A Decade of Fighting Invasive Meningococcal Disease: A Narrative Review of Clinical and Real-World Experience with the MenACWY-CRM Conjugate Vaccine

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ABSTRACT

The quadrivalent A, C, W and Y meningococcal vaccine conjugated to nontoxic mutant of diphtheria toxin (MenACWY-CRM) has been licensed since 2010 for the prevention of invasive meningococcal disease (IMD), an uncommon but life-threatening condition. Here, we summarize the experience accrued with MenACWY-CRM during the first decade since its licensure, by providing an overview of clinical trials investigating the safety, immunogenicity and co-administration of MenACWY-CRM with other vaccines as well as presenting real-world evidence regarding the impact of MenACWY-CRM vaccination on carriage and IMD incidence. MenACWY-CRM has demonstrated an acceptable clinical safety profile across a wide range of age groups; no safety concerns have been reported in special populations, such as immunocompromised infants and toddlers, or pregnant women. MenACWY-CRM has also been proven to be immunogenic in various age groups and geographic settings, and a booster dose has been shown to elicit strong anamnestic responses in all studied populations, irrespective of the vaccine used for priming. With no clinically relevant vaccine interactions reported, MenACWY-CRM is being conveniently integrated into existing vaccination programs for various age and risk groups; this possibility of co-administration helps improving vaccine coverage and streamlining the healthcare process of fighting preventable infectious diseases. Vaccination of adolescents and adults has been proven to reduce nasopharyngeal carriage for serogroups C, W and Y, which is an important element in reducing transmission. Real-world evidence indicates that MenACWY-CRM can reduce IMD incidence even in high-exposure groups. When combined with vaccines against serogroup B meningococci, MenACWY-CRM can offer protection against five of the most common serogroups responsible for IMD, which is an important advantage in the continuously evolving landscape of meningococcal serogroup epidemiology.

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PLAIN LANGUAGE SUMMARY

Invasive meningococcal disease is an uncommon but life-threatening infection that appears as meningitis and/or sepsis. It is caused by Neisseria meningitidis, a bacteria commonly present in the throat or nose. Vaccination with MenACWY-CRM (Menveo, GSK) helps to prevent invasive meningococcal disease caused by four of the most common N. meningitidis serogroups (A, C, W and Y). This vaccine has been licensed for 10 years: we summarized here all available evidence gathered since the vaccine has been available in general practice, from clinical development to real-world experience. Information gained during clinical trials of MenACWY-CRM confirms that vaccination is well tolerated, has an acceptable safety profile and would induce significant protection when given to individuals of various ages such as infants, toddlers, children, adolescents and adults, and when administered at the same time as routine or traveler vaccinations as well as vaccines against serogroup B meningococci (4CMenB). Vaccination with MenACWY-CRM has been shown to decrease the number of serogroup C, W and Y meningococci found in the nose and throat in adolescents and adults as well as the occurrence of invasive meningococcal disease in a high-exposure population from a real-world setting. MenACWY-CRM can conveniently be integrated into most of the existing vaccination schedules for various age and risk groups. When combined with vaccination against serogroup B meningococci, MenACWY-CRM can contribute to providing protection against five of the most common serogroups responsible for invasive meningococcal disease.

Keywords: Carriage; Co-administration; Immunogenicity; Invasive meningococcal disease; MenACWY-CRM; Menveo; Quadrivalent meningococcal conjugate vaccine; Real-world evidence; Safety; Traveler vaccine

Key Summary Points

The quadrivalent A, C, W and Y meningococcal vaccine conjugated to nontoxic mutant of diphtheria toxin (MenACWY-CRM) has been licensed since 2010 for the prevention of invasive meningococcal disease (IMD), an uncommon but life-threatening condition.

Reported evidence indicates that MenACWY-CRM has demonstrated an acceptable safety profile, has been proven as immunogenic in a wide range of age groups and in various geographic settings and can reduce IMD incidence even in high-exposure groups.

Since no clinically relevant interactions were observed between MenACWY-CRM and a broad selection of routine immunizations, traveler vaccines and a vaccine against meningococcal serogroup B (4CMenB), this vaccine is being conveniently integrated into existing vaccination programs for various age and risk groups.

Even though access to healthcare might be challenging in many countries due to the COVID-19 pandemic, guidance from the World Health Organization recommends countries to prioritize routine immunization of children and urgent catch-up vaccinations.

When co-administered with 4CMenB, a vaccine against serogroup B meningococci, MenACWY-CRM can contribute to providing protection against five of the most common serogroups responsible for IMD, an important advantage in the continuously evolving landscape of meningococcal serogroup epidemiology.
INTRODUCTION

Invasive meningococcal disease (IMD), caused by Neisseria meningitidis, is an uncommon but life-threatening and unpredictable disease that can lead to death in 24 h [1–3]. Due to the similarity of its early, non-specific symptoms to those of viral illnesses, IMD can easily be misdiagnosed; even with timely and appropriate intervention, the case fatality rate can reach up to 20% [4] and a high proportion of IMD survivors may experience significant long-term sequelae such as neurological impairment, seizures, limb amputation or hearing loss [3]. Infants, young children, adolescents and/or young adults, immunocompromised patients and those with underlying medical conditions, individuals living in crowded conditions (such as students in college dormitories or military recruits), travelers to endemic or epidemic regions and laboratory personnel working with N. meningitidis isolates are considered at an increased risk for developing IMD [5–11].

Based on the capsular polysaccharide structure, N. meningitidis can be classified in 12 serogroups. Worldwide, six of these serogroups, A, B, C, W, X and Y, are responsible for most IMD cases [12, 13]. The distribution of the various serogroups fluctuates and varies over time and geographically [13–27] (Fig. 1).

Immunization with polysaccharide-protein conjugated vaccines is an effective means to prevent meningococcal disease caused by serogroups A, C, W and Y, while vaccines based on subcapsular protein antigens can provide protection against serogroup B [12, 28]. Currently, four quadrivalent meningococcal ACWY conjugate vaccines are licensed in various regions worldwide. These vaccines differ in the protein carrier to which the polysaccharide antigens are conjugated: MenACWY-TT (Nimenrix, Pfizer and the recently licensed MenQuadfi, Sanofi Pasteur) uses tetanus toxoid (TT), MenACWY-DT (Menactra, Sanofi Pasteur) uses diphtheria toxoid (DT), and MenACWY-CRM (Menveo, GSK) uses a nontoxic mutant of diphtheria toxin (CRM197) [29].

To provide a comprehensive overview of the MenACWY-CRM clinical development and real-world experience accrued during the first decade since its licensure, this review summarizes evidence of the vaccine’s safety, immunogenicity, co-administration with other vaccines, effect on carriage and real-world impact in a broad range of populations (Fig. 2). This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

MENACWY-CRM COMPOSITION, DEVELOPMENT AND LICENSURE

MenACWY-CRM Composition

Each dose of MenACWY-CRM contains 10 μg of serogroup A meningococcus (MenA) polysaccharide and 5 μg of each of serogroup C, W and Y meningococcus (MenC, MenW and MenY) polysaccharides, individually conjugated to Corynebacterium diphtheriae cross-reactive material (CRM197), in an approximate dose of 47 μg per vaccine. CRM197 is a mutant form of diphtheria toxin that differs from the wild type by a single amino acid (AA), AA 197 [30–32].

Before administration, the lyophilized MenA component has to be reconstituted using the liquid MenCWY component, contained in 0.5 ml of phosphate-buffered saline [31].

MenACWY-CRM Development

The development of purified capsular polysaccharide-based vaccines in the 1970s [33] represented a major advance in the fight against IMD at that time. However, the use of polysaccharide vaccines was initially limited to controlling epidemics and outbreaks of IMD, as they did not induce immunological memory, the
protection offered was short-lived and, with the exception of MenA, they were poorly immunogenic in infants and young children, and they induced hyporesponsiveness [28, 34–36].

The approach of conjugating the capsular polysaccharide to an immunogenic carrier protein was first used for developing a vaccine against Hemophilus influenzae type b [37, 38] and has been successfully applied to other pathogens as well, including N. meningitidis. By inducing a T-cell dependent immune response, polysaccharide-protein conjugate vaccines are highly immunogenic in infants, prime for immunological memory that can be effectively boosted without hyporesponsiveness and interfere with N. meningitidis transmission by decreasing carriage [1, 31, 34, 39]. The first conjugated meningococcal vaccines were developed against MenC [40]. The UK was the first country to introduce a MenC conjugate vaccine in its national immunization program (NIP) in 1999, leading to a substantial decrease of IMD caused by MenC as well as serogroup C nasopharyngeal carriage, in a very short time [41]. To further expand protection against IMD, quadrivalent ACWY conjugate vaccines, including MenACWY-CRM, were subsequently developed.

Initial Licensure of MenACWY-CRM

MenACWY-CRM was first licensed in 2010 for the active immunization against N. meningitidis serogroups A, C, W and Y of individuals aged between 11 and 55 years in the USA and Canada and of individuals aged 11 years or older at risk of exposure in the European Union (EU) [42]. Similarly to other meningococcal vaccines, evidence of MenACWY-CRM efficacy for licensure was provided based on serologic correlates of protection [35, 43, 44]. Historically, the first correlate of protection was established against MenC by a serum bactericidal assay using human complement (hSBA) and was defined as an hSBA titer ≥ 4 [5]. Subsequently, this titer...
was accepted as a correlate of protection against other serogroups [2, 45, 46]. In the clinical development program of MenACWY-CRM, serogroup-specific anticapsular antibody hSBA titers of ≥ 8 are used as correlates of protection.

**Distribution Footprint of MenACWY-CRM**

In the decade since its first approval, MenACWY-CRM has continued its clinical development program and has been licensed in over 60 countries [47], where over 58 million doses have been distributed. Age indications for MenACWY-CRM have also been expanded and currently range from 2 years onwards in the EU, between 2 months and 55 years in the USA and from 2 months onwards in several other countries, such as Argentina, Brazil, Australia and Saudi Arabia. Increasingly more countries have introduced meningococcal vaccination programs over the past years. MenACWY-CRM is the quadrivalent meningococcal vaccine specifically included in the NIP for both infants

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**Fig. 2** Summary of the MenACWY-CRM experience accrued during the first decade since its licensure. For more details, see video file 1 in the online/HTML version of the manuscript or follow the digital features link. *MenACWY-CRM inadvertently administered within 28 days prior to conception or during pregnancy. MenACWY-CRM is not indicated in pregnant women. MenACWY-CRM quadrivalent meningococcal vaccine against serogroups A, C, W and Y, conjugated to the nontoxic mutant of diphtheria toxin, HAV hepatitis A vaccine, HBV hepatitis B vaccine, Hib Haemophilus influenzae type b vaccine, IPV inactivated poliomyelitis vaccine, DTaP combined diphtheria, tetanus, acellular pertussis, PCV7 7-valent pneumococcal conjugate vaccine, PCV13 13-valent pneumococcal conjugate vaccine, Rotavirus rotavirus vaccine, MMR measles-mumps-rubella vaccine, V varicella vaccine, MMRV measles-mumps-rubella-varicella vaccine, Tdap tetanus-diphtheria-acellular pertussis vaccine, Td tetanus-diphtheria toxoid, HPV human papillomavirus vaccine, MenB Neisseria meningitidis serogroup B, 4CMenB multicomponent vaccine against meningococcal serogroup B, IMD invasive meningococcal disease.
SAFETY AND REACTOGENICITY

Within the last decade, the safety profile of MenACWY-CRM has been assessed in clinical trials and observational studies across all age groups: healthy [50–59] or immunocompromised infants and toddlers [7], children [56, 58–66], adolescents and adults [56, 59, 61–63, 67–72], including pregnant women [73] and elderly individuals up to 75 years of age [61].

Since the initial licensure of MenACWY-CRM, two studies assessing the safety of the vaccine across all age groups have been conducted. The first was a post-marketing study involving 3920 individuals aged 2 months to 55 years who received MenACWY-CRM according to local clinical practice in South Korea [56]; the other study analyzed 2614 reports of adverse events (AEs) in MenACWY-CRM recipients between 2010 and 2015, collected from the USA Vaccine Adverse Event Reporting System (VAERS) [59]. In the USA, different post-marketing studies assessed the safety of MenACWY-CRM in various age groups, including 138 infants with an indication for meningococcal vaccination, 42% of whom had impaired immunity (i.e., anatomic/functional asplenia or DiGeorge syndrome) [7], 327 children aged 2–10 years [66], 48,899 adolescents and young adults aged 11–21 years [74] and 92 women who inadvertently received MenACWY-CRM during pregnancy [73]. No major safety concerns were identified in any of the investigated populations and age groups. While a temporal association was observed between the occurrence of Bell’s palsy and receipt of MenACWY-CRM in the 11–21 years age group, the risk was significantly higher only for those who received MenACWY-CRM concomitantly with other vaccines. In this case, co-administration represents a confounding factor, considering that several of the co-administered vaccines have facial palsy reported as a potential AE in their labels [74]. These results are also included in a systematic review of post-licensure safety studies conducted in the USA, the conclusions of which further support the favorable safety profile of MenACWY-CRM in a real-world setting [75].

Administration of MenACWY-CRM concomitantly with routine infant vaccines [50–54, 76, 77], tetanus-diphtheria-containing boosters in adolescents and adults [76, 78–80], a quadrivalent human papilloma virus (HPV) vaccine in adolescents [76], traveler vaccines [81–83] and a multicomponent vaccine against meningococcal serogroup B (4CMenB) in infants [84] and high-exposure adults [11, 85] was well tolerated and no safety concerns were identified.

Overall, the most frequent solicited AEs reported after MenACWY-CRM were tenderness and irritability in infants and younger children [7, 50, 51, 53–56, 58, 60–63, 65] and pain, headache and myalgia in older children, adolescents and adults [56, 60–64, 67–70, 72]. These AEs, well known after any vaccine administration, were not severe and generally lasted for one to two days, as reflected in the MenACWY-CRM patient leaflet [86].

IMMUNOGENICITY

Immunogenicity of MenACWY-CRM has been confirmed during the first decade post-licensure across all age groups: infants and toddlers [50–54, 57, 58, 87–89], children [58, 60–65], adolescents and adults [62, 63, 67–69, 72, 90–92], including older adults up to 75 years of age [61]. In addition, a booster dose of MenACWY-CRM induced strong anamnestic responses [58, 64, 65, 68, 69, 72, 91] (Fig. 3). Recently, it has been demonstrated that MenACWY-CRM vaccination elicits protective bactericidal titers against hypervirulent MenC field strains that contributed to IMD outbreaks in Italy [93].

Immunogenicity of Different Dosing Schedules in Infants

Infants in their first year of life are a high-risk group for IMD. One of the main purposes of developing quadrivalent conjugate vaccines was...
to provide protection against IMD as early as possible in this vulnerable population [53]. Immunogenicity of the four-dose infant/toddler MenACWY-CRM schedule has been well established, and immune responses elicited by a three-dose schedule administered at 2, 6 and 12 months [51] or at 2, 4 and 12 months [53] were found to be noninferior to those of a four-dose schedule. In certain settings, depending on the regional epidemiology of IMD, a three-dose vaccination schedule that allows for more flexibility, while potentially reducing the number of vaccination visits, can represent an alternative to the four-dose schedule [53].

**Antibody Persistence and Booster Vaccination**

Serogroup-specific bactericidal antibodies induced by vaccination wane gradually over the
first 5 years post-vaccination; this waning is less marked following vaccination of adolescents (> 11 years of age) compared to vaccination in early childhood [64, 69]. A booster dose of MenACWY-CRM induced robust immune responses with high seroprotection rates, regardless of whether it was administered 6—12 months or 5 years after priming, or whether the children were primed in infancy (with a 3- or 4-dose schedule) or in toddlerhood [58, 64, 65, 87].

Teenagers represent another group at increased risk for IMD. To ensure a protective level of antibodies throughout the age groups at higher risk of IMD, a booster dose of quadrivalent conjugate vaccine in adolescence is recommended in different countries, including the USA [94] and the UK [95]. Given the country-specific particularities of meningococcal vaccination programs, several studies have explored the use of a MenACWY-CRM booster dose in adolescents primed with different mono- or quadrivalent meningococcal conjugate vaccines. A MenACWY-CRM booster dose administered 3–6 years after vaccination with either MenACWY-DT or MenACWY-CRM induced a fast and robust anamnestic response, from as early as 6 days [68, 72]; evidence has also been generated for persistence of antibody titers following booster administration [96]. In MenC-primed teenagers who received a booster dose of MenACWY-CRM 13 years after primary vaccination, boostability of the immune response against serogroup C was demonstrated [91].

**CO-ADMINISTRATION OF MENACWY-CRM WITH OTHER VACCINES**

**Co-administration with Routine Childhood/Adolescent Vaccinations**

Co-administration of vaccines targeting different infectious agents has the benefit of reducing the number of vaccination visits to a minimum, thus facilitating the implementation of busy infant vaccination schedules. Therefore, evidence is needed to show that vaccines can be administered during the same visit without any significant negative impact on the safety and immunogenicity of either vaccine [52].

In infants and toddlers, no clinically relevant vaccine interactions and/or impact on vaccine reactogenicity and safety were observed when MenACWY-CRM was co-administered with routine vaccines such as hepatitis A and B vaccines (HAV, HBV), combined diphtheria-tetanus-acellular pertussis vaccine (DTaP), inactivated poliomyelitis vaccine (IPV), vaccines against *H. influenzae* type b (Hib), combined DTaP-IPV-HBV/Hib, 7- and 13-valent pneumococcal conjugate vaccines (PCV7, PCV13), measles-mumps-rubella (MMR), varicella (V) and combined MMRV vaccines and rotavirus vaccine [50–54, 76, 77] (Fig. 4).

Immunological interference may arise when conjugated polysaccharide vaccines using TT, DT and CRM as carrier proteins are administered after tetanus-diptheria-containing vaccines. This is thought to be the result of an antigenic competition between the polysaccharide and the carrier protein epitopes, resulting in an increased antibody response to the carrier and a decreased response to the conjugated polysaccharides [97]. To explore whether such interference also appears in the case of MenACWY-CRM, studies designed to identify whether immune responses against the four vaccine serogroups are influenced by the concomitant or sequential administration of MenACWY-CRM with tetanus-diptheria-containing vaccines have been conducted in adolescents and adults. In Korean military recruits, while administration of tetanus-diphtheria toxoids (Td) 3 days before MenACWY-CRM led to lower antibody levels against MenA and C, seroprotection rates against MenC were not significantly influenced [78], and the differences are not considered to be clinically relevant. When co-administered with the tetanus-diptheria-acellular pertussis vaccine (Tdap), no interference of immune responses against either of the four meningococcal serogroups was observed in adolescents and young adults [76]. Similarly, no clinically relevant vaccine interactions or safety concerns were observed following concomitant administration of MenACWY-CRM, Tdap and HPV vaccine in
adolescents [76, 98, 99]. Co-administration of MenACWY-CRM with Tdap and PCV13 induced similar serogroup W-specific immune responses and was well tolerated, regardless of prior, concurrent or sequential administration of Tdap in Australian adults [79, 80].

Based on these results that show no significant interference of the immune responses against the vaccine antigens after completion of the vaccination course, concurrent administration of MenACWY-CRM and routine adolescent and adult vaccines, such as tetanus-diphtheria-containing vaccines, HPV vaccine and pneumococcal vaccines, is generally considered as both immunogenic and practical [76, 80, 100].

Co-administration with Traveler Vaccines

For travelers, concomitant administration of multiple vaccines is essential for maximizing protection against diseases within the often limited timeframe available before the start of travel. However, assessment of potential interactions between vaccines is required before routinely recommending co-administration [76]. In adolescents or adults, co-administration of MenACWY-CRM with several traveler vaccines (including vaccines against typhoid fever, yellow fever, Japanese encephalitis and rabies), HAV, HBV or the combined HAV-HBV vaccines did not interfere with the immunogenicity or safety of the individual vaccines [81–83] (Fig. 4).

**Fig. 4** Available evidence on the co-administration of MenACWY-CRM with other vaccines. MenACWY-CRM quadrivalent meningococcal vaccine against serogroups A, C, W and Y, conjugated to the nontoxic mutant of diphtheria toxin, DTap combined diphtheria, pertussis and tetanus vaccine, IPV inactivated poliomyelitis vaccine, Hib Haemophilus influenzae type b vaccine, HBV hepatitis B vaccine, HAV hepatitis A vaccine, PCV7 7-valent pneumococcal conjugate vaccine, PCV13 13-valent pneumococcal conjugate vaccine, MMR measles-mumps-rubella vaccine, V varicella vaccine, MMRV measles-mumps-rubella-varicella vaccine, Rotavirus rotavirus vaccine, Tdap tetanus-diphtheria-acellular pertussis vaccine, Td tetanus-diphtheria toxoid, HPV human papillomavirus vaccine, MenB Neisseria meningitidis serogroup B, 4CMenB multicomponent vaccine against meningococcal serogroup B.
Co-administration with Vaccines Against MenB

Development of 4CMenB, a vaccine against meningococcal serogroup B, has broadened the spectrum of vaccine-preventable IMD-causing meningococcal serogroups. The first studies assessing the sequential administration of a three-dose schedule of 4CMenB, followed by MenACWY-CRM after 1 month [85], and the concomitant administration of MenACWY-CRM with the first dose of 4CMenB [11] were conducted in laboratory workers routinely exposed to meningococcal isolates. Results of these studies revealed no immunological interference between 4CMenB and MenACWY-CRM and their co-administration also showed an acceptable safety profile [11, 85].

Co-administration of quadrivalent and serogroup B meningococcal vaccines in infants has the benefit of providing immunization against five of the most prevalent meningococcal serogroups during the first year of life, when the risk of IMD is the highest. Co-administration of 4CMenB and MenACWY-CRM at 3, 5, 7 and 13 months of age demonstrated an acceptable safety profile, with no notable increase in reactogenicity observed in participants who received both vaccines compared to those who received 4CMenB only; immune responses elicited following co-administration were noninferior compared to those following separate administration [84].

These data confirm that 4CMenB and MenACWY-CRM are safe and immunogenic with no interference when administered during the same vaccination visit. This combination is successful in inducing seroprotection in individuals who are at increased risk of IMD by virtue of their young age or their occupation (Fig. 4).

EFFECT OF MENACWY-CRM ON CARRIAGE AND TRANSMISSION

The rate of meningococcal carriage varies among the different age groups in a population and is strongly influenced by factors such as living in crowded conditions (e.g., college dormitories, military camps) or various social mixing behaviors. In developed countries, carriage rate peaks in adolescents and young adults, while in developing countries, carriage appears to be more common in early childhood and adulthood, with carriage rates being more evenly distributed across age groups [101, 102]. Since asymptomatic carriers are the main source of transmission, reducing the nasopharyngeal carriage of pathogenic meningococci has the potential to significantly reduce transmission [34].

Significant decreases in cross-sectional carriage rates of vaccine serogroups have been previously documented following mass vaccination with monovalent vaccines against MenC and MenA in the UK and sub-Saharan Africa, respectively [103–106]. To date, two studies have evaluated the impact of MenACWY-CRM vaccination on carriage. In students from the UK aged between 18 and 24 years, administration of MenACWY-CRM resulted in a significant decrease of 36% in MenC, W and Y carriage rates during the 12 months after vaccination [70]. In Poland, carriage rates for serogroups C, W and Y were significantly lower in professional soldiers (considered to be a high-exposure group) who had been vaccinated with MenACWY-CRM (1%) compared to their unvaccinated counterparts (10%) [9].

REAL-WORLD EVIDENCE OF MENACWY-CRM IMPACT

As IMD is an uncommon and life-threatening disease, the efficacy of MenACWY-CRM could not be assessed through randomized controlled trial designs and its licensure relied on immunological correlates of protection. Accordingly, observational studies are the only available method to assess the vaccine’s effect in reducing the incidence and risk of IMD caused by serogroups A, C, W and Y.

A recent study in a high-exposure group—the Armed Forces in South Korea—showed a reduction of 88% in meningococcal disease incidence after 95% of soldiers (amounting to a
population of 1624,000 person-years) were vaccinated with MenACWY-CRM during a 4-year period [107]. No cases of IMD resulting from serogroups A, C, W and Y, and no deaths occurred during the study period, compared to four deaths in the 5 years before vaccination was implemented. No new safety signals were detected, and the safety profile of the vaccine matched the one observed in clinical trials. As soldiers only stayed on duty for 2 years, the duration of protection could only be demonstrated for this follow-up period.

CONCLUSION

As more time passes since the introduction of NIPs in an increasing number of countries, the population-level effects of immunization are becoming clearer. These effects contribute to selecting the best approach for reducing IMD incidence. While access to healthcare services may currently be challenging in many countries due to the COVID-19 pandemic, it is essential to prioritize routine immunization, since high vaccination rates help to ensure that no additional pressure is placed on the already overloaded healthcare systems; guidance from the World Health Organization (WHO) also recommends countries to prioritize routine immunization of children and urgent catchups. Especially in the context of the increased contact and socialization that will follow the lifting of lockdowns and the reopening of schools, accent should be placed on protecting children and adolescents, two age groups who are at increased risk of IMD. This is also important since initial non-specific symptoms of IMD might resemble those of COVID-19, potentially preventing early diagnosis, which in the case of IMD, is essential for a fast and appropriate treatment.

With the continuously evolving epidemiology of meningococcal serogroups responsible for IMD, protection against the most common N. meningitidis serogroups becomes crucial. MenACWY-CRM can play an important role in generating such a protection, with the added benefit of being easily integrated into current vaccination programs. Co-administration of MenACWY-CRM with 4CMenB will help protect against five of the most common serogroups responsible for IMD, thus facilitating the implementation of public health strategies to fight this uncommon but life-threatening disease.

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