An Advisory Committee Statement (ACS)

National Advisory Committee on Immunization (NACI)

NACI Rapid Response: Update on the Use of Quadrivalent Conjugate Meningococcal Vaccines in Children Under 2 Years of Age

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Public Health Agency of Canada
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Preamble

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

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I. Background

Invasive meningococcal disease (IMD) is a rare but life-threatening disease that often presents as meningococcal meningitis or sepsis[1]. Worldwide, IMD is primarily caused by serogroups A, B, C, W, X, and Y of *Neisseria meningitidis*. Meningococcal disease caused by the different serotypes varies widely by geography and through time. In Canada, serogroup C predominated in the pre-vaccination period but there has been a decrease of serogroup C and an increase of serogroups B and W since vaccine programs were established[1]. Recently, serogroup Y appears to have increased in Quebec[2]. Serogroup A, which is not endemic in Canada, once predominated globally, but has largely disappeared following immunization programs in Africa[3,4]. These changes in incidence highlight the importance of active surveillance and updating immunization programs to optimize the prevention of IMD. In Canada, young children, particularly those under 5 years of age, have the highest incidence of IMD which is partially due to limited prior pathogen exposure[5]. In individuals under 5 years of age, approximately 10% of IMD cases result in death[6]. Survivors may experience long-term sequelae such as hearing loss, cognitive impairments, limb amputations, and skin scarring[1,7,8].

Since the early 2000s, Canada has implemented routine immunization programs against serogroup C which have dramatically reduced the incidence of serogroup C IMD in children and adolescents[1,9]. For routine immunization of healthy individuals aged 2 to 23 months, the National Advisory Committee on Immunization (NACI) currently recommends one dose of monovalent conjugated serogroup C vaccine (Men-C-C) at 12 to 23 months of age, regardless of any doses given during the first year of life. For individuals 2 to 23 months of age who are at high risk of IMD due to underlying medical conditions or increased risk of exposure to *Neisseria meningitidis*, NACI recommends Men-C-ACYW-CRM (Menveo) and/or 4CMenB (Bexsero) depending on the risk[10]. For details on the latest NACI recommendations, please consult the Canadian Immunization Guide: Meningococcal Vaccines Chapter.

When Canada's routine meningococcal vaccine program was initially recommended for children under 2 years of age, only Men-C-C vaccines were authorized for use in this age group. Since NACI's last updated guidance on the use of quadrivalent conjugate meningococcal vaccines containing serogroups A, C, Y and W (Men-C-ACYW), Men-C-ACYW-TT vaccines (Nimenrix® and MenQuadfi®) have been authorized for use in children under 2 years of age in Canada[11,12]. In addition, PHAC was notified by the market authorization holders that all Men-C-C vaccines marketed in Canada (i.e. Menjugate Liquid, NeisVac-C®) will no longer be available for provincial purchase starting in April 2026. In light of expected vaccine supply changes, authorization of Men-C-ACYW-TT vaccines (Nimenrix® and MenQuadfi®) for children under 2 years of age and evolution of IMD epidemiology in Canada, NACI has been requested to provide updated recommendations on the use of Men-C-ACYW vaccines in children under 2 years to inform provincial and territorial meningococcal vaccine programs for infants and toddlers.

OBJECTIVE

This rapid response was undertaken to provide guidance on the use of quadrivalent meningococcal vaccines in routine and high-risk immunization programs in Canada. To provide timely advice to provinces/territories (P/Ts), the scope of this guidance was limited to children under 2 years of age and to quadrivalent conjugate meningococcal vaccines containing serogroups A, C, Y, and W antigens.

As indicated in its workplan, NACI will conduct a more comprehensive review of existing meningococcal ACYW and B recommendations (including routine immunization programs for infants and toddlers, and adolescent and young adults, as well as high-risk immunization programs) in a future NACI statement.

II. Methods

This NACI advisory committee statement was prepared through the following activities:

- Analysis of the burden of IMD using data submitted to the National Enhanced Invasive Meningococcal Disease Surveillance System (eIMDSS), and P/T isolate submissions to the National Microbiology Laboratory (NML).
- Retrieval, quality assessment, and synthesis of individual studies on the benefits and harms of Men-C-ACYW vaccines (including data comparing the immunogenicity and safety of Men-C-ACYW-CRM versus Men-C-ACYW-TT vaccines).
- Review of vaccine guidance from national and international bodies through an environmental scan.
- Consideration of vaccine principles.
- Translation of evidence into recommendations.

The main policy questions addressed in this rapid response were:

1. For routine programs: Should NACI recommend the use of quadrivalent Men-C-ACYW conjugate vaccines in routine immunization schedules of children under 2 years of age, in place of the currently recommended monovalent Men-C-C vaccines?

2. For high-risk programs: Should NACI maintain the current preferential recommendation for Men-C-ACYW-CRM (Menveo) in children under 2 years of age who are at high risk of IMD, or can the other Men-C-ACYW vaccines (Nimenrix®, MenQuadfi® and Menactra®) be considered in this population?

Knowledge synthesis was performed by the NACI Secretariat and supervised by the NACI IMD Working Group (WG). This included considerations such as the burden of disease, vaccines' safety and immunogenicity, and other aspects of the overall immunization strategy (economics, ethics, equity, feasibility and acceptability). NACI reviewed the evidence, discussed the recommendations as proposed by the IMD WG, and voted on February 17, 2026.

Note on language: In this rapid response, vaccine trade names are sometimes used to help differentiate meningococcal vaccines using the same carrier protein. The use of trade names is for identification only and does not indicate endorsement of any specific vaccine product.

III. Evidence Summary

III.1 Burden of disease

In Canada, IMD is reported year-round with most cases occurring in the fall and winter, with periodic peaks in the winter months[13]. The incidence of serogroup C IMD decreased, following the introduction of routine Men-C-C vaccine programs in the early 2000s[1,9]. Canada has observed a 96% reduction of serogroup C IMD, and an overall average 66% IMD reduction from 0.83 cases per 100,000 population in 1997–2001 to 0.28 per 100,000 in 2017–2021 in all age groups[1]. While additional reductions in IMD incidence were observed during the COVID-19 pandemic years, there has been a gradual increase since 2022, although absolute rates remain low[6].

Figure S1 in Appendix A presents the reported IMD cases and IMD incidence rates in Canada. From 2015 to 2024, a total of 1,075 IMD cases (all ages) were reported to the eIMDSS, corresponding to an average annual incidence of 0.28 cases per 100,000 population[6]. During this period, infants under 1 year of age consistently had the highest age-specific annual incidence, with a mean of 2.79 cases per 100,000, while incidence in other age groups was lower (Figures S2 and S3 in appendix A). Among children 1 to 4 years of age, average annual incidence during this period was 0.87 cases per 100,000, among adolescents 15 to 19 years of age incidence was 0.63 cases per 100,000, and among adults over 40 years of age incidence was 0.29 cases per 100,000. While representing only 1% of the population, infants under 1 year of age accounted for roughly 9% of all national IMD cases and children 1 to 4 years of age accounted for 12% of cases over this period.

Consistent with previous findings[13], national data from 2015 to 2024 continue to show that serogroups B and W together account for the majority of reported IMD cases, with serogroup B responsible for 33% of cases and serogroup W for 27%, followed by serogroups Y (14%) and C (5%)[6]. Among children 5 years of age and younger, serogroup B disease remains the predominant cause of IMD (accounting for approximately 50% of cases), with an average annual incidence of 0.48 cases of serogroup B IMD per 100,000 between 2015 and 2024. While less common than serogroup B disease, serogroups W and Y remain important causes of IMD disease in children 5 years of age and younger (Figures S4 and S5 in Appendix A). In terms of case counts, over the past decade among children under 5 years of age, serogroup B was responsible for 104 out of 210 cases, serogroup W caused 53 cases and Y caused 8 cases. Between 2015 and 2024, the case fatality rate (CFR) for serogroup C IMD across all age groups was 17%, while serogroup B, Y, and W cases had a CFR of around 8%.

Regional IMD epidemiology and outbreaks

Over the last decade, there have been notable differences in the epidemiology of IMD across Canada. Age-standardized rates (2015 to 2024) were highest in Nunavut (1.29 per 100,000), followed by Manitoba (0.63 cases per 100,000), Nova Scotia (0.55 per 100,000), Northwest Territories (0.45 per 100,000), Quebec (0.38 cases per 100,000) and Newfoundland and Labrador

(0.34 per 100,000)[6]. Serogroup distribution also varied from west-to-east, with serogroup W accounting for all culture-confirmed IMD in Yukon, 61% of cases in Manitoba, 58% of cases in British Columbia and 54% in Alberta. In contrast, serogroup B accounted for over 75% of cases in Newfoundland, Nova Scotia, New Brunswick and Northwest territories[6]. An increase in the incidence of serogroup Y IMD caused by a virulent clone belonging to the clonal complex ST-23 has also been observed in Quebec starting in 2022[2].

From 2015 to 2024, there were six IMD outbreaks reported to eIMDSS. All but one involved serogroups B or W. The outbreaks occurred in community or institutional settings[6].

III.2 Immunogenicity and Safety of Men-C-ACYW vaccines authorized for use in Canada

As of March 26, 2026, there were three quadrivalent Men-C-ACYW vaccines authorized in Canada: Menveo (Men-C-ACYW-CRM), Nimenrix® (Men-C-ACYW-TT) and MenQuadfi® (Men-C-ACYW-TT). Marketing of Menactra® (Men-C-ACYW-DT) in Canada has been discontinued since December 19, 2025, but its use is anticipated until the latest lot expiry date (August 31, 2026). Table S1 and Table S2 in Appendix A present details on vaccines characteristics and authorized schedules.

NACI reviewed available evidence on the safety and immunogenicity from 14 clinical trials in which Men-C-ACYW vaccines currently authorized for use in Canada were compared to each other or to Men-C-C vaccines[14-37]. NACI reviewed data on Men-C-ACYW-TT and Men-C-ACYW-CRM vaccine. Men-C-ACYW-DT[11] is expected to be discontinued in December 2026. Below is a high-level summary of relevant immunogenicity and safety outcomes from these studies. Additional details from these studies are available in Appendix A (Tables S3A to S3C and S4A to S4C). Data on comparative efficacy and effectiveness was not available. For conjugate meningococcal vaccines, efficacy is inferred from immunogenicity using serum bactericidal antibody (SBA) assays which measure functional antibodies that are capable of bacterial killing in the presence of human (h) or rabbit (r) complement (hSBA or rSBA). Unless otherwise stated, all reported immune response parameters (e.g., seroresponse rates, proportion of participants with seroprotection, geometric mean titres [GMTs]) were measured 1 month after the dose for which results are described.

The descriptions of vaccine schedules below includes the number of infant doses administered before 12 months of age *plus* the toddler dose administered at 12 months of age or older (e.g., 3+1, 2+1, 1+1 or 0+1).

Immunogenicity

Immunogenicity data was available from 13 trials[14-36]. Overall, Men-C-ACYW-TT vaccines were found to elicit robust immune responses that were generally comparable or superior to the comparators Men-C-ACYW-CRM or Men-C-C (Tables S3A to S3C).

Immunogenicity of Men-C-ACYW vs. Men-C-C

Six clinical trials compared immune responses following quadrivalent Men-C-ACYW-TT vaccines with responses after monovalent Men-C-C vaccines (TT or CRM conjugates) in infants or toddlers, starting at 6 weeks and 12 months of age, using 3+1, 2+1 or 0+1 schedules. Across these studies and regardless of the schedule, Men-C-ACYW-TT vaccines met pre-defined non-inferiority criteria for both the proportion of study participants achieving seroprotection against serogroup C as well as serogroup C antibody titres, based on immune responses measured 30 to 42 days after the last dose in the series (see Table S3A for more details).

Comparison of immunogenicity between Men-C-ACYW vaccines (MenQuadfi®, Nimenrix® or Menveo)

Eight clinical trials compared the immunogenicity of Men-C-ACYW vaccines: MenQuadfi® versus Menveo (n=4) and MenQuadfi® vs. Nimenrix® (n=4). These trials enrolled infants starting at 2, 6 or 12 months of age and used schedules of 3+1, 2+1, 1+1 or 0+1 doses with or without routine paediatric vaccines[14-19,24-27,29,31]. All the vaccines generated very high (≥94%) seroprotection across all serogroups 30 days after the toddler dose. Compared to Menveo, MenQuadfi® met non-inferiority for all four serogroups. While there were some assay- and serogroup-specific differences in GMTs, the clinical significance of these differences is unknown (Table S3B). Compared to Nimenrix®, MenQuadfi® met non-inferiority for seroprotection against all four serogroups, with MenQuadfi® often generating higher GMTs (Table S3C).

Safety

Safety data were available from 14 trials[14-37] (Tables S4A to S4C). Across all clinical trials, the safety profiles of Men-C-ACYW-TT vaccines (MenQuadfi® and Nimenrix®) were found to be comparable to each other and to the comparator vaccines, including Menveo, NeisVac-C® vaccine, Menjugate Liquid, and Meningitec®. Most reported adverse events (AEs) were non-serious, affecting between 70% and 92% of study vaccine recipients. In all studies, injection-site reactions such as pain, tenderness, and redness were the most frequently reported local reactions, while irritability, drowsiness, crying, and fever were the most commonly reported systemic reactions. These reactions were generally mild to moderate and resolved spontaneously within a few days of vaccination. Where seizures or convulsions were reported, they frequently occurred outside the expected risk-window or were associated with concomitant infection or underlying medical history. Most serious adverse events (SAEs) were considered unrelated to the study vaccines, predominantly consisting of common childhood infections and injuries.

Concurrent administration of Men-C-ACYW vaccines with routine vaccines

Seven studies and one review of ten studies compared the immunogenicity and safety after the concurrent administration of Men-C-ACYW vaccines with other vaccines to non-concurrent administration (sequential administration or each vaccine alone)[14,24,28,33,35,38-41]. In these Phase 2/3 clinical trials, Men-C-ACYW-CRM and Men-C-ACYW-TT vaccines were concurrently administered with DTaP-IPV-HB-Hib, Pneu-C-7, Pneu-C-10, Pneu-C-13, rotavirus, MMR or varicella vaccines. There was no observed significant immune interference (i.e. immune responses to all concurrently-administered vaccine antigens met non-inferiority criteria when compared to immunogenicity of non-concurrently administered vaccines). However, in three trials where Men-

C-ACYW-CRM was administered at 2, 4, 6, and 12 months with different routine vaccines (DTaP, IPV, HB, Hib, and Pneu-C-7 or Pneu-C-13), GMTs for some pertussis antigens[40,42] and select pneumococcal serotypes (i.e., 6B, 23F, and 19A) were slightly lower one month after the 6-month dose[40,43-45]; differences in immune responses resolved one month after the toddler booster and non-inferiority met for all antigens. The clinical significance of the lower titres after 6 months is unknown as there are no correlates of protection. Reactogenicity was comparable with or without concurrent administration.

Overall, the available evidence suggests that Men-C-ACYW vaccines can be administered concurrently with routine vaccines given that no interference has been observed with doses administered at or after 12 months of age. However, evidence remains limited in relation to immune interference when CRM-containing vaccines are concurrently administered with Men-C-ACYW-CRM, and when TT-containing vaccines are concurrently administered with Men-C-ACYW-TT before 12 months of age. No studies were identified that included pneumococcal conjugated (Pneu-C) vaccines with higher valency (e.g., Pneu-C-15 and Pneu-C-20).

Vaccine schedules and interchangeability

Four clinical trials compared 2+1 and 3+1 schedules in healthy children under 2 years of age. In the two trials in which Men-C-ACYW-CRM vaccine was evaluated, one assessed non-inferiority after the infant series before 12 months of age and the other after the toddler dose given at 12 months of age or older; in both, immune responses after the 2+1 schedule were non-inferior to those elicited by the 3+1 schedule for all serogroups except serogroup A[42,45]. In a trial in which Nimenrix® was provided in 3+1 (doses at 2, 3, 4, and 12 months) and 2+1 (doses at 2, 4, and 12 months) schedules, high antibody titres (meeting or exceeding the seroprotective threshold) were achieved for all four serogroups one month after both primary schedules and after the toddler dose, with a favorable safety profile[32]. Another trial compared MenQuadfi® 3+1 vs. 2+1 (with Nimenrix® 2+1 as a control)[28]. Seroresponse rates for serogroups C, W and Y after the toddler dose were high (≥95%), with MenQuadfi® 2+1 meeting non-inferiority compared to control. Overall, for serogroups C, W, and Y, immune responses after the 2+1 schedule were non-inferior compared to the 3+1 schedule, for both Men-C-ACYW-CRM and Men-C-ACYW-TT products. For serogroup A, there was more variation across studies, with a modest incremental benefit with three priming infant doses than two, but the differences narrowed substantially following the toddler dose in every study. After series completion, 2+1 and 3+1 schedules produced high seroresponse rates in all four trials (typically ≥88–100%), with generally similar GMTs and comparable safety, for both Men-C-ACYW-CRM and Men-C-ACYW-TT.

In a randomized study in toddlers 12 to 15 months of age, a single dose of Men-C-ACYW-CRM elicited robust immune responses at 29 days post-vaccination, with seroprotection rates and GMTs generally comparable to Men-C-ACYW-TT (Nimenrix®) across all serogroups[30]. By 180 days post-vaccination, seroresponse rates for Men-C-ACYW-CRM were higher for serogroup A (62% vs 29%; GMT 13 vs 4.67), but lower for C (85% vs 93%; GMT 24 vs 41), W (83% vs 99%; GMT 21 vs 56) and Y (74% vs 95%; GMT 16 vs 26) compared with Men-C-ACYW-TT, with overall comparable safety profiles.

Although no studies specifically evaluated mixed-product schedules (i.e. interchangeability within a series) in infants, a study assessing a Men-C-ACYW-TT (MenQuadfi®) booster dose in toddlers 12 to 23 months of age (mean age of 14.3 months; n=71) previously primed with either Nimenrix® or Menveo® demonstrated robust immune responses across all serogroups, with 100% of participants achieving protective antibody titers one month post-booster and substantial increases in GMTs from baseline[46]. The toddler booster dose was well tolerated, with mostly mild to moderate injection site and systemic reactions. Together with the comparisons of different Men-C-ACYW conjugate vaccines described above, these findings suggest that products containing different carrier proteins could be interchanged, if necessary, to complete a series.

III.3 Ethics, equity, feasibility and acceptability

Ethics

This NACI guidance was developed using processes that uphold and integrate ethical procedural considerations. NACI evaluated the following core ethical principles for public health: promoting well-being and minimizing risk of harm; maintaining trust; respect for people and fostering autonomy; and promoting justice and equity. No significant ethical issues were identified through this evaluation.

Equity

Replacing Men-C-C vaccines with quadrivalent Men-C-ACYW vaccines is not expected to create equity issues. Transition to a quadrivalent conjugate meningococcal vaccine program addresses equity considerations by ensuring the continuity of existing infant/toddler programs. Broader serogroup coverage (A, Y, W in addition to C) aligns with the ethical principle of maximizing health benefits. In addition, a universal recommendation may improve equity by standardizing the access of care across Canada and ensuring that protection against emerging serogroups (e.g. W) is not limited to those in groups at high risk of IMD or those who can afford it.

Feasibility

Men-C-ACYW vaccines are already procured and used in all provinces and territories. Using the same product for infants/toddlers and adolescents could reduce logistical complexity, lower the risk of administration errors, and simplify public health messaging. Feasibility may be further improved if any Men-C-ACYW vaccine can be used, since there would be more product choices for programs. Using a 2+1 instead of a 3+1 schedule for individuals at high risk of IMD may further improve program feasibility and reduce costs.

Acceptability

National Men-C-C coverage in children under 2 years of age (children receiving at least one dose of Men-C-C by their second birthday) is approximately 90%. Feedback received from provincial and territorial consultations indicated no major feasibility concerns and there was general support for the switch to Men-C-ACYW programs. Acceptability among parents and providers is expected to remain high, provided clear guidance is given on schedules and interchangeability. It is also expected that coverage of more *N. meningitis* serogroups, and therefore more protection against IMD, will be seen positively by parents. Men-C-ACYW vaccines with simpler schedules (e.g. 2+1 instead of 3+1 for individuals at high risk) are likely to be more acceptable to both parents and vaccine providers.

III.4 Economics

NACI reviewed economic considerations in the context of the discontinuation of Men-C-C vaccine supply and the need to identify a replacement product to maintain protection against IMD in infants and toddlers. Given that Men-C-C vaccines will no longer be broadly available in Canada, a formal economic evaluation of a routine infant Men-C-ACYW program was not conducted. Instead, economic considerations focused on the anticipated budget implications of replacing Men-C-C with Men-C-ACYW, informed by current procurement volumes and publicly available vaccine price information.

Publicly available list prices indicate that, based on average prices, Men-C-ACYW vaccines are approximately 1.6 times as costly as Men-C-C vaccines (range: 1.1-2.8, based on smallest and largest differences in list prices across products). Based on these list prices, replacing Men-C-C with Men-C-ACYW was estimated to increase vaccine acquisition costs by approximately $3.7 million additional per 100,000 doses procured, with estimates ranging from $0.5 million to $6.9 million, depending on product-specific list prices and price assumptions. The number of procured doses of Men-C-C and Men-C-ACYW in Canada are currently roughly equivalent, therefore replacing Men-C-C with Men-C-ACYW would be expected to approximately double the number of Men-C-ACYW doses procured.

Factors that could partially offset higher vaccine acquisition costs were identified but not formally evaluated. These included: the potential for lower per-dose prices resulting from higher overall purchase volumes through bulk procurement if Men-C-ACYW vaccines were used across multiple age groups, prevention of additional IMD cases due to protection against serogroups W and Y, and administrative efficiencies associated with the use of a single vaccine for both infant/toddler and adolescent programs.

Iv. Recommendations

Following the thorough review of available evidence summarized above, NACI makes the following recommendations for public health programs.

Please note:
A **strong recommendation** applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.

A **discretionary recommendation** may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

Please see Table 1 for a more detailed explanation of strength of NACI recommendations.

Recommendations for public health program decision-making

(i.e. Provinces and Territories making decisions for publicly funded immunization programs)

Routine programs

1. NACI recommends that all children 12 to 23 months of age should receive one dose of Men-C-ACYW vaccine, regardless of any doses given during the first year of life.

(Strong NACI Recommendation)

Considerations

- Menactra® (Men-C-ACYW-DT), MenQuadfi® (Men-C-ACYW-TT), Menveo (Men-C-ACYW-CRM) or Nimenrix® (Men-C-ACYW-TT) can be used in their authorized age groups. See table 2 for the recommended routine vaccine schedule.
- Men-C-ACYW vaccines can be administered concurrently with other vaccines.
- Toddlers who have already received a Men-C-C vaccine between 12 to 23 months of age are not recommended to be revaccinated with an additional dose of Men-C-ACYW.
- Depending on the provincial or territorial schedule and the incidence of IMD in their jurisdiction, infants may receive Men-C-ACYW doses before 12 months of age.
- All jurisdictions should maintain the adolescent Men-C-ACYW program to sustain herd immunity and ensure individual protection during adolescence and young adulthood when the risk of IMD increases again.

Summary of evidence and rationale

- Recent epidemiological data continue to show that IMD incidence is highest among young children. Canada's routine meningococcal infant immunization programs against serogroup C have successfully and dramatically reduced the incidence of serogroup C IMD in children under 5 years of age.

- One dose of Men-C-C vaccine has previously been recommended for all children at 12 to 23 months of age, regardless of any doses given during the first year of life. Replacing the recommended Men-C-C vaccines with Men-C-ACYW vaccines will provide additional coverage for serogroups W and Y, which currently account for more reported IMD cases than serogroup C.
- Evidence from randomized clinical trials show that Men-C-ACYW vaccines provide comparable or superior serogroup-C immune responses compared to Men-C-C vaccines, while also protecting against serogroups A, W and Y. Reactogenicity of Men-C-ACYW and Men-C-C vaccines was similar across reviewed studies.

Programs for individuals at high risk of invasive meningococcal disease

2. NACI recommends that children 6 weeks to 23 months of age who are at high risk of invasive meningococcal disease due to an underlying medical condition or increased risk of exposure to serogroups A, C, Y or W should be immunized using a Men-C-ACYW vaccine.
(Strong NACI recommendation)

Considerations

- Menactra® (Men-C-ACYW-DT), MenQuadfi® (Men-C-ACYW-TT), Menveo (Men-C-ACYW-CRM) or Nimenrix® (Men-C-ACYW-TT)® can be used in their authorized age groups. For children who are at high risk of IMD, the recommended vaccine schedule by age is specified in Table 2. The list of individuals at high-risk of IMD is available below.
- Men-C-ACYW conjugate vaccines containing different carrier proteins (i.e., DT, TT or CRM) can be interchanged. When possible, the vaccine series should be completed with the same vaccine, however in situations where the originally used product is not available for a subsequent dose or unknown, another Men-C-ACYW vaccine may be administered to complete the schedule.
- Men-C-ACYW vaccines can be concurrently administered with other vaccines.

Summary of evidence and rationale

- Men-C-ACYW vaccines authorized for use in Canada provide robust immune responses against serogroups A, C, Y, W of *Neisseria meningitidis.*
- In healthy infants, immune responses to serogroups C, Y, W were comparable after a 2+1 or 3+1 schedule. For serogroup A, immune responses were sometimes higher with three priming doses than two. However, these differences narrowed substantially following the toddler dose, and both 2+1 and 3+1 schedules produced high antibody titres against serogroup A. The clinical significance of these lower antibody titres after the infant series is unknown. Serogroup A is not currently endemic in Canada and its incidence has decreased globally following the introduction of immunization programs.
- Some Men-C-ACYW vaccines available in Canada are authorized with a 3+1 schedule but can be used off-label with a 2+1 schedule in individuals at high risk of IMD, based on evidence of robust immune responses following completion of a 2+1 schedule.

Table 1. Strength of NACI recommendation

Strength of Recommendation	Strong	Discretionary
Wording	"should/should not"	"may/may not"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), OR Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

Table 2. Recommended Men-C-ACYW[a] vaccine schedules for children under 2 years of age

Age at vaccination	Recommended vaccine schedules by age	
	Routine schedule[b]	**Schedule for individuals at high risk of invasive meningococcal disease**
6 weeks to 6 months	-	**2 +1 doses** (2 doses 8 weeks[c] apart + 1 booster dose at 12 to 23 months[d] of age)
7 to 11 months	-	**1+1 doses** (1 dose + 1 booster dose at 12 to 23 months[d] of age)
12 to 23 months	**1 dose**	**1 dose[e]**

[a]Menactra® (Men-C-ACYW-DT), MenQuadfi® (Men-C-ACYW-TT), Menveo (Men-C-ACYW-CRM) or Nimenrix® (Men-C-ACYW-TT) can be used in their authorized age groups (consult the product's leaflet or information contained within Health Canada's authorized product monographs available through the Drug Product Database).
[b] Infants may receive Men-C-ACYW doses before 12 months of age, depending on the provincial or territorial schedule and the incidence of IMD in their jurisdiction
[c] Men-C-ACYW vaccines may be given a minimum of 4 weeks apart if accelerated immunization is needed (e.g. close contacts of IMD and/or outbreak management)
[d] Booster dose is recommended to be given at 12 to 23 months of age but can be given at ≥24months of age if the child was not immunized at the recommended age. Dose is recommended to be administered 8 weeks or more from the previous dose. However, a minimum interval of 4 weeks can be used if accelerated immunization is needed.
[e] Previously unimmunized individuals 12 months of age and older who are at high risk of IMD *due to underlying medical conditions* are recommended to receive two doses of Men-C-ACYW vaccine

List 1. Individuals at high risk of invasive meningococcal disease

Underlying medical conditions

- Functional or anatomic asplenia or sickle cell disease
- Congenital immunodeficiencies (e.g., complement, properdin, factor D, combined T and B cell immunodeficiencies or primary antibody deficiencies)
- Acquired complement deficiency due to receipt of terminal complement inhibitors
- HIV, especially if perinatally acquired

Increased risk of exposure

- Travellers to areas with high rates of endemic meningococcal disease or transmission, including meningitis belt of sub-Saharan Africa and pilgrims for the purposes of Hajj or Umrah in Mecca, Saudi Arabia
- Research, industrial and clinical laboratory personnel who are potentially routinely exposed to N. meningitidis
- Military personnel during recruit training and on certain deployments
- Most close contacts of a case of IMD and for outbreak control, if the disease is caused by a serogroup contained in the vaccine

V. RESEARCH PRIORITIES

To address current knowledge gaps resulting from absent or limited data and to strengthen future recommendation development, NACI has identified the following areas where further research is needed:

- Immunogenicity, effectiveness and durability of protection of different Men-C-ACYW schedules in infants and toddlers who are immunocompromised.
- Impact on immunogenicity of concurrent administration of Men-C-ACYW vaccines with Pneu-C-15, Pneu-C-20 and other higher valency pneumococcal vaccines.
- Meningococcal carriage by age and serogroup.

LIST OF ABBREVIATIONS

AEs	Adverse events
AEFI	Adverse event following immunization
CFR	Case fatality rate
CI	Confidence interval
CRM	CRM197 carrier protein
DT	Diphtheria Toxoid carrier protein
DTaP	Diphtheria toxoid, tetanus toxoid, acellular pertussis
DTaP-IPV-HB-Hib	Diphtheria toxoid, tetanus toxoid, acellular pertussis, hepatitis B, inactivated poliomyelitis, *Haemophilus influenzae* type b
EEFA	Ethics, Equity, Feasibility, Acceptability
eIMDSS	National Enhanced Invasive Meningococcal Disease Surveillance System
GMT	Geometric mean titre
hSBA	Serum bactericidal antibody assay with human complement
HB	Hepatitis B
Hib	*Haemophilus influenzae* type b
IMD	Invasive meningococcal disease
IPV	Inactivated poliomyelitis vaccine
Men-C-C	Monovalent conjugate meningococcal serogroup C vaccine
Men-C-ACYW	Quadrivalent conjugate meningococcal serogroups A, C, Y and W vaccine
Men-C-ACYW-DT	Men-C-ACYW with Diphtheria Toxoid carrier protein (Menactra®)
Men-C-ACYW-CRM	Men-C-ACYW with CRM_{197} carrier protein (Menveo)
Men-C-ACYW-TT	Men-C-ACYW with Tetanus Toxoid carrier protein (Nimenrix® or MenQuadfi®)
MMR	Measles-mumps-rubella
N. meningitis	*Neisseria meningitis*

NACI	National Advisory Committee on Immunization
PHAC	Public Health Agency of Canada
Pneu-C	Pneumococcal conjugate vaccines
Pneu-C-7	Pneumococcal conjugate 7-valent vaccine
Pneu-C-10	Pneumococcal conjugate 10-valent vaccine
Pneu-C-13	Pneumococcal conjugate 13-valent vaccine
Pneu-C-15	Pneumococcal conjugate 15-valent vaccine
Pneu-C-20	Pneumococcal conjugate 20-valent vaccine
rSBA	Serum bactericidal antibody assay with rabbit complement
ST-11	Sequence Type 11
TT	Tetanus toxoid carrier protein
USA	United States of America
VE	Vaccine effectiveness
VS	Versus
WG	Working group
WHO	World Health Organization

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Appendix A

Figure S1: Reported IMD Cases and Incidence Rates (IR) in Canada, 2015-2024

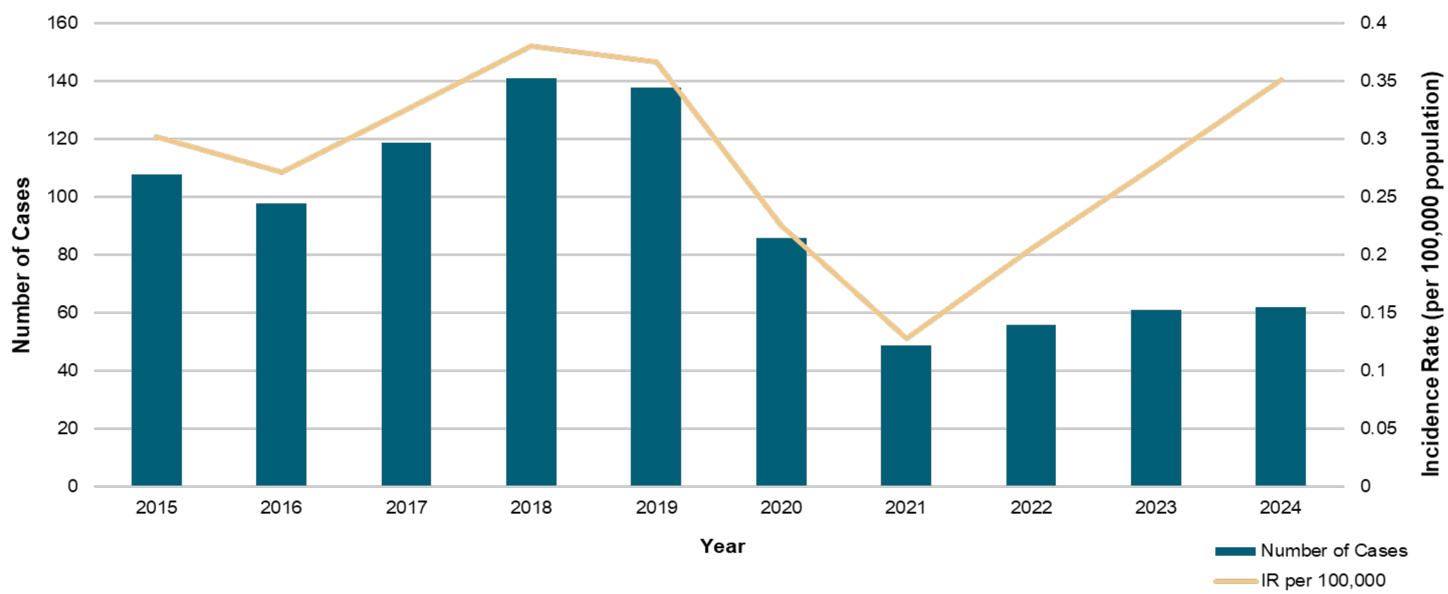

Figure S2: IMD Incidence Rates by Age Group, 2015-2024

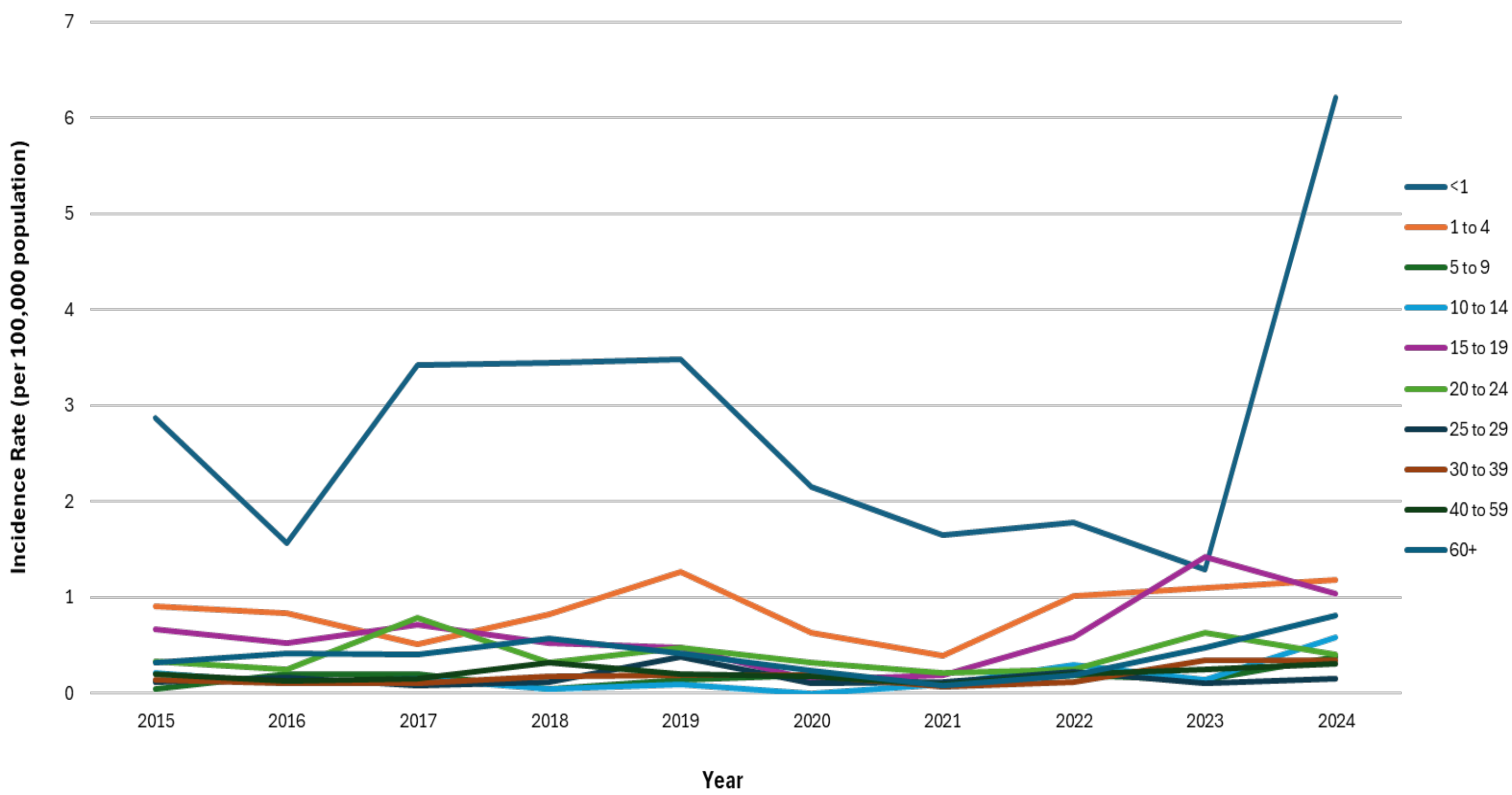

Figure S3: IMD Incidence in Children Under 5 Years of Age, 2015-2024

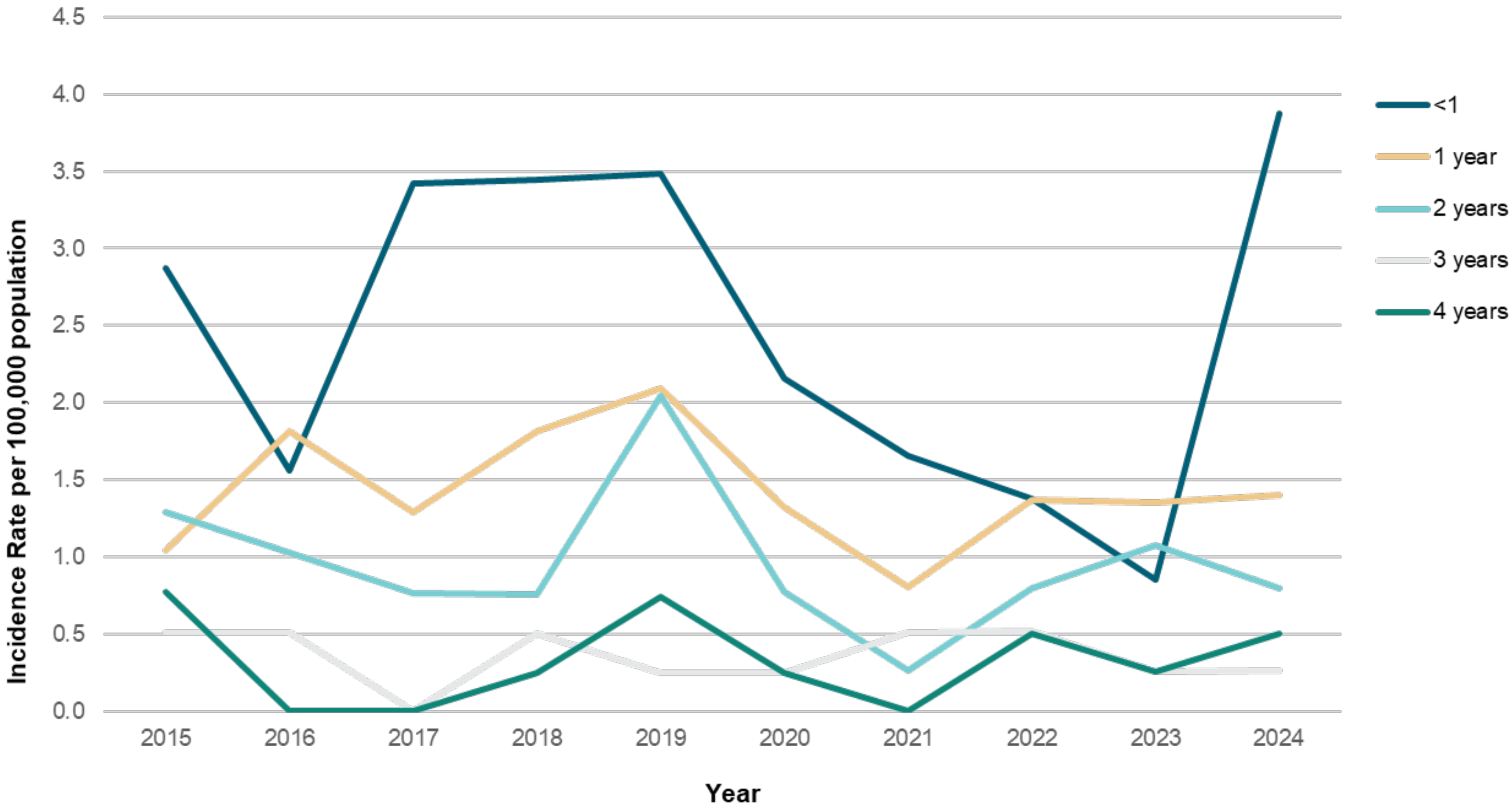

Figure S4: IMD Serogroup Distribution by Age Group, 2015-2024

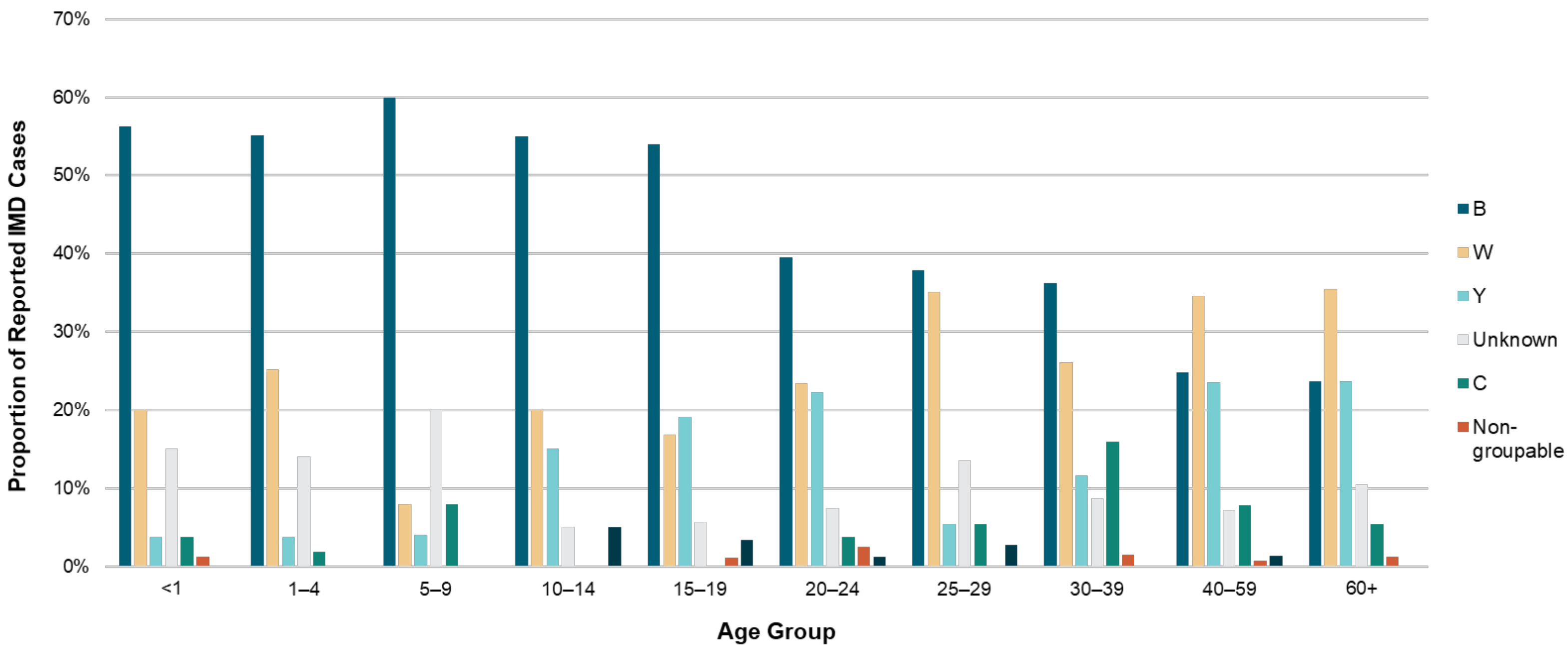

Figure S5: IMD Serogroup Distribution in Children 5 Years and Under, 2015-2024

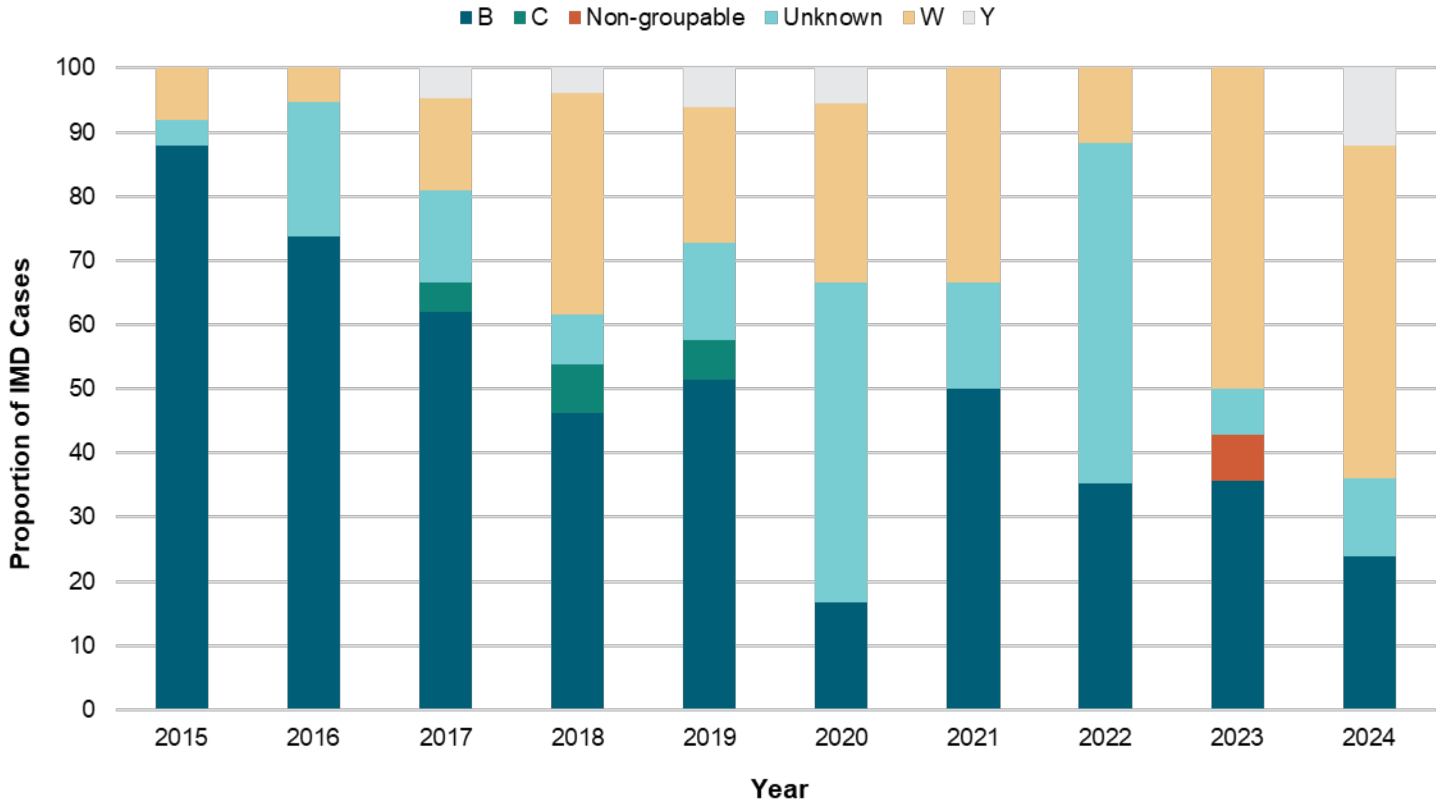

Table S1. Quadrivalent conjugate meningococcal vaccines available for use in Canada (as of March 26, 2026)

	Menactra®* [47] MenC-ACYW-DT	**Menveo**[48] Men-C-ACYW-CRM	**Nimenrix®** [49] Men-C-ACYW-TT	**MenQuadfi®** [50] Men-C-ACYW-TT
Manufacturer	Sanofi Pasteur Limited	GlaxoSmithKline Inc.	Pfizer Canada ULC	Sanofi Pasteur Limited
Date of authorization in Canada	May 3, 2006	May 21, 2010	March 5, 2013	October 29, 2020
Vaccine serotypes and carrier protein	Meningococcal (Groups A, C, Y and W) Polysaccharide Diphtheria Toxoid Conjugate Vaccine	Meningococcal (Groups A, C, Y and W) Oligosaccharide CRM_{197} Conjugate Vaccine	Meningococcal (Groups A, C, Y and W) Polysaccharide Tetanus Toxoid Conjugate Vaccine	Meningococcal (Groups A, C, Y and W) Polysaccharide Tetanus Toxoid Conjugate Vaccine
Concentration of Polysaccharide	4 µg of each serogroup	10 µg of serogroup A 5 µg of each of serogroups C, Y,W	5 µg of each serogroup	10 µg of each serogroup
Adjuvant	N/A	N/A	N/A	N/A
Authorized Age Groups	9 months through 55 years of age[a]	2 months through 55 years of age[a]	6 weeks to 55 years of age[a]	6 weeks of age and older
Authorized dosage and route of administration	0.5 mL IM[b]	0.5 mL IM[b]	0.5 mL IM[b]	0.5 mL IM[b]
Minimum interval as per authorized indication	At least 3 months apart	At least 2 months apart	At least 2 months apart	At least 2 months apart
Storage Requirements	Store at 2° to 8°C Do not freeze	Store at 2° to 8°C Do not freeze Protect from light	Store at 2° to 8°C Do not freeze Protect from light Diluent may be stored at ambient temperature (25°C)	Store at 2°C to 8°C Do not freeze
Dosage form	Solution for injection	Powder and diluent solution for injection **OR** Solution for injection	Powder and diluent for solution for injection	Solution for injection

* Marketing of Menactra in Canada has been discontinued since December 19, 2025, but its use is anticipated until the latest lot expiry date (August 31, 2026).

[a] Men-C-ACYW vaccines (except MenQuadfi®) are not authorized for use in those 56 years of age and older; however, based on limited evidence and expert opinion their use is considered appropriate above these authorized ages.

[b] Intramuscularly

For complete information, consult the product's leaflet or information contained within Health Canada's authorized product monographs available through the Drug Product Database.

Table S2 – *Authorized Men-C-ACYW vaccine schedules for unvaccinated children <2 years of age (as of March 26, 2026).**

Vaccine	2 to 6 months of age	7 to 11 months of age	12 to 23 months of age
Menactra®**	Not authorized	2 doses[a]	2 doses[a]
Menveo	3[b] +1[c] doses	1+1[b,c] doses	1+1[b,c] doses
Nimenrix®	2[b,d] +1[c] doses	1+1[b,c] doses[e]	1 dose
MenQuadfi®	3[b,d] +1[c] doses	1+1[c] doses[e]	1 dose

*NACI's recommended schedule may differ from authorized schedules
** Marketing of Menactra in Canada has been discontinued since December 19, 2025, but its use is anticipated until the latest lot expiry date (August 31, 2026).
a *Menactra®: For infants and toddlers from 9 months through 23 months of age, administered with an interval of at least 3 months between doses*
b Administered with an interval of at least 2 months between doses
c The "+1" dose should be given between 12 and 23 months of age. For more details, refer to the vaccines' product monographs available through Health Canada's *Drug Product Database*.
d *Nimenrix® and MenQuadfi® administered to infants starting at 6 weeks of age.*
e Nimenrix® and MenQuadfi®: For infants 6 to 11 months of age

Vaccine immunogenicity and safety studies

Table S3A: Summaries of clinical trials reporting vaccine immunogenicity for Men-C-ACYW-TT vs Men-C-C (N=1,627 Men-C-ACYW recipients)

Trial (period, location)	Intervention (n, mean age)	Comparator (n, mean age)	Schedule	Key immunogenicity findings
NCT03890367, Europe 2019–2023[31]	MenQuadfi (232; 16.5 mo);	NeisVac-C (240; 16.7 mo)	0+1	MenQuadfi produced similar seroprotection rates for serogroup C compared to NeisVac-C (99.5% [95%CI: 97.4 to 100] vs. 99.5% [95% CI: 97.4 to 100]) measured by hSBA, meeting non-inferiority criteria. MenQuadfi also produced significantly higher antibody GMTS via rSBA (2,143 [95% CI: 1,870 to 2,456] vs. 1,624 [95% CI: 1,425 to 1,850]) and hSBA (515 [95% CI: 450 to 591] vs. 227 [95% CI: 198 to 260]), meeting superiority criteria.
NCT01144663, Europe 2012–2013[20,32]	Nimenrix (524; 8.6 wk)	NeisVac-C (527; 8.6 wk) Menjugate (516; 8.7 wk)	2+1	Nimenrix seroprotection rates for serogroup C were non-inferior to Menjugate (difference in vaccine rSBA post-primary series response rate -0.88% [95% CI: -2.45 to 0.43]), and had similar rSBA response rates post-booster (Nimenrix: 99.8%; Menjugate: 98.4%;). Post-booster dose, Nimenrix had similar antibody rSBA GMTs (1,177.0 [95% CI: 1,059.1 to 1,308.0] vs. 1,051.4 [95% CI: 919.6 to 1,202.1]) and hSBA GMT (4,992.3 [95% CI:

				4,085.7 to 6,100] vs. 5,438.2 [95% CI: 4,412.4 to 6,702.3]). Nimenrix seroprotection rates for serogroup C were non-inferior to NeisVac-C (difference in vaccine rSBA post-primary series response rate -1.32% [95% CI: -2.84 to -0.48]), and had similar rSBA response rates post-booster (Nimenrix: 99.8%; NeisVac-C: 100.0%). Post-booster dose, Nimenrix had significantly lower antibody rSBA GMTs (1,177.0 [95% CI: 1,059.1 to 1,308.0] vs. 1,960.2 [95% CI: 1,776.4 to 2,163.1]) and similar hSBA GMT (4,992.3 [95% CI: 4,085.7 to 6,100] vs. 5,542.3 [95% CI: 4,765.2 to 6,446.2]).
NCT00474266, Finland 2007–2008[33]	Nimenrix (374; 14.4 mo)	Meningitec (125; 14.4 mo)	0+1	Nimenrix seroprotection rates for serogroup C were non-inferior to Meningitec (difference in vaccine rSBA response rate 2.2% [95% CI: -0.29 to 6.78]), and had significantly higher antibody rSBA GMTs (477.6 [95% CI: 437.3 to 521.6] vs. 212.3 [95% CI: 170 to 265.2]) and hSBA GMT (196 [95% CI: 175.4 to 219] vs. 40.3 [95% CI: 29.5 to 55.1]).
NCT00427908, Finland 2007[21]	Nimenrix (229; 19.1 mo)	Meningitec (75; 19.3 mo)	0+1	Nimenrix seroprotection rates for serogroup C were non-inferior to Meningitec (difference in vaccine rSBA response rate 1.47% [95% CI: -0.27 to 7.89]), and had significantly higher antibody rSBA GMTs (878.7 [95% CI: 779.4 to 990.7] vs. 415 [95% CI: 296.9 to 580]) and

				hSBA GMT (190 [95% CI: 164.7 to 219.2] vs. 21.2 [95% CI: 13.9 to 32.3]).
NCT00508261, Europe 2007–2008[22]	Nimenrix (220; 15 mo)	Meningitec (127; 14.6 mo)	0+1	RSBA GMTs for serogroup C were similar after vaccination with Nimenrix compared to Meningitec (828.7 [95% CI: 672.4 to 1021.4] vs. 691.4 [95% CI: 520.8 to 917.9]).
NCT00126984, Europe 2005-2008[36]	Nimenrix (48, 12.7 mo)	Meningitec (48; 12.6 mo)	0+1	Vaccine response rates against serogroup C were similar between groups and rSBA-MenC GMTs were approximately 3-fold higher with Nimenrix group compared to Menigitec.

Table S3B: Summaries of clinical trials reporting vaccine immunogenicity for Men-C-ACYW-TT vs Men-C-ACYW-CRM (N=1,917)

<table>
<tr><th>Trial (period, location)</th><th>Intervention (n, mean age)</th><th>Comparator (n, mean age)</th><th>Schedule</th><th>Key immunogenicity findings</th></tr>
<tr><td>NCT03630705, Mexico 2018–2022[14]</td><td>MenQuadfi (190; 2.2 mo)</td><td>Menveo (92; 2.3 mo)</td><td>2+1 MenQuadfi and 3+1 Menveo</td><td>MenQuadfi achieved non-inferior seroprotection (hSBA) for all serogroups A, C, W and Y compared to Menveo.
<table>
<tr><td>Serogroup</td><td>% MenACYW-TT (95% CI)</td><td>% MenACYW-CRM (95% CI)</td></tr>
<tr><td>A</td><td>97.6 (93.2 to 99.5)</td><td>95.0 (86.1 to 99.0)</td></tr>
<tr><td>C</td><td>99.2 (95.7 to 100)</td><td>93.3 (83.8 to 98.2)</td></tr>
<tr><td>Y</td><td>100 (97.1 to 100)</td><td>100 (94.0 to 100)</td></tr>
<tr><td>W</td><td>100 (97.1 to 100)</td><td>100 (94.0 to 100)</td></tr>
</table></td></tr>
</table>

				Compared to Menveo, study participants who received MenQuadfi had significantly lower rSBA GMTs for serogroups A at all time points, and higher for serogroups C (all time points) and W (post dose provided at 6 months of age).

Serogroup and time point	% MenACYW-TT (95% CI)	% MenACYW-CRM (95% CI)
Serogroup A		
Post 6 month dose	387 (293 to 510)	1328 (708 to 2489)
Post 12 month dose	1102 (808 to 1502)	5113 (2999 to 8717)
Serogroup C		
Post 6 month dose	1366 (1138 to 1640)	235 (173 to 319)
Post 12 month dose	2023 (1551 to 2639)	572 (338 to 969)
Serogroup Y		
Post 6 month dose	1056 (872 to 1280)	549 (336 to 897)
Post 12 month dose	1156 (913 to 1464)	2288 (1343 to 3900)
Serogroup W		
Post 6 month dose	2587 (2071 to 3231)	763 (509 to 1143)
Post 12 month dose	3135 (2196 to 4474)	1938 (1075 to 3493)

NCT03537508, USA 2018–2023[24,25]	MenQuadfi (1,330; 65.3 d)	Menveo (623; 65.3 d)	3+1	MenQuadfi's hSBA seroresponse rates post-booster dose were similar to Menveo for all serogroups, except for serogroup C where they were higher (difference in the percentage of participants 8.75 [95% CI: 4.80 to 13.60]).

Serogroup	% MenACYW-TT (95% CI)	% MenACYW-CRM (95% CI)

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<table>
<tr><td>A</td><td>79.4 (75.6 to 82.9)</td><td>77.6 (71.5 to 82.9)</td></tr>
<tr><td>C</td><td>97.0 (95.1 to 98.3)</td><td>88.2 (83.4 to 92.0)</td></tr>
<tr><td>Y</td><td>96.4 (94.4 to 97.8)</td><td>92.3 (88.1 to 95.4)</td></tr>
<tr><td>W</td><td>97.6 (95.9 to 98.7)</td><td>96.4 (93.3 to 98.3)</td></tr>
</table>
Study participants who received MenQuadfi had higher hSBA GMTs for all serogroups post dose 3 and prior to booster dose.
<table>
<tr><th>Serogroup and timepoint</th><th>GMT MenACYW-TT (95% CI)</th><th>GMT MenACYW-CRM (95% CI)</th></tr>
<tr><td>Day 30 post 3rd dose</td><td></td><td></td></tr>
<tr><td>Serogroup A</td><td>24.9 (21.6 to 28.6)</td><td>16.3 (13.5 to 19.6)</td></tr>
<tr><td>Serogroup C</td><td>365 (325 to 411)</td><td>51.4 (42.9 to 61.5)</td></tr>
<tr><td>Serogroup Y</td><td>83.0 (75.0 to 91.8)</td><td>42.9 (36.7 to 50.0)</td></tr>
<tr><td>Serogroup W</td><td>92.8 (84.8 to 102)</td><td>51.4 (43.9 to 60.0)</td></tr>
<tr><td>Day 0 before 4th dose</td><td></td><td></td></tr>
<tr><td>Serogroup A</td><td>9.33 (8.45 to 10.3)</td><td>6.43 (5.64 to 7.33)</td></tr>
<tr><td>Serogroup C</td><td>57.8 (51.5 to 64.8)</td><td>4.82 (4.22 to 5.50)</td></tr>
<tr><td>Serogroup Y</td><td>42.9 (39.3 to 46.7)</td><td>10.4 (9.15 to 11.9)</td></tr>
<tr><td>Serogroup W</td><td>57.8 (52.7 to 63.3)</td><td>9.27 (8.15 to 10.5)</td></tr>
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<tr>
<td>NCT03691610, USA 2018–2023[18,29]</td>
<td>MenQuadfi (298; 6.01 mo)</td>
<td>Menveo (290; 6.02 mo)</td>
<td>1+1</td>
<td>
MenQuadfi’s hSBA seroresponse rates post-booster dose were similar to Menveo for all serogroups.
<table>
<tr><th>Serogroup</th><th>% MenACYW-TT (95% CI)</th><th>% MenACYW-CRM (95% CI)</th></tr>
<tr><td>A</td><td>89.4 (83.1 to 93.9)</td><td>82.9 (75.1 to 89.1)</td></tr>
<tr><td>C</td><td>99.3 (95.9 to 100)</td><td>97.6 (93.2 to 99.5)</td></tr>
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Y	98.6 (94.9 to 99.8)	97.7 (93.3 to 99.5)
W	99.3 (96.2 to 100)	92.9 (87.0 to 96.7)

Study participants who received MenQuadfi had higher hSBA GMTs for serogroups C and Y post dose 1, and serogroups C, Y and W post dose 2.

Serogroup and timepoint	GMT MenACYW-TT (95% CI)	GMT MenACYW-CRM (95% CI)
Pre-dose 1:A	4.73 (3.92 to 5.72)	4.64 (3.74 to 5.74)
Post dose 1: A	8.26 (6.55 to 10.4)	5.45 (4.42 to 6.72)
Pre dose 2: A	20.1 (14.7 to 27.4)	14.9 (11.0 to 20.3)
Post dose 2: A	184 (143 to 237)	119 (90.6 to 157)
Pre-dose 1: C	2.57 (2.21 to 2.99)	2.48 (2.20 to 2.79)
Post dose 1: C	167 (129 to 217)	41.3 (32.8 to 52.1)
Pre dose 2: C	150 (117 to 193)	12.7 (9.63 to 16.8)
Post dose 2: C	1473 (1236 to 1756)	319 (263 to 388)
Pre-dose 1: Y	2.54 (2.27 to 2.83)	2.37 (2.16 to 2.60)
Post dose 1: Y	8.36 (6.61 to 10.6)	3.79 (3.20 to 4.49)
Pre dose 2: Y	46.2 (36.3 to 58.6)	6.74 (5.43 to 8.36)
Post dose 2: Y	423 (358 to 499)	133 (107 to 166)
Pre-dose 1: W	2.23 (2.05 to 2.42)	2.31 (2.13 to 2.51)
Post dose 1: W	5.51 (4.39 to 6.92)	3.82 (3.22 to 4.52)

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<tr><td>Pre dose 2: W</td><td>46.8 (36.1 to 60.5)</td><td>6.16 (4.87 to 7.80)</td></tr>
<tr><td>Post dose 2: W</td><td>442 (367 to 533)</td><td>106 (83.4 to 135)</td></tr>
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<tr><td>NCT01994629, Italy 2013–2014[19]</td><td>Nimenrix (99; 12.7 mo)</td><td>Menveo (99; 12.8 mo)</td><td>0+1</td><td>
Study participants who received Nimenrix had similar hSBA seroresponse rates for all serogroups at all time points except for Day 180 (lower seroresponse for A and higher for W and Y).
<table>
<tr><th>Serogroup and timepoint</th><th>% MenACYW-TT (95% CI)</th><th>% MenACYW-CRM (95% CI)</th></tr>
<tr><td>A Day 29</td><td>87 (78.3 to 93.1)</td><td>88 (79 to 93.7)</td></tr>
<tr><td>A Day 180</td><td>29 (20.3 to 39.8)</td><td>62 (51.6 to 71.9)</td></tr>
<tr><td>C Day 29</td><td>84 (74.8 to 90.7)</td><td>95 (87.8 to 98.2)</td></tr>
<tr><td>C Day 180</td><td>93 (86.3 to 97.6)</td><td>85 (76.3 to 91.6)</td></tr>
<tr><td>W Day 29</td><td>73 (61.8 to 82.5)</td><td>54 (42.9 to 65.4)</td></tr>
<tr><td>W Day 180</td><td>99 (93.3 to 99.97)</td><td>83 (73.3 to 90.5)</td></tr>
<tr><td>Y Day 29</td><td>54 (42.4 to 64.5)</td><td>39 (28.8 to 50.5)</td></tr>
<tr><td>Y Day 180</td><td>95 (88.6 to 98.7)</td><td>74 (63.4 to 82.7)</td></tr>
</table>
Study participants who received Nimenrix also had similar hSBA GMTs for all serogroups at all time points except for Day 180 (lower antibody concentrations for A and higher for C and W).
<table>
<tr><th>Serogroup and timepoint</th><th>GMT MenACYW-TT (95% CI)</th><th>GMT MenACYW-CRM (95% CI)</th></tr>
<tr><td>A Day 1</td><td>2.04 (1.89 to 2.21)</td><td>2.19 (2.02 to 2.38)</td></tr>
<tr><td>A Day 29</td><td>30 (23 to 40)</td><td>41 (31 to 55)</td></tr>
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	A Day 180	4.67 (3.43 to 6.36)	13 (9.5 to 18)
	C Day 1	2.24 (1.99 to 2.52)	2.44 (2.16 to 2.76)
	C Day 29	20 (16 to 26)	30 (23 to 39)
	C Day 180	41 (32 to 53)	24 (18 to 30)
	W Day 1	2.4 (1.96 to 2.95)	2.58 (2.12 to 3.15)
	W Day 29	14 (9.91 to 19)	9.34 (6.72 to 13)
	W Day 180	56 (45 to 70)	21 (17 to 27)
	Y Day 1	2.16 (1.94 to 2.40)	2.23 (2.02 to 2.48)
	Y Day 29	8.20 (5.96 to 11)	5.89 (4.27 to 8.13)
	Y Day 180	26 (20 to 34)	16 (12 to 21)

Table S3C: Summaries of clinical trials reporting vaccine immunogenicity for Men-C-ACYW-TT vs Men-C-ACYW-TT (N=2,400 Men-C-ACYW-TT recipients)

Trial (period, location)	Intervention (n, mean age)	Comparator (n, mean age)	Schedule	Key immunogenicity findings
NCT03547271, Europe 2019–2023[17]	MenQuadfi (554; 72.6 d)	Nimenrix (579; 72.4 d)	2+1	Compared to Nimenrix, hSBA seroresponses following immunization with MenQuadfi were higher for serogroup C at all measured time points, and lower for serogroup A post-dose 2.

Serogroup and timepoint	% MenQuadfi (95% CI)	% Nimenrix (95% CI)
Post-dose 2		
A	46.7 (42.3 to 51.2)	60.9 (56.5 to 65.2)
C	97.4 (95.7 to 98.6)	86.8 (83.5 to 89.6)

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<tr><td>W</td><td>92.6 (90.0 to 94.7)</td><td>88.4 (85.4 to 91.1)</td></tr>
<tr><td>Y</td><td>87.1 (83.9 to 89.9)</td><td>81.4 (77.8 to 84.7)</td></tr>
<tr><td>Post-dose 3</td><td></td><td></td></tr>
<tr><td>A</td><td>90.6 (87.8 to 92.9)</td><td>91.7 (89.1 to 93.8)</td></tr>
<tr><td>C</td><td>98.7 (97.4 to 99.5)</td><td>91.3 (88.7 to 93.5)</td></tr>
<tr><td>W</td><td>99.4 (98.4 to 99.9)</td><td>98.4 (97.0 to 99.3)</td></tr>
<tr><td>Y</td><td>98.7 (97.4 to 99.5)</td><td>96.9 (95.1 to 98.1)</td></tr>
</table>
After dose 3, hSBA GMTs were higher post immunization with MenQuadfi for all serogroups except for serogroup A.
<table>
<tr><td>Serogroup</td><td>GMT Ratio (95% CI)(MenACYW / Nimenrix)</td></tr>
<tr><td>A</td><td>0.690 (0.565 to 0.842)</td></tr>
<tr><td>C</td><td>4.73 (4.00 to 5.58)</td></tr>
<tr><td>W</td><td>1.54 (1.33 to 1.78)</td></tr>
<tr><td>Y</td><td>1.78 (1.55 to 2.04)</td></tr>
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<tr>
<td>NCT03890367, Europe 2019–2021[31]</td>
<td>MenQuadfi (232; 16.5 mo)</td>
<td>Nimenrix (235; 16.6 mo)</td>
<td>0+1</td>
<td>Following immunization with MenQuadfi, hSBA GMT (GMT ratio 16.3 [97.5% CI: 12.7 to 21.0]) and proportion of children achieving seroprotective antibody levels (difference in percentage 10.43% [97.5% CI: 5.68 to 16.2]) were higher for serogroup C when compared to Nimenrix, meeting non-inferiority and superiority criteria. When measured by rSBA, these differences in immune responses were less pronounced (GMT ratio 6.80 [97.5% CI: 5.04 to 9.18]) and proportion of children achieving seroprotective antibody levels (difference in percentage 5.24% [97.5% CI: 1.83 to 9.85]) for serogroup C.</td>
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				Non-inferiority criteria were still met and superiority was also met for rSBA GMTs.
NCT03205358, Finland 2015[27]	MenQuadfi (94; 1.44 yr)	Nimenrix (94; 1.47 yr)	0+1	When measured by hSBA, compared to Nimenrix, immunization with MenQuadfi resulted in a higher seroprotection rate for serogroup C.

Serogroup	% MenQuadfi (hSBA) (95% CI)	% Nimenrix (hSBA) (95% CI)
A	97.8 (92.3, 99.7)	91.9 (83.9, 96.7)
C	100 (96.0, 100.0)	89.5 (81.1, 95.1)
W	98.9 (94.0, 100.0)	96.5 (90.1, 99.3)
Y	98.9 (94.0, 100.0)	100 (95.8, 100.0)

When measured by hSBA, compared to Nimenrix, immunization with MenQuadfi resulted in higher GMTs for serogroups C and W.

Serogroup	MenQuadfi (hSBA) GMT (95% CI)	Nimenrix (hSBA) GMT (95% CI)
A	76.8 (63.0 to 93.7)	61.5 (45.5 to 83.1)
C	492.9 (405.9 to 598.5)	28.4 (21.4 to 37.5)
W	71.7 (56.3 to 91.5)	44.5 (36.6 to 54.2)
Y	96.6 (75.8 to 123.1)	76.4 (61.4 to 95.1)

When measured by rSBA, immunization with MenQuadfi and Nimenrix resulted in similar seroprotection rates for all serogroups.

Serogroup	% MenQuadfi (rSBA) (95% CI)	% Nimenrix (rSBA) (95% CI)

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<table>
<tr><td>A</td><td>100 (96.0, 100.0)</td><td>100 (95.8, 100.0)</td></tr>
<tr><td>C</td><td>100 (96.0, 100.0)</td><td>98.8 (93.7, 100.0)</td></tr>
<tr><td>W</td><td>100 (96.0, 100.0)</td><td>100 (95.8, 100.0)</td></tr>
<tr><td>Y</td><td>100 (96.0, 100.0)</td><td>100 (95.8, 100.0)</td></tr>
</table>
When measured by rSBA, compared to Nimenrix, immunization with MenQuadfi resulted in higher GMTs for serogroup C and lower serogroup A.
<table>
<tr><th>Serogroup</th><th>MenQuadfi (rSBA)
GMT (95% CI)</th><th>Nimenrix (rSBA)
GMT (95% CI)</th></tr>
<tr><td>A</td><td>3137.5 (2667.9 to 3689.7)</td><td>7377.1 (6151.5 to 8846.8)</td></tr>
<tr><td>C</td><td>2440.1 (2055.4 to 2897.0)</td><td>418.6 (327.1 to 535.5)</td></tr>
<tr><td>W</td><td>5306.8 (4318.8 to 6520.8)</td><td>4333.7 (3520.1 to 5335.5)</td></tr>
<tr><td>Y</td><td>2633.3 (2129.1 to 3256.7)</td><td>2759.6 (2254.8 to 3377.4)</td></tr>
</table>
</td>
</tr>
<tr>
<td>NCT02955797,
Europe 2017–2020[16,26]</td>
<td>MenQuadfi
(306; 16.1 mo)</td>
<td>Nimenrix
(306; 16.2 mo)</td>
<td>0+1</td>
<td>
Seroprotection rates as defined by hSBA titres ≥ 1:8 were similar between groups of meningococcal vaccine-naïve participants except for serogroup C where immunization with MenQuadfi led to superior immune responses.
<table>
<tr><th>Serogroup</th><th>% MenQuadfi
(95% CI)</th><th>% Nimenrix
(95% CI)</th><th>% difference
(95% CI)</th></tr>
<tr><td>A</td><td>90.8 (86.9 to 93.8)</td><td>89.5 (85.4 to 92.7)</td><td>1.3 (-3.6 to 6.2)</td></tr>
<tr><td>C</td><td>99.3 (97.6 to 99.9)</td><td>81.4 (76.4 to 85.6)</td><td>18 (13.6 to 22.8)</td></tr>
<tr><td>Y</td><td>93.2 (89.7 to 95.8)</td><td>91.6 (87.8 to 94.5)</td><td>1.6 (-2.76 to 6.03)</td></tr>
<tr><td>W</td><td>83.6 (78.9 to 87.7)</td><td>83.4 (78.7 to 87.5)</td><td>0.2 (-5.85 to 6.18)</td></tr>
</table>
</td>
</tr>
</table>

	Antibody concentrations were similar between meningococcal vaccine-naïve groups except for serogroup C and W where immunization with MenQuadfi led to higher GMTs. Serogroup / MenQuadfi GMT (95% CI) / Nimenrix GMT (95% CI) / GMT ratio (95% CI): A / 28.7 (25.2 to 32.6) / 28.0 (24.4 to 32.1) / 1.03 (0.85 to 1.24) C / 436 (380 to 500) / 26.4 (22.5 to 31.0) / 16.5 (13.4 to 20.4) Y / 38.0 (33.0 to 43.9) / 32.2 (28.0 to 37.0) / 1.18 (0.97 to 1.44) W / 22.0 (18.9 to 25.5) / 16.4 (14.4 to 18.6) / 1.34 (1.1 to 1.63)

Serogroup	MenQuadfi GMT (95% CI)	Nimenrix GMT (95% CI)	GMT ratio (95% CI)
A	28.7 (25.2 to 32.6)	28.0 (24.4 to 32.1)	1.03 (0.85 to 1.24)
C	436 (380 to 500)	26.4 (22.5 to 31.0)	16.5 (13.4 to 20.4)
Y	38.0 (33.0 to 43.9)	32.2 (28.0 to 37.0)	1.18 (0.97 to 1.44)
W	22.0 (18.9 to 25.5)	16.4 (14.4 to 18.6)	1.34 (1.1 to 1.63)

Table S4A: Summaries of clinical trials reporting vaccine safety for Men-C-ACYW-TT vs Men-C-ACYW-CRM (N=4,479 Men-C-ACYW-TT recipients)

Trial (period, location)	Intervention (n, mean age)	Comparator (n, mean age)	Schedule	Safety observations
NCT03630705, Mexico 2018 to 2022[14]	MenQuadfi (201; 2.2 mo)	Menveo (99; 2.3 mo)	2+1	Non-serious adverse events (AEs) were common with 90% of infants in the MenQuadfi group and 79% of infants in the Menveo group reporting at least one non-serious AE. Injection-site pain was commonly reported (over 60%) by study participants in both groups. Fever was reported by 42.2% of MenQuadfi and 33.5% of Menveo recipients. Irritability and abnormal crying were reported in more than 50% of study participants in both groups. No deaths occurred in any study group.
NCT03673462, USA 2018–2023[15,37]	MenQuadfi (2,080; 64.7 d)	Menveo (697; 64.9 d)	3+1	Non-serious adverse events were reported by 90.8% study participants in the MenQuadfi and 92.1% in the Menveo group. Injection-site pain was the most frequent reaction, occurring in

				77.8% of MenQuadfi and 77.2% of Menveo recipients, followed by injection-site erythema that was reported in approximately 54% of recipients in both groups. At least one SAE was reported by 5.19% and 3.01% of vaccine recipients in the MenQuadfi and Menveo group, respectively. There were two febrile seizures that were assessed as possibly related to MenQuadfi. In total three deaths were reported during the study period, all in the MenQuadfi group, with none considered to be vaccine related.
NCT03537508, USA 2018–2023[25]	MenQuadfi (1,727; 65.3 d)	Menveo (867; 65.3 d)	3+1	Safety profiles were comparable between groups. Within 30 minutes of any vaccination, 2 participants (1 in each group) experienced a non-related immediate AE. In the MenQuadfi group, 5.7% of study participants and in the Menveo group 4.4% of study participants reported SAEs during the study period (0.8% and 0.6% were reported as an adverse event of special interest). All SAEs and deaths were considered to be unrelated to the study vaccines.
NCT03691610, USA 2018–2023[18,29]	MenQuadfi (370; 6.01 mo)	Menveo (361; 6.02 mo)	1+1	At least one non-serious adverse event was reported for 77.84% infants in the MenQuadfi and 71.19% infants in the Menveo group. Injection-site pain was most commonly reported (54.59% and 49.86% in MenQuadfi and Menveo recipient, respectively) followed by injection-site erythema and swelling in approximately 45% and 32% of vaccine recipients in each group, respectively. Most common systemic AEs were crying (43.24% vs 38.23%) and pyrexia (18.38% vs.19.67%, in the MenQuadfi and Menveo groups, respectively). All SAEs were considered unrelated to the study vaccines. No deaths were reported in the study.
NCT01994629, Italy 2013–2014[30]	Nimenrix (101; 12.7 mo)	Menveo (99; 12.8 mo)	0+1	Similar proportion (approximately 65%) of study participants reported at least one solicited AE within 7 days post vaccination. A greater number of subjects in the Menveo group (34.3%) reported local solicited AEs than in the Nimenrix group (28.7%). Tenderness at the injection site was the most common local solicited AE, reported by 29.9% of study participants in the Menveo and 26% of study participants in the

				Nimenrix group. The incidence of erythema and induration were similar in both groups. There was only one severe local reaction (induration) reported by one individual in the Menveo group. Systemic solicited AEs were reported by approximately 56% of study participants in both groups, with irritability, sleepiness, and change in eating habits being most commonly reported. A total of three individuals in the Menveo group reported eight severe systemic AEs, while two individuals in the Nimenrix group reported four severe systemic AEs. Fever was reported by approximately 14% study participants. There were no instances of severe fever (≥ 40 °C). Most reported solicited AEs were mild to moderate and resolved by Day 7. Percentages of possibly related unsolicited AEs and medically attended AEs were similar between groups. The 11 reported SAEs were considered unrelated to the study vaccines.

Table S4B: Summaries of clinical trials reporting vaccine safety for Men-C-ACYW-TT vs Men-C-ACYW-TT (N=3,362 Men-C-ACYW recipients)

Trial (period, location)	Intervention (n, mean age)	Comparator (n, mean age)	Schedule	Safety observations
NCT03547271, Europe 2019–2023[28]	MenQuadfi (714; 72.6 d)	Nimenrix (726; 72.4 d)	2+1	Overall, the safety profile between groups was comparable. Across groups, the most common solicited site injection reaction was tenderness (approximately 58%) and the most common solicited systemic reaction was irritability (approximately 86%). Most solicited reactions were observed within 3 days of vaccination and resolved spontaneously after 1–3 days. No AEs that led to study discontinuation were reported within 30 days of any vaccination. All reported SAEs were considered unrelated to study vaccine, and no deaths were reported during the study.

NCT03890367, Europe 2019–2021[31]	MenQuadfi (232; 16.5 mo)	Nimenrix (235; 16.6 mo)	0+1	Overall, the safety profile was comparable between vaccine groups with solicited reactions observed in approximately 80% of vaccine recipients. The proportion of participants who reported at least one unsolicited adverse reaction was 6.5% (15/230) in the MenQuadfi group and 4.7% (11/232) in the Nimenrix group. No immediate unsolicited AEs were reported within 30 minutes of vaccination in any group. The two reported SAEs (one in each of the groups) were considered unrelated to the vaccine. No deaths were reported during the study.
NCT03205358, Finland 2015[27]	MenQuadfi (94; 1.44 yr)	Nimenrix (94; 1.47 yr)	0+1	There were no immediate unsolicited AEs or reactions after vaccination in either vaccine group. Solicited injection site and systemic reactions were reported within 7 days of vaccination. In both vaccine groups the majority of injection site and systemic reactions were Grade 1 and lasted one to three days. All unsolicited AEs were non-serious, and most were Grade 1 or Grade 2 in intensity. At least one unsolicited non-serious systemic reaction was reported for 5.3% (5/94) of toddlers who received MenQuadfi and 4.3% (4/94) of whom received Nimenrix. The most frequently reported unsolicited event was diarrhea, reported by 2.1-4.3% of participants. One toddler who received MenQuadfi experienced two SAEs (accidental injuries), neither of which was considered related to the vaccine. There were no reported deaths.
NCT02955797, Europe 2017–2020[26]	MenQuadfi (306; 16.1 mo)	Nimenrix (306; 16.2 mo)	0+1	There were no immediate, unsolicited AEs or adverse reactions in either vaccine group, or any discontinuations from the study or death due to an adverse event. None of the reported SAEs were considered as related to the investigational vaccines. The percentages of participants who reported at least 1 SAE were less than 1% and comparable between the groups. Two AESI were reported in the MenQuadfi group: febrile partial seizure with concomitant viral upper respiratory tract infection

	(23 days after vaccination) and generalised non-febrile convulsions following accidental trauma (6 days after vaccination); neither was considered as related to the vaccination. The most commonly reported AEs were related to infection, and were reported by approximately 12% of participants both groups. The proportion of participants who had reported at least one Grade 3 unsolicited non-serious systemic AE were similar in both groups (6.1% in the MenQuadfi and 5.4% in the Nimenrix group). None of the AEs were Grade 3 intensity or led to the discontinuation of study participation.

Table S4C: Summaries of clinical trials reporting vaccine safety for Men-C-ACYW-TT vs Men-C-C (N=1,862 Men-C-ACWT-TT recipients)

Trial (period, location)	Intervention (n, mean age)	Comparator (n, mean age)	Schedule	Safety observations
NCT03890367, Europe 2019–2023[31]	MenQuadfi (232; 16.5 mo); Nimenrix (235; 16.6 mo)	NeisVac-C (240; 16.7 mo)	0+1	Overall, the safety profile was comparable between vaccine groups. Solicited systemic reactions were observed in 80.4% of the MenQuadfi and 74.9% of the NeisVac-C group. The proportion of participants who reported at least one unsolicited adverse reaction was 6.5% (15/230) in the MenQuadfi group and 5.0% (12/239) in the NeisVac-C group. No immediate unsolicited AEs were reported within 30 minutes of vaccination in any group. All reported SAEs were considered unrelated to the study vaccines. No deaths were reported during the study.

NCT01144663, Europe 2012–2013[32]	Nimenrix (524; 8.6 wk)	NeisVac-C (527; 8.6 wk) Menjugate (516; 8.7 wk)	2+1	The percentages of participants reporting local and general symptoms were similar between groups. The most frequently reported solicited local AE was redness, reported by approximately one third of participants after the primary series and by up to 45% after booster vaccination. Grade 3 local symptoms were reported after 0.1%–3.5% and 0.2%–7.9% of primary and booster doses, respectively. The most frequently reported solicited general symptom was irritability, which was reported after approximately 60% of doses (with Grade 3 intensity between 7 and 9%). Percentage of infants with unsolicited AEs (52.1%–56.4%) and grade 3 unsolicited AEs (3.2%–5.3%) were similar between groups. No fatal SAEs were reported.
NCT00474266, Finland 2007–2008[33]	Nimenrix (374; 14.4 mo)	Meningitec (125; 14.4 mo)	0+1	Unsolicited symptoms (both serious and non-serious) reported within 43 days of the first vaccination were reported by 60.2% in the Nimenrix group and 54.4% in the Meningitec group (15.0% and 12.8% deemed related to the vaccine in the Nimenrix and Meningitec, respectively). The most frequently reported unsolicited symptoms with a causal relationship to vaccination were diarrhoea in the Nimenrix group (4.5%) and Meningitec group (8.8%). Redness and swelling of Grade 3 intensity were reported after vaccination with Nimenrix by 4.4% and 4.1% of individuals, respectively, and by 0.8% each after Meningitec. General solicited symptoms of Grade 3 intensity were infrequent, and reported by 1.6% of study participants. The two

				SAEs reported were considered unrelated to vaccination. No deaths occurred during the study.
NCT00427908, Finland 2007[34]	Nimenrix (229; 19.1 mo)	Meningitec (75; 19.3 mo)	0+1	Injection site redness was the most frequently reported solicited local symptom in both groups, and was reported in 32.9% and 36.8% of toddlers in the Meningitec and Nimenrix groups, respectively. The most common solicited general symptom was irritability reported in 38.6% of toddlers in the Nimenrix group and 39.7% of toddlers in the Meningitec group. Grade 3 solicited symptoms were each reported in no more than 3.5% of the toddlers in each group. Unsolicited AEs were reported in approximately half of toddlers in each group. The most frequently reported unsolicited symptoms were rhinitis in the Nimenrix group (8.3%) and pyrexia in the Meningitec group (13.3%). No SAEs were considered to be causally related to vaccination and no deaths were reported throughout the study.
NCT00508261, Europe 2007–2008[35]	Nimenrix (220; 15 mo)	Meningitec (127; 14.6 mo)	0+1	There were no differences in the frequency of reported local AEs between groups. Drowsiness and irritability were the most frequently reported solicited general symptoms in both groups, with symptoms of grade 3 intensity being infrequent and reported by less than 1.8% of study participants in each group. The percentage of subjects reporting SAEs, new onset of chronic illnesses, rash and emergency room visits from was 15.5% and 17.3% in the Nimenrix and Meningitec groups, respectively. None of the SAEs reported during the study was considered to be causally related to vaccination.

NCT00126984, Europe 2005-2008[36]	Nimenrix (48, 12.7 mo)	Meningitec (48; 12.6 mo)	0+1	The incidence of solicited local and general symptoms was within the same range in both groups. Redness at the injection site was the most commonly reported solicited local symptom. Drowsiness and irritability were the most commonly reported general solicited AEs. No unsolicited symptoms of grade 3 intensity and related to vaccination were reported during the course of the study. None of the reported SAEs were considered by the investigator to be related to vaccination.