunization in adolescents and young adults [50]. Based on clinical trial data (which included antibody persistence 3 years post-vaccination) and the known duration of protection of 3–5 years for the MPSV4 vaccine, MenACWY-D duration of protection was estimated as 8–10 years, as MenACWY-D induced higher responses than MPSV4 [50]. The WG additionally noted the use of routine adolescent visits for other vaccinations (e.g. tetanus diphtheria [Td] booster), for a preexisting vaccination platform that could be used for administering MenACWY-D [50].

Based on these considerations, and to maximize the individual benefit of the vaccine during the years of increased risk, the WG recommended routine use of MenACWY-D in 11–12-year-olds [14]. While a national catch-up program was not initially recommended, routine vaccination of individuals at increased risk was recommended, along with revaccination every 3–5 years for those remaining at high risk [14].

ACIP members expressed concerns about the WG recommendation. As at the time IMD incidence peaked among 17–18-year-olds, the advisability of immunizing a group at lower risk for the disease was questioned, especially because the duration of protection and the ability of the vaccine to achieve herd protection were unknown. Some members suggested targeting either an older age group or two age cohorts to more quickly reach individuals at highest risk. However, the lack of an older adolescent vaccination visit platform was a concern, and young adolescents were considered easier to reach than older adolescents, who often miss routine preventive care visits [50].

MenACWY-D was approved by the U.S. Food and Drug Administration (FDA) in January 2005 for 2–55-year-olds [51,52]. In February 2005, the WG revisited the debate about the optimal age for the administration of the vaccine [14]. In addition to epidemiological data from 1991 to 2002, the importance of strengthening the adolescent vaccination visit to support overall vaccination coverage during adolescence, cost per life year gained, and concerns about limited MenACWY vaccination supply were discussed [14]. It was noted that a survey of 587 primary care family physicians and pediatricians indicated providers' preference for vaccination at 11–12 years of age, but providers recognized the greater disease burden for older adolescents [14].

The ACIP voted unanimously in favor of routine vaccination for 11–12-year-olds, adolescents at high school entry, college freshmen living in dormitories and other high-risk groups, and for any other adolescents wishing to decrease their risk for meningococcal disease [14]. Under this recommendation, adolescents would be vaccinated prior to the period of increased risk (16–21 years of age) [52], which could promote high coverage rates and potentially herd protection.

2.3. Interval period (2005–2010) and updated recommendations

Following this recommendation, vaccine supply issues were encountered in May 2006 and resolved by November 2006 [53,54]. In addition, concerns were raised about a possible increase in the incidence of Guillain–Barré syndrome (GBS) after vaccination

Table 2. The ACIP milestone recommendations for meningococcal vaccines and indicated rationale: high-risk individuals.

Recommendation	Date of the ACIP meeting	Rationale
MenACWY		
MenACWY-D use preferred in persons aged 11–55 years (MPSV4 accepted as an alternative for persons aged 11–55 years if MenACWY-D was not available); MPSV4 recommended in children aged 2–10 years and persons aged >55 years. The following populations were indicated as at increased risk: • College freshmen living in dormitories • Microbiologists routinely exposed to isolates of *N. meningitidis* • Travelers to or residents of countries with epidemic or hyperendemic *N. meningitidis*, particularly in the case of prolonged contact with the local population • Military recruits • Patients with terminal complement component deficiencies and patients with anatomic or functional asplenia	February 2005 [14,43]	• Demonstrated disease risk in the specific risk groups
Addition of a booster recommendation for: • Children 2–10 years of age at increased risk for IMD, including those with complement deficiencies, anatomic or functional asplenia, HIV infection, travelers to, or residents of countries in which meningococcal disease is hyperendemic or epidemic, and due to an outbreak of a vaccine-preventable serogroup	October 2010 [15]	• Clarification of the eligible groups for meningococcal vaccination • Update to the primary vaccination recommendations for highrisk children • Update to the recommendations regarding vaccination of adolescents and revaccination • Clarification of the use of conjugate versus polysaccharide meningococcal vaccines
MenB		
MenB series Category A (for all persons at risk) recommendation for individuals 10 years old and older, including: • Persons with persistent complement component deficiencies Persons with anatomic or functional asplenia • Microbiologists routinely exposed to isolates of *N. meningitidis* • Persons identified to be at increased risk because of a serogroup B meningococcal disease outbreak	February 2015 [45]	• Demonstrated disease risk in the specific risk groups • Concurrent recommendation for those groups to receive MenACWY vaccines • Presence of an immune response to MenB vaccines in the general adolescent population • Lack of theoretical safety concerns for individuals older than 25 years of age, compared with 10–25-year-olds
MenB booster dose recommendation, one year after completion of MenB primary series, followed by MenB booster doses every 2–3 years for the duration of risk, for: • Persons with persistent complement component deficiencies • Persons with anatomic or functional asplenia • Microbiologists routinely exposed to isolates of *N. meningitidis* MenB booster dose recommendation, one year or more after completion of MenB primary series (a booster after 6 months or more may be considered), for: • Persons identified to be at increased risk because of a serogroup B meningococcal disease outbreak	February 2019 [44,46]	• Evidence that antibody persistence was likely to be at least 2–3 years and could be longer in healthy adolescents and adults

Abbreviations: ACIP, Advisory Committee on Immunization Practices; HIV, human immunodeficiency syndrome; MenACWY-D, quadrivalent meningococcal conjugate vaccine; MPSV4, meningococcal polysaccharide vaccine; MenACWY, meningococcal serogroups A, C, W, and Y vaccine; MenACWY-D, meningococcal conjugate vaccine (quadrivalent); MenB, meningococcal serogroup B vaccine.

[55]. However, evidence from two large studies showed that GBS was not associated with vaccination, and persons with a history of GBS were not at higher risk for recurrence after receiving MenACWY-D versus any other vaccine [56].

In 2007, the ACIP recommended a preventative visit for 11–12-year-olds, during which they would receive other immunizations [57].

3. 2010 milestone: routine MenACWY booster at 16 years of age

3.1. Context and unmet need

In 2005, the ACIP expected that MenACWY-D would offer longer protection than MPSV4, noting the need to confirm this assumption definitive data on persistence of protection were not available [59].

In June 2009, MenACWY-D effectiveness was estimated to exceed 80%, although this estimate only pertained to persons up to 3 years post-vaccination [58]. In 2010, data were presented suggesting that MenACWY-D protection was less durable than expected, which could leave older adolescents who were vaccinated at 11–12 years of age vulnerable to IMD; in addition, no data were available on whether herd protection had been achieved in this group [56]. The duration of protection was conservatively reassessed as 3–5 years [56], and there were 14 reports of IMD caused by serogroups C or Y among vaccinated persons (median age: approximately 18 years at vaccination and 20 years at having IMD) [58].

3.2. WG and ACIP discussions

A new Meningococcal Conjugate Vaccine, Quadrivalent vaccine (MenACWY-CRM), which uses CRM197 (a mutant

diphtheria toxin) as the protein conjugate, was licensed in February 2010 and added as an option in the immunization schedule [56]. Strategies for updating the MenACWY immunization schedule (using either MenACWY-D or MenACWY-CRM) were considered, including adding a booster at 17 years of age (either for first-year college students living in dormitories or for all adolescents), or moving the first vaccine dose to an older age (11–15 or 14–15 years of age) [56].

The WG considered that vaccinating an additional age group would increase the program cost, resulting in a high cost per quality-adjusted life year (QALY) gained [56]. In addition, it was noted that reaching older adolescents would be more difficult, and ACIP members acknowledged that moving meningococcal vaccination to an older age group would risk delaying other vaccines, like human papillomavirus (HPV), which were recommended for pre-adolescents [56]. Notably, a cost-effectiveness analysis showed that, compared with a single dose at either 11 or 15 years of age, a booster dose at 16 years of age had a similar cost per QALY gained but would prevent twice as many IMD cases and deaths [60]. This consideration supported vaccination of 16-year-olds in addition to 11-year-olds.

In 2010, the ACIP voted in favor of retaining routine vaccination at 11–12 years of age and adding a booster dose at 16 years of age; six members were in favor, five members were against, and three members abstained [15].

In 2011, the ACIP assessed MenACWY vaccination for infants but decided against a routine recommendation for all healthy infants, noting that approximately 60% of meningococcal disease cases among children in the first year of life were caused by serogroup B and that the highest incidence in the first 5 years of life occurs in infants aged 0–5 months, which is too young to have received the 2–3 required doses of vaccine [52]. A MenB recommendation for infants was not evaluated by ACIP at that time or since then, as no MenB vaccine has been approved by the FDA for use in this age group [61].

4. 2015 milestone: optional use of MenB at 16–23 years of age

4.1. Context and unmet need

Implementation of the primary and booster program for MenACWY was followed by a decline in IMD cases caused by serogroups C, W, and Y from 2005 to 2011 [8]. IMD caused by serogroup A is rare in the U.S. [62]. However, the incidence of serogroup B cases increased from 2009 to 2014. By 2014, serogroup B accounted for the highest proportion of IMD cases in adolescents [63]. Over the preceding 5 years, five college campus outbreaks due to serogroup B had been reported [63]. Between 2009 and 2013, the case fatality rate for IMD cases, of which most were caused by serogroups B and C, was 19.1% in organization-based outbreaks and 27.3% in community-based outbreaks [64]. This change in IMD epidemiology highlighted the need for a MenB vaccine.

As the serogroup B polysaccharide is poorly immunogenic due to structural similarity between the capsule and human tissue [65], MenB vaccine development was protracted and had to be based on subcapsular proteins [66]. An additional challenge to vaccine development was that strains differ significantly in the antigenicity and subcapsular protein expression [66].

At the time, the meningococcal serogroup B-factor H binding protein vaccine (MenB-FHbp) was in late development, and the MenB 4-component vaccine (MenB-4C) was licensed in Europe, Canada, and Australia [67–70]. In June 2014, interim guidance was presented for use of MenB-4C in response to outbreaks under the CDC-sponsored expanded access Investigational New Drug (IND) protocol [71]. In October 2014, MenB-FHbp was licensed in the U.S. for use with a 3-dose schedule [72]. MenB-4C was licensed for use with a two-dose schedule in 2015 [73].

The WG outlined several concerns about a routine recommendation for MenB vaccines, indicating the need for additional data to inform policy-making: breadth of strain coverage, duration of protection, impact on carriage, impact of vaccine pressure on other circulating strains, difficulties implementing multi-dose schedules, and the low burden of disease [74]. Although it was noted that only one-third of cases occurred in college students, the occurrence of the majority of cases among non-college students was not discussed [74].

4.2. WG and ACIP discussions

In February 2015, the WG discussed immunization of high-risk groups, including those exposed during outbreaks [45]. They proposed a Category A recommendation (for all persons in an age- or risk-factor-based group, now referred to as a 'routine recommendation') for individuals 10 years of age or older at increased risk (due to complement component deficiencies, asplenia, occupational exposure to *Neisseria meningitidis* isolates, or a MenB outbreak) [45]. This recommendation went beyond the licensed age indication (10–25 years of age) and was justified based on the lack of theoretical safety concerns in persons older than 25 years and the potential benefits [45]. The ACIP voted unanimously in favor of the recommendation [45].

In June 2015, a recommendation for broader use among adolescents and college students was discussed [16]. In addition to previously outlined challenges regarding the use of MenB, the cost of vaccination was cited [16]. A cost-effectiveness analysis estimated that a routine adolescent immunization program would prevent 15–30 IMD cases and 2–5 deaths; 100,000–400,000 individuals would need to be vaccinated to prevent one case, and nearly 1–3 million would need to be vaccinated to prevent one death [16]. The cost per QALY gained was estimated as $4–9 million [16].

The WG favored recommending vaccination at 16–18 years of age due to the likelihood that 16-year-olds may still be under the care of a pediatrician, the established recommendation for a MenACWY booster at 16 years of age, and the likelihood of completing the series before entering college [16]. In part due to MenB cases occurring in 18–23-year-olds not attending college, the WG supported a policy of vaccinating all adolescents, rather than only college students [16].

The ACIP voted in favor of a Category B recommendation (for individual clinical decision-making, now referred to as

SCDM); 14 members were in favor and one abstained [16]. The ACIP advised that a MenB series may be administered to 16–23-year-olds to provide short-term protection against most MenB strains, with the preferred age being 16–18 years to maximize protection during the highest-risk period [16].

The WG acknowledged controversy around previous Category B recommendations, noting that they are difficult to understand and implement and could possibly convey lower importance of MenB compared with MenACWY [16]. However, Category B recommendation was favored due to the previously outlined challenges associated with the use of MenB in the U.S.

4.3. Interval period (2015–2023) and updated recommendations

A discussion about MenB booster doses was initiated in 2017. The need for boosters for persons at increased risk was based on evidence of antibody waning [75].

In February 2018, the WG considered the epidemiology of IMD among college students, noting that the incidence was low but college students were at increased risk compared with peers not attending college [76]. The incidence of IMD caused by serogroups C, W, and Y combined was lower, and was similar in both college students and non-college students, likely at least in part due to the success of the adolescent MenACWY program [76]. The WG concluded that routine vaccination of all college students would be difficult [76]. They advocated for more CDC guidance on SCDM to help patients, caregivers, and healthcare providers make better-informed decisions [76].

In June 2019, the WG reviewed data on the persistence of immunogenicity, Grading of Recommendation Assessment, Development, and Evaluation (GRADE), Evidence to Recommendations (EtR), and policy options for MenB booster doses [44]. Data that had been presented to the ACIP (for MenB-FHbp) and published evidence (for an investigational MenABCWY booster dose with a MenB-4C component) suggested that antibody persistence after a MenB booster is likely to last at least 2–3 years and may be longer in healthy adolescents and adults [44,77–79]. The WG concluded that additional safety and effectiveness data would be necessary for the ongoing evaluation of the recommendation [44].

ACIP unanimously voted in favor of a recommendation for persons 10 years of age or older at increased risk due to medical conditions to receive a booster 1 year after completing the initial series, and booster doses every 2–3 years for the duration of risk [44]. In addition, guidance was provided on vaccination during outbreaks. A one-time booster 1 year or more since completion of the MenB primary series was recommended for persons 10 years of age or older at increased risk during outbreaks, noting that a booster may be given at least 6 months after completion of the primary series [44].

5. 2023 milestone: MenABCWY recommendation and upcoming assessments

A comprehensive program to prevent IMD in the U.S. needs to address all five serogroups primarily responsible for causing IMD. Initially, this goal could only be accomplished through the use of both MenACWY and MenB, with their differing products, dosing schedules, and recommendations. In October 2023, a MenABCWY vaccine manufactured by Pfizer, Inc. was licensed by the FDA for use in 10–25-year-olds with a two-dose schedule [80], prompting review by the ACIP.

5.1. WG and ACIP discussions

Between October 2022 and October 2023, the WG and the ACIP discussed the potential introduction of MenABCWY to the adolescent immunization schedule [81–83]. In February 2023, Pfizer, Inc. presented data demonstrating the satisfactory safety profile and non-inferiority of MenABCWY versus MenB-FHbp and MenACWY-CRM [84,85]. MenABCWY was assessed based on its ability to replace either MenB, MenACWY, or both vaccines if administered at the same time [85]. Several schedule options were considered by the WG, including the use of MenABCWY at 11–12 years of age or at 16 years of age, as either a two-dose series or one dose followed by a MenB dose: QPB (MenACWY at 11 years of age, followed by MenABCWY and MenB at 16 years of age), PPB (MenABCWY at 11 years of age, followed by MenABCWY and MenB at 16 years of age), and QPP (MenACWY at 11 years of age, followed by two doses of MenABCWY at 16 years of age) [82].

Discussions at the ACIP in June 2023 and October 2023 focused primarily on three domains of the EtR framework: resource use, feasibility, and public health impact [82,83]. Resource use was the main factor in the ACIP deliberations. Cost-effectiveness modeling found that reasonable pricing and duration of protection of the vaccine, alongside reconsidered vaccination interventions, would determine the cost or cost-saving value of MenABCWY [82,83]. While the consideration of MenABCWY cost is beyond the scope of this review, cost-effectiveness analyses for MenABCWY have shown that vaccination strategies varied in cost per health outcome, with QPB and QPP being considered as probably reasonable and efficient allocation of resources, while PPB was not [83]. Both interventions (QPB and QPP) were considered as the ones that could be incrementally or likely cost-saving, respectively, relative to standard of care (two doses of MenACWY and two doses of MenB) [86]. The WG and the ACIP raised concerns about the implications of adding MenB protection at 11 years of age, and, most importantly, programmatic costs related to the introduction of a more expensive vaccine in an already complex and costly vaccination program [82,85].

Feasibility of implementation was another consideration as part of the EtR; the WG assessed QPB and QPP to be equally feasible to implement in clinical practice [82,83]. Further considerations for the feasibility of the QPB schedule (such as the financial and storage burden on providers to carry three vaccines, the ease of integrating into individual provider practices, and the complexity of the recommendation) were not presented as part of the EtR. Acceptability to key stakeholders, such as healthcare providers, professional societies, and the public, was considered to be comparable for the QPB recommendation and for the PPB recommendation; it was considered unknown for the QPP option [82,83]. In addition to these factors, members of the ACIP highlighted the lack of studies

for MenABCWY in individuals at high-risk of IMD due to medical conditions, as well as low IMD incidence in light of the overall cost of the meningococcal vaccination schedule for adolescents [82,83].

In October 2023, the WG proposed two options for meningococcal vaccination schedule (following MenACWY at 11–12 years of age): 1) 1 dose of MenABCWY followed by a dose of MenB at 16 years of age, and 2) 2 doses of MenABCWY at 16–18 years of age to achieve protection against the five serogroups [87]. ACIP members approved MenABCWY as an option when both MenACWY and MenB are indicated at the same visit (10 were in favor, four were against) [87]. MenABCWY became an option for healthy 10–25-year-olds who are recommended to receive MenACWY and MenB at the same visit [87]; MenB would then be given for subsequent doses when MenACWY is not indicated [88]. In essence, this recommendation is most applicable to 16-year-olds receiving a MenACWY booster who also opt to initiate the MenB series.

6. Context for reassessment of meningococcal vaccination policy

The reassessment of the meningococcal vaccination schedule for adolescents was requested by ACIP members for the years 2024–2025, who cited the difficulties with implementation of the SCDM recommendation for MenB vaccines, waning protection of the MenACWY and MenB vaccines, and the low incidence of IMD in adolescents, especially between 11 and 15 years of age [12].

A second MenABCWY vaccine, developed by GSK, is undergoing review by the FDA and evaluation by the WG/ACIP on the same timeline as the reassessment of the meningococcal vaccination schedule [89,90]. The availability of two MenABCWY vaccines has the potential to modernize the approach to preventing IMD. Currently, the U.S. meningococcal policy is at an inflection point due to the convergence of epidemiological factors, differing coverage rates for vaccines, availability of new vaccines, and new data on attitudes toward and implementation of vaccine recommendations. The following issues add to the need for reassessing the meningococcal vaccination policy: 1) a routine vaccination program for the less common serogroups (A, C, W, and Y) but an optional vaccination program for the most common serogroup (B); 2) confusion among individuals eligible to be vaccinated and providers regarding MenB recommendation; and 3) low MenB coverage rates among healthy individuals and high-risk individuals, possibly stemming from this confusion. A concerted effort to prevent IMD using MenABCWY could mitigate those problems and produce a more streamlined and comprehensive approach to IMD prevention, maintaining protection against serogroups A, C, W, and Y and improving protection against serogroup B.

6.1. Changes in serogroup epidemiology from pre-2005 to 2023

Meningococcal serogroup distribution is unpredictable and varies over time; the past 2 decades have seen changes in IMD epidemiology [62]. Incidence of IMD in the U.S. steadily decreased starting in the late 1990s (1.3 cases per 100,000 population in 1996 to 0.42 per 100,000 in 2005 [91]), and to 0.06 cases per 100,000 population in 2021 [92].

The decline in IMD incidence preceded the introduction of routine vaccination with MenACWY. However, vaccination with MenACWY has significantly contributed to this decrease. IMD incidence among 11–15-year-olds declined by 16% prior to the vaccine recommendation in 2005 and by 28% after 2005 [8]. Similarly, IMD incidence among persons 16–22 years of age declined by 11% annually in the post-primary dose period and by 36% annually in the post-booster period (2011–2017) [8].

By comparison to IMD caused by serogroups A, C, W, and Y, IMD caused by serogroup B only slightly declined in 2006–2010, and then increased in 2015–2019; it is now the leading cause of IMD among adolescents and young adults in the U.S. [12]. Unlike the routine recommendation for MenACWY and the resulting rapid increase in vaccination coverage, the SCDM recommendation for MenB led to a slow increase in vaccination coverage over the past 9 years, precluding a population-level impact on disease incidence. Furthermore, while IMD incidence decreased during the COVID-19 pandemic, it is worrisome that in 2023, 416 cases were diagnosed across all ages (the highest number of cases since 2014) [12].

7. Prevention of IMD caused by serogroups A, B, C, W, and Y from 2015 to 2023

7.1. Establishing two new age platforms for routine immunization of adolescents

The initial consideration by ACIP members in 2005 was that an immunization platform for pre-adolescents would ensure vaccination of more pre-adolescents, compared with the number of young adults who would be reached if vaccination were recommended in later adolescence [14]. This assumption has proven to be correct. MenACWY vaccination rates rose quickly and plateaued at 80–90% in 2015 (reflective of the pre-adolescent platform) (Figure 1). In contrast, booster vaccination of older adolescents increased much more slowly, reaching only 60.8% in 2022 [93]; ACIP members had predicted this, expecting approximately 55% coverage based on hepatitis B vaccine coverage and expressing concerns regarding vaccination coverage in older adolescents [14].

School mandates and state-driven education on IMD, along with raised awareness about this uncommon but serious disease, contributed to the success of the immunization platform at 11 – 12 years of age [94]. This success was evidenced by a faster increase in vaccine coverage for MenACWY versus other routinely recommended vaccines (i.e., HPV) in this same age group [93].

A study evaluating the determinants of MenACWY vaccination in U.S. adolescents found that factors associated with vaccine completion included more than one annual healthcare visit, the presence of a booster dose vaccine mandate, and a higher ratio of pediatricians to children [94], highlighting

disparities in access to vaccination, which may translate to disparities in vaccination coverage rates.

7.2. MenACWY and MenB vaccine safety, effectiveness, and persistence

7.2.1. MenACWY vaccines

MenACWY-D and MenACWY-CRM vaccines have been licensed in the U.S. since 2005 and 2010, respectively [51,56]. Clinical trials and real-world use have demonstrated that both are well tolerated, with similar reactogenicity [48,95,96]. The overall effectiveness of MenACWY-D in adolescents is estimated as 69% up to 8 years after the primary dose [97,98]. Antibody persistence has also been assessed for both vaccines. MenACWY-D administration was shown to result in serogroup-specific antibody waning after primary vaccination, with robust increases of antibody titers against all serogroups following booster administration [97]. MenACWY-CRM administration was demonstrated to provide antibody persistence for at least 5 years post-vaccination in all age groups; the booster dose resulted in robust increases of antibody titers for the A, C, W, and Y serogroups [99]. In addition, robust functional antibody responses were seen up to 12 months after administration of one MenACWY-CRM dose in university students [100].

Evidence on the impact of MenACWY vaccination on carriage in non-U.S. countries is also available. A repeated cross-sectional survey of 15–19-year-olds found that the prevalence of oropharyngeal carriage of serogroups W and Y decreased by 73% and 69%, respectively, following MenACWY introduction in the United Kingdom (UK) [101]. Notably, a study of adolescents in South Australia found that meningococcal carriage was not impacted by public health strategies, such as social distancing due to the COVID-19 pandemic [102], highlighting that MenACWY vaccination effectively reduces meningococcal carriage, relative to public health measures.

A third quadrivalent meningococcal conjugate vaccine, MenACYW-TT (MenQuadfi), was licensed in 2020 [97], while MenACWY-D was retired [103], but persistence following its administration in adolescents is assumed to be similar to the other licensed MenACWY vaccines. Data on persistence following booster administration have also become available. A phase 4, open-label study demonstrated that 4 years after MenACWY-D booster vaccination, 89.9–98.2% of the participants had serum bactericidal activity against human complement (hSBA) titers ≥1:4, the threshold associated with protection against IMD, and 81.7–97.2% had hSBA titers ≥1:8, which is an even more conservative threshold for protection [104].

7.2.2. MenB vaccines

Concerns of the WG and ACIP after MenB licensure were related to the limited safety data and theoretical concerns for autoimmune side effects, unknown breadth of coverage, duration of protection, impact on carriage, impact of vaccine pressure on other circulating strains, challenging implementation of schedules, and low burden of disease [74]. In the intervening years since these vaccines were first recommended, evidence has addressed many of these initial concerns.

Safety data on MenB are now available from large clinical trials and vaccine safety surveillance systems. In clinical trials, MenB-4C and MenB-FHbp have a similar safety profile. The most commonly reported local reactions after either vaccine are injection site pain, erythema, swelling, and induration [97]. Most symptoms resolve within 5 days of vaccination [97]. A similar safety profile was demonstrated by a real-world study of MenB-4C in college students and individuals at high risk [105]. No safety signals of increased autoimmune disease symptoms or diagnosis have been associated with either vaccine. Similarly, no cases of GBS have been reported for either MenB vaccine after 9 years of use in adolescents and young adults since the vaccines' licensure.

The breadth of coverage was assessed for both MenB vaccines. A 2017 study on MenB-FHbp concluded that vaccine-elicited immune responses provide broad protection against IMD [66]. In addition, a 2018 study showed that >91% of serogroup B isolates ($n = 1,814$) from vaccinated young adults were susceptible to MenB-FHbp-induced antibodies [106]. For MenB-4C, an assay for evaluating MenB effectiveness against diverse strains has been developed and a phase 3 clinical trial demonstrated that MenB-4C induced bactericidal activity against a 110-strain MenB panel [107]. Both studies have effectively addressed the initial concern among ACIP members. Additionally, MenB-FHbp vaccination has elicited bactericidal responses in 53–100% of C, W, Y, and X strains [108], and antibodies induced by MenB-4C vaccination of 11–17-year-old adolescents have also shown bactericidal activity against 55–74% of C, W, and Y strains [108,109]. These results may suggest that meningococci antigens may not be strain-specific and MenB vaccines may favor cross-reactivity.

Duration of protection has also been assessed. An open-label extension study of a phase 2 randomized study on MenB-FHbp in 11–18-year-old adolescents found that immune responses declined by 12 months after the completion of the primary 2- or 3-dose series; 18.0–61.3% of the participants had hSBA titers ≥ lower limit of quantitation (LLOQ) [110]. The study also found that a booster dose at 48 months after the primary series produced robust immune responses that were similar between 2- and 3-dose schedules [110]. A follow-up study, which developed a power law model (PLM), supports that the persistence of hSBA titers is maintained for at least 5 years post-primary MenB-FHbp vaccination and post-booster [111]. Another extension study of a phase 2 randomized study tested persistence of the immune response induced by MenB-4C in 15–24-year-olds. At 4 years and 7.5 years after administration of two doses of MenB-4C in 15–24-year-olds, antibody levels declined but remained higher than in vaccine-naïve participants (hSBA titers ≥4 were observed among 30–84% participants from Canada and Australia after 4 years and among 44–84% participants from Chile after 7.5 years) [77]. Similarly, a booster of MenB-4C at 4 or 7.5 years after the primary series induced a robust immune response, suggesting induction of an anamnestic response [77]. In addition, a recent real-world data modeling study estimated the duration of protection for MenB-4C as 6.3–11.3 years, which is greater than previously published immunogenicity data and suggests that this increased duration may extend to the MenABCWY vaccine [112]. Current data suggest that breakthrough cases in immunized individuals are uncommon [6].

Outside of the U.S., MenB-4C vaccines are part of several national and regional immunization programs for infants, young children, and adolescents, providing real-world effectiveness data [113–118]. These data are not yet available for MenB-FHbp. Specifically for the adolescent age group, South Australia implemented an immunization program in all 15–20-year-olds in 2019 [118]. Vaccine effectiveness of 89% for MenB-4C, among adolescents aged 15–18 years, and a reduction of 79% in incidence of IMD caused by serogroup B were observed 3 years after the program was implemented [118]. This evidence provides reassurance on the duration of protection by MenB and addresses concerns about persistence.

Finally, data on impact on carriage have become available: immunization with MenB-4C was shown not to impact oropharyngeal carriage among adolescents 15–18 years of age in South Australia, suggesting a lack of herd protection and a necessity for protection among adolescents [119]. To our best knowledge, data on impact of carriage for MenB-FHbp are not yet available.

8. Discussion

8.1. Context behind meningococcal vaccination recommendations

We have presented a timeline of how IMD prevention efforts have evolved in the past 2 decades, emphasizing the recommendation milestones in 2005 (modified in 2007), 2010, 2015, and 2023. Understanding how IMD epidemiology, vaccination landscape, and scientific framework have evolved is a necessary step toward reassessing vaccine recommendations. It is important to consider the different clinical development timelines of each vaccine due to technical and research challenges, and to acknowledge that ACIP evaluations and recommendations have stemmed from the available vaccines and the best data available at each timepoint.

At each milestone, meningococcal WG and ACIP members considered a wide range of data and immunization scenarios and made recommendations based on concurrent scientific, economic, and societal context. The success of the MenACWY recommendation at 11–12 years of age, together with the ensuing establishment of a strong platform for immunization for MenACWY, HPV, and Tdap at this age, are a testament to the ACIP process and public policy expertise of CDC and the ACIP.

The doubts related to the safety and effectiveness of MenB were legitimate at the time of MenB recommendation (2015). They were based on the limited data available for MenB at that time, but also on the ACIP's recent experience with MenACWY, which had proven not to have the 8–10 years of persistence initially considered likely in 2005. The recent evidence on the breadth of coverage and duration of protection of MenB has addressed many of the challenges and uncertainties originally outlined by the ACIP.

8.2. The current state of meningococcal vaccination in the U.S.

The two different recommendations corresponding to the two types of vaccines (MenACWY and MenB) for the prevention of one disease (IMD) have created confusion among patients, caregivers, and providers [19–21], as well as a unique paradigm in the current CDC immunization schedule, with different vaccines (MenACWY, MenB, and MenABCWY), recommendations (routine and SCDM), individuals (healthy and high-risk), and dosing schedules (two- and three-dose), for the same disease. Furthermore, there are knowledge gaps among adolescents, their caregivers, and young adults, some of whom believe MenACWY vaccination fully protects against meningococcal disease, even if MenB vaccination was not received [19–21]. This confusion may result in individuals remaining vulnerable to IMD.

The SCDM recommendation has advantages and disadvantages. It guarantees insurance coverage for MenB under the Patient Protection and Affordable Care Act and the Vaccines for Children Program [120]. However, all medical decision-making is shared, and, therefore, it is unclear how SCDM implementation differs from other recommendations; in addition, the implementation of SCDM by providers may be heavily influenced by whether patients are planning to attend college [21]. Therefore, while SCDM allows adolescents and young adults to receive MenB, misunderstanding of SCDM may create barriers to vaccination due to perceptions that this particular vaccine is 'optional.' Although the term 'SCDM' was thought to be better understood by clinicians than 'Category B' [44], evidence has accumulated over time that misunderstandings related to implementing SCDM for MenB persist among healthcare providers, including physicians in different specialties, nurse practitioners, and physician assistants [19,21,121–123]. In addition, caregivers of adolescents and young adults may not understand or be fully aware of the concept of SCDM, leading to missed opportunities to discuss and obtain MenB vaccination [20].

Healthy adolescents and young adults are at increased risk for IMD caused by the most common serogroups in the U.S. (B, C, W, and Y), compared with other age groups, with serogroup B causing the highest proportion of cases [97]. However, only an estimated 11.9% of U.S. 17-year-olds had completed a MenB vaccine series in 2022 [93]. Moreover, a claims data analysis showed that in a large cohort of 16–23-year-olds, only 44.7–56.7% completed MenB series in 2017–2018 [70]. Despite a large vaccination effort, this age group remains largely unprotected against IMD caused by serogroup B. Further, individuals living with specific conditions such as functional or anatomical asplenia, HIV, or complement deficiency are at increased risk for IMD compared with the general population, invoking health equity considerations [124]. Even with a routine recommendation for MenB vaccination among individuals at increased risk for IMD, vaccination rates among high-risk 16–23-year-olds are low. Analyses of claims data showed that only 9.7% of newly diagnosed eligible patients with asplenia received MenB within 3 years [125], and only 2.2% of the patients newly diagnosed with complement component deficiencies received MenB within 3 years [126].

Although there was a decrease in meningococcal disease incidence during the COVID-19 pandemic, there has been a resurgence of cases beginning in 2022 [127,128]. In 2023, 422 cases were reported (the highest annual figure since 2014) [127]. The increase in incidence is driven by serogroup Y in >

24-years-olds, with Black/African American populations disproportionately affected [128]. IMD in adolescents between 2022 and 2023 remained predominantly caused by serogroup B, further highlighting the need for improved MenB vaccination rates among adolescents [128].

IMD is uncommon, but it has catastrophic consequences for survivors and their caregivers. Particularly tragic are instances in which adolescents were vaccinated with MenACWY and were assumed to be fully protected from IMD but died from IMD caused by serogroup B [129]. Among survivors, long-term sequelae may severely impact day-to-day functioning, employability, and quality of life. Caregivers' employability and daily life may also be impacted. IMD can have profound impact on patients, caregivers, and the society overall. Fortunately, IMD is preventable.

8.3. What is the future of IMD prevention in the U.S.?

The recent approval of MenABCWY in 2023 presents an opportunity to reassess vaccination recommendations and ensure more equitable protection against all serogroups. In preparation, the ACIP re-assessed the terms of reference for the adolescent meningococcal vaccination schedule in February 2024 [130].

Recently, doubts about the need to vaccinate against IMD have been raised. During MenABCWY discussions in 2023–2024, the ACIP expressed concerns about the current economic burden of IMD prevention [83]. The debate over the optimal age to vaccinate adolescents for prevention of IMD has been conducted within the ACIP periodically since 2005 (as shown above), so this discussion is neither new nor unexpected. It has been previously postulated that vaccination at an earlier age (e.g. 11–12 years) is best from a public health perspective because it encourages greater vaccination coverage. As shown by the most recent NIS-Teen data, routinely vaccinating with MenACWY at 16–18 years of age only reaches 61% of the adolescents [93], despite a long period for implementation (2010–2022) and state/school mandates. This trend is not likely to change, irrespective of meningococcal recommendations, because it is influenced by patterns of adolescent care, transition to adulthood from both personal and health system perspectives, and changes in insurance coverage.

Recent discussions about removing the routine vaccine recommendation from the pediatric schedule (MenACWY at 11–12 years of age) [12] are unprecedented in the history of the U.S. immunization program. Arguments for such a dramatic change note that disease incidence is now low and vaccination is no longer needed [12], economic cost is high [83], and other vaccinations at this age (HPV and Tdap) can be administered at an earlier age [131,132]; hence, a specific vaccination visit at 11–12 years of age may not be necessary. Arguments against this change highlight that the current low incidence is at least partially due to the success of the immunization program; that disease recurrence and deaths in this age group will likely reemerge without high vaccination uptake; and that the beneficial impact of MenACWY on carriage could be negated and lead to increased cases at other ages (both younger and older). Importantly, removing a routine recommendation with widespread state mandates could trigger a downstream vaccine hesitancy wave that might affect other mandated immunization policies, damaging general trust in vaccination.

These public discussions, evaluations, and reassessments are at the core of ACIP's informal mission: to reflect on the values of the society and the available scientific evidence, in order to make a recommendation in the present that is adaptable and beneficial to future children and adults, promoting health equity, while considering cost-effectiveness.

Although the focus of the U.S. recommendations is on adolescents and young adults, infants and young children have the greatest incidence of meningococcal disease in the U.S. and many other countries [133–135]. Meningococcal vaccine recommendations in European countries, especially for MenB vaccines, address IMD prevention only in this younger age group [136]. In the U.S., MenACWY vaccines are indicated for infants as young as 2 months of age, but the ACIP specifically recommends against vaccinating healthy infants, for the reasons previously presented, allowing only for vaccination of infants at high risk because of medical conditions or travel to endemic areas [88,137]. MenB vaccines are not indicated at this time for U.S. infants, and hence no ACIP recommendation can be made. An ongoing phase 3 study in U.S. infants (NCT03621670) may allow for expansion of MenB-4C to this age group [138]. Future recommendations of meningococcal vaccination in this age group in the U.S. may help to address the occurrence of IMD [133,134].

8.4. Why is MenABCWY best for IMD prevention?

There is a need for a concerted effort toward prevention of IMD caused by the five serogroups. For primary care providers, the clinical presentation and treatment of IMD is serogroup-agnostic and IMD is one clinical entity. As such, many providers and caregivers may not understand why two separate vaccines are needed and why the CDC schedules appear to place them at different levels of importance. A 2019 survey revealed that while most parents are aware of IMD as a serious disease, there is a lack of awareness regarding vaccination for different IMD serogroups, and many parents are unsure of their children's vaccination status [139]. Education on vaccination and recommendation by healthcare providers is an important step in addressing the knowledge gaps of caregivers and encouraging vaccine completion [139]. In addition, patient advocacy groups (PAGs) can help raise awareness around meningococcal vaccination. The National Meningitis Association (active until December 2022) released public comments in support of meningococcal vaccination recommendations [14,50,140]. Active PAGs, including the American Society for Meningitis Prevention (formerly known as the Meningitis B Action Project), Immunize.org, and the National Foundation for Infectious Diseases [141–143], have significantly contributed to raising awareness and developing accessible resources on vaccination.

Combination vaccines bring important benefits to immunization practice. The ACIP outlined potential advantages and disadvantages of combination vaccines in 2023 [83,144].

Potential advantages include improved vaccine coverage rates; timely vaccination coverage for children behind the schedule; reduced costs; and facilitation of introducing new vaccines into vaccination programs [145]. Potential disadvantages include possible increased frequency of adverse events due to administration of a combination vaccine (compared with administration of separate antigens at the same visit); confusion associated with vaccine combinations and schedules for subsequent doses; reduced immunogenicity for vaccine components; and shorter shelf life of the vaccine, compared with individual component vaccines [145]. The expected economic impact is unclear, but a better overall economic value is anticipated with the use of combination vaccines due to avoiding costs related to extra injections, additional visits, delayed or missed vaccinations, and additional handling and storage logistics [145].

The use of MenABCWY could alleviate issues related to logistics, transition of adolescents out of pediatric care, administrative errors, and a regimen of 2–3 different vaccines for the same disease. Improved clarity and simplicity of the schedule through a routine recommendation of MenABCWY may also boost meningococcal vaccination completion rates (11.9% for MenB among 17-year-olds in 2022) [93], and help combat the existing disparities in vaccination completion [70].

Finally, in light of the clinical and real-world evidence regarding the use of MenACWY and MenB over the past 2 decades, one must consider that if a pentavalent vaccine had been available at the various meningococcal vaccine milestones (2005, 2010, 2015), it might have been routinely recommended.

8.5. Special vaccination circumstances

This review has focused on meningococcal vaccination recommendations for healthy adolescents and young adults in the U.S., due to age-characteristic behavioral risks (such as socializing in close physical proximity). However, considerations for populations at increased risk have been important in decision-making regarding vaccine recommendations. Certain challenges that were previously outlined for MenB are relevant for MenABCWY, including limited data on duration of protection. Therefore, it is unknown whether populations at increased risk for IMD may benefit from MenABCWY booster for the duration of risk in adolescence and young adulthood. Given the current recommendation for a MenACWY booster for individuals at increased risk for IMD, together with the evidence of diminishing immune response after the completion of the MenB primary series, administration of MenABCWY may provide long-term protection against the five serogroups. This consideration may shape future discussions regarding MenABCWY recommendations.

9. Expert opinion

Invasive meningococcal disease (caused by five common serogroups in the United States) progresses rapidly and can lead to death or devastating long-term sequelae among survivors, such as amputations and neurological damage. This disease, however, can be prevented via vaccination, with three types of vaccines available and recommended for use in the U.S. There is a continued need to protect adolescents and young adults, who are at increased risk for this disease, in addition to those at high risk due to medical conditions or occupation. This need calls for a concerted approach balancing scientific evidence with the values and preferences of patients and their caregivers.

Two decades have passed since the routine recommendation for MenACWY conjugates was first issued, and nearly a decade since the Category B/SCDM recommendation for MenB. Now, a reassessment of meningococcal vaccine recommendations is warranted, considering the evolution of IMD epidemiology, the availability of new vaccines offering broader serogroup coverage, and emerging evidence from clinical trials and real-world observational studies. Specifically, the recommendation for MenB under SCDM deserves reconsideration. Serogroup B has become the leading cause of IMD among adolescents and young adults in the U.S. However, MenB recommendation under SCDM, rather than as a routine recommendation, introduces confusion among individuals to be vaccinated, their caregivers, and healthcare providers of various specialties, leaving many adolescents and young adults vulnerable to IMD. In addition, MenB vaccine coverage rates are low even among high-risk populations, for whom the vaccine is recommended routinely, highlighting the challenges of implementing risk-based recommendations. Although ACIP experts outlined challenges associated with the use of MenB in the U.S. at the time of its recommendation in 2015 (limited safety data and theoretical concerns about autoimmune side effects, unknown breadth of coverage, duration of protection, impact on carriage, impact of vaccine pressure on other circulating strains, challenging implementation of multi-dose schedules, and perceived low burden of disease), data have since become available addressing those challenges, which may inform the re-assessment of meningococcal vaccination recommendations.

A routine recommendation for the pentavalent MenABCWY vaccine at an age supported by disease epidemiology and vaccine characteristics would grant protection against the five most common meningococcal serogroups. This recommendation would present a promising solution for issues associated with administration of separate meningococcal vaccines under different ACIP recommendations. The use of MenABCWY could rectify barriers associated with knowledge gaps on meningococcal vaccination and with logistical issues, improving health equity and protecting future generations. It is possible that if MenABCWY was available 2 decades ago, a routine recommendation might have been made. Future research may assess knowledge, attitudes, and practices regarding MenABCWY among adolescents, young adults, caregivers, and healthcare providers, as well as the impact of MenABCWY use on meningococcal vaccination coverage rates in the U.S.

ACIP recommendations are never intended to exist in perpetuity. Ideally, immunization guidelines should be updated periodically, based on disease epidemiology or product improvements and availability. Examples include

cessation of the universal smallpox immunization program in response to disease elimination [146], routine recommendation of Mpox vaccine for high-risk adults in response to an outbreak [147,148], modification of polio vaccination recommendation to increase reliance on inactivated vaccine due to progress in global polio eradication efforts [149], retirement of live viral herpes zoster vaccine when a new adjuvanted subunit vaccine became available [150–152], and adjustments in pneumococcal and hepatitis B vaccine recommendations for different age and risk groups [153,154].

The evolution of meningococcal vaccines provides another example, and opportunity, for such policy adjustments. In 5 years, it is likely that providers will embrace the evolution of meningococcal immunization recommendations to include an all-MenABCWY schedule. The driving motivation would be their interest in protecting adolescents and young adults equitably from all relevant strains that cause IMD in the U.S. In particular, MenABCWY would be seen as a vehicle to greatly increase protection against serogroup B disease, as MenB uptake would increase 'on the coattails' of MenACWY. A secondary driver would be simplification of the immunization schedule at a time when, as new vaccines are developed and recommended, the schedule is likely to become more complicated. A routine recommendation for use of MenABCWY in the most appropriate age groups would increase vaccine uptake and ultimately protection against IMD in the U.S. This could significantly alter the epidemiological landscape of IMD in the U.S. and perhaps encourage wider conversations globally. Widespread use of such vaccines might further reduce the incidence of IMD, avoiding tragic deaths and devastating lifelong sequelae from a vaccine-preventable disease. Willingness to revisit established immunization policies could also help streamline vaccine delivery and endorse focusing programmatic efforts upon specific populations, for IMD and other vaccine-preventable diseases.

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Declaration of interest

DE Clements, T Olaiya, O Herrera-Restrepo, and WY Sohn are GSK employees and hold financial equities in GSK. C Burman is a GSK employee and holds financial equities in GSK, and is a Pfizer former employee and current stockholder. T Folaranmi is a GSK employee and holds financial equities in GSK, and received GSK support for attending meetings and congresses. V Abbing-Karahagopian is a GSK employee. GS Marshall received grants/contracts (paid to institution) from GSK, Merck, Pfizer, Sanofi, and Seqirus; advisory board consulting fees and travel/meeting support from GSK, Merck, Moderna, Pfizer, Sanofi, and Seqirus; and medical writing support (sponsored by GSK). JH Conway received scientific advisory and honoraria consulting fees from GSK, Merck, Pfizer, and Moderna. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Author contributions

Substantial contributions to study conception and design: DE Clements, T Olaiya, C Burman, O Herrera-Restrepo, WY Sohn, T Folaranmi, V Abbing-Karahagopian, GS Marshall, JH Conway; substantial contributions to analysis and interpretation of the data: DE Clements, T Olaiya, C Burman, O Herrera-Restrepo, WY Sohn, T Folaranmi, V Abbing-Karahagopian, GS Marshall, JH Conway; drafting the article or revising it critically for important intellectual content: DE Clements, T Olaiya, C Burman, O Herrera-Restrepo, WY Sohn, T Folaranmi, V Abbing-Karahagopian, GS Marshall, JH Conway. All authors approved the final version to be published and are fully accountable for all aspects of the work.

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