Annexes to the WHO Recommendations on the Use of Multivalent Meningococcal Conjugate Vaccines in Countries of the African Meningitis Belt

Grading of evidence -

Evidence to recommendations tables

World Health Organization

Background

Annexes 1-3 contain tables that summarize the grading of recommendations, assessment, development and evaluations (GRADE). Annexe 4 contains the SAGE evidence-to-recommendation framework tables (ETR tables). The ETR tables are based on the DECIDE Work Package 5: Strategies for communicating evidence to inform decisions about health system and public health interventions. Evidence to a recommendation (for use by a guideline panel) (www.decide-collaboration.eu/, accessed 11 January 2021).

Contents

Annex 1. GRADE table: Efficacy and safety of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5): 2-29 years of age

Author(s): Haidara FC, Umesi A, Sow SO

Date of review: 3 September 2023

Population: Immunocompetent children, adolescents and adults 2 to 29 years of age

Intervention: A single dose of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5)

Comparison: A single dose of Meningococcal Serogroup ACWY-D Conjugate Vaccine (MenACWY-D), (Menactra, Sanofi Pasteur)

Outcomes: Serogroup A, C, W, Y or X meningococcal disease

Question: What is the efficacy of a single dose of pentavalent meningococcal conjugate (ACWYX) vaccine, vs currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines in preventing meningococcal disease?

Quality assessment							No of patients (%)		Effect		
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other consi-derations**	**NmCV-5 28 days after a single dose for each serogroup A, C, W, Y and X[b]**	**MenACWY-D 28 days after a single dose for each serogroup A, C, W and Y[b]**	**Relative Difference (96% CI)**	**Abso-lute**	**Quality**
Efficacy/effectiveness											
1	Randomised controlled trial[a]	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	A: 814/1154 (70.5) C: 1109/1133 (97.9) W: 1081/1097 (98.5) Y: 1019/1051 (97.0) X: 1099/1131 (97.2)	A: 286/572 (50.0) C: 531/556 (95.5) W: 520/534 (97.4) Y: 494/537 (92.0) X: 48/507 (9.5)	20.5 (15.4, 25.6) 2.4 (0.6, 4.7) 1.2 (-0.3, 3.1) 5.0 (2.5, 7.9) 47.2 (42.8, 51.6)	-	⊕⊕⊕⊕ HIGH

Absence of serious adverse effects

1	Randomised controlled trial	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	0/1200 (0%)[c,d]	0/600 (0%)[c,d]	-	-	⊕⊕⊕⊕ HIGH

a. In this clinical trial, immunogenicity is used instead of clinical endpoints. The evaluation of efficacy in this trial was based on non-inferiority to bactericidal antibody levels produced by licensed quadrivalent meningococcal ACWY conjugate vaccines, using serum bacterial antibody titer determined in the presence of rabbit complement (rSBA).

b. Seroresponse rate (defined as percentage of participants with a postvaccination SBA titer of at least 32 in those with a prevaccination titer of less than 8 or a titer that was at least four times as high as the prevaccination titer in those with a prevaccination titer of at least 8).The noninferiority of NmCV-5 to MenACWY-D was assessed on the basis of the difference in the percentage of participants with a seroresponse (defined as prespecified changes in titer; margin, lower limit of the 96% confidence interval [CI] above −10 percentage points) or geometric mean titer (GMT) ratios (margin, lower limit of the 98.98% CI >0.5). Serogroup X responses in the NmCV-5 group were compared with the lowest response among the MenACWY-D serogroups, after regulatory review. The overall GMT ratios for the four shared serogroups ranged from 1.7 (98.98% CI, 1.5 to 1.9) for serogroup A to 2.8 (98.98% CI, 2.3 to 3.5) for serogroup C. For all four serogroups in common with the MenACWY-D vaccine, the NmCV-5 vaccine elicited immune responses that were noninferior to those elicited by the MenACWY-D vaccine in the overall population and in each age group 2-10 years, 11-17 years and 18-29 years. The serogroup X component of the NmCV-5 vaccine also generated seroresponses and GMTs that met the prespecified noninferiority criteria.

c. Additional data on the safety and immunogenicity of the NmCV-5 vaccine have been documented in immunocompetent adults in two other randomised controlled trials, using the same control vaccine (MenACWY-D).
   - In a first-in-man phase 1 study in adults 18-45 years conducted in the United States of America, 0/20 (0%) and 0/20 (0%) serious adverse effects were reported in the NmCV-5 and MenACWY-D vaccine group. Within 28 days of NmCV-5 vaccination, the immune responses induced were predicted to confer protection against the five targeted serogroups of invasive meningococcal disease.
   - In a lot-to-lot consistency study (adults 18-29 years) and immunogenicity study in adults 18-85 years conducted in India, 0/1233 (0%) and 0/407 (0%) serious adverse effects were reported in the NmCV-5 and MenACWY-D vaccine group. At 28 days following vaccination, for all four serogroups in common with the MenACWY-D vaccine, the NmCV-5 vaccine elicited immune responses that were noninferior to those elicited by the MenACWY-D vaccine in the overall population. The serogroup X component of the NmCV-5 vaccine also generated seroresponses and GMTs that met the prespecified noninferiority criteria. Lot-to-lot immunological consistency was also demonstrated in the age group 18-29 years.

d. NmCV-5 clinical development studies were not designed to include pregnant or lactating women. However, pregnancies were reported during the conduct of three of the trials.
   - In the phase 1 study (USA), one subject had a positive pregnancy test approximately one month after receiving the MenACWY-D vaccine. The subject had a normal full-term delivery without a birth defect.
   - In the phase 3 study (Gambia and Mali), a total of 13 subjects became pregnant after vaccination, with the date of the last known menstrual period being either 12 days or more after receiving the study vaccine, or unknown but likely to be after vaccination, based on ultrasound results after pregnancy diagnosis. Of these 13 pregnancies, 10 were reported in the NmCV-5 group and 3 in the MenACWY-D group. Eleven subjects had a normal full-term delivery without birth defects. Two subjects decided to terminate the pregnancy, both from the NmCV-5 group.

- In the phase 3 study (India), a total of 6 pregnancies, with the date of the last known menstrual period being 25 days or more after receiving the study vaccine for 5 subjects, and 6 days before receiving the study vaccine for 1 subject. Of these 6 pregnancies, 5 were reported in the NmCV-5 group and 1 in the MenACWY-D group. Of these 6 pregnancies, the outcome was reported for 5 pregnancies. There were 4 normal full-term deliveries without birth defects: 3 in the NmCV-5 group (including pregnancy that could have been conceived within 2 weeks of receiving NmCV-5) and 1 in the MenACWY-D group. One subject decided to terminate the pregnancy, and for one pregnancy the outcome was unknown, both from the NmCV-5 group.

Summary of Findings	**Statement on quality of evidence**	Protection against invasive meningococcal disease is mediated by bactericidal antibodies to meningococcal capsular polysaccharides or protein antigens in the presence of complement. This complement-dependent bactericidal activity is measured by use of a Serum Bactericidal Activity (SBA) assay with a rabbit (rSBA) or human (hSBA) complement source. SBA activity correlates with immunity to meningococcal disease and is well established as a correlate of protection. Therefore, it was decided not to downgrade.
	Conclusion	High scientific evidence that a single dose of NmCV-5 is safe and elicits a robust immune response in individuals as 2 to 29 years of age to prevent meningococcal disease. High certainty of evidence around the safety of the intervention.

References

1. Haidara FC, Umesi A, Sow SO, Ochoge M, Diallo F, Imam A et al. Meningococcal serogroup ACWYX conjugate vaccine in 2-to-29-Year-Olds in Mali and Gambia. N Engl J Med 2023; 388: 1942-55.
2. Chen WH, Neuzil KM, Boyce CR, Pasetti MF, Reymann MK, Martellet L et al. Safety and immunogenicity of a pentavalent meningococcal conjugate vaccine containing serogroups A, C, Y, W, and X in healthy adults: a phase 1, single-centre, double-blind, randomised, controlled study. Lancet Infect Dis 2018; 18: 1088-96.
3. NmCV-5_2.5 Clinical Overview. 2023.
4. Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med 1969;129:1307–26. https://doi.org/10.1084/jem.129.6.1307
5. Borrow R, Balmer P, Miller E. Meningococcal surrogates of protection — serum bactericidal antibody activity. Vaccine 2005; 23: 2222-7.
6. Lucidarme J, Louth J, Townsend-Payne K, Borrow R. Meningococcal serogroup A, B, C, W, X, and Y serum bactericidal antibody assays. Methods Mol Biol 2019; 1969: 169-79.

Annex 2. GRADE table: Efficacy and safety of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5): 12-16 months of age

Author(s): Tapia MD, Sow SO, Naficy A

Date of review: 3 September 2023

Population: Immunocompetent children 12 to 16 months of age

Intervention: A single or two doses of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5)

Comparison: A single or two doses of Meningococcal Serogroup ACWY-D Conjugate Vaccine (MenACWY-D), (Menactra, Sanofi Pasteur)

Outcomes: Serogroup A, C, W, Y or X meningococcal disease

Question: What is the efficacy of a single dose of pentavalent meningococcal conjugate (ACWYX) vaccine, vs currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines in preventing meningococcal disease?

Quality assessment							No of patients (%)		Effect		
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other consi-derations**	nonadjuvanted **NmCV-5** **28 days after a single dose for each serogroup A, C, W, Y and X[b]**	**MenACWY-D** **28 days after a single dose for each serogroup A, C, W and Y[b]**	**Relative** **Difference (95% CI)**	**Abso-lute**	**Quality**
Efficacy/effectiveness											
1	Randomised controlled trial[a]	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	A: 143/144 (99.3) C: 141/144 (98.6) W: 140/144 (97.9) Y: 140/144 (97.2) X: 144/144 (100)	A: 70/72 (97.2) C: 50/72 (69.4) W: 65/72 (90.3) Y: 63/72 (87.5) X: 12/72 (16.7)	2.1 (-1.48, 8.96) 29.2 (19.4, 40.7) 7.6 (1.6, 16.9) 9.7 (2.8, 19.6) -	-	⊕⊕⊕⊕ HIGH

Absence of serious adverse effects

1	Randomised controlled trial	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	0/149 (0%)[c]	0/76 (0%)	-	-	⊕⊕⊕⊕ HIGH

a. In this clinical trial, immunogenicity is used instead of clinical endpoints. The evaluation of efficacy in this trial was based on non-inferiority to bactericidal antibody levels produced by licensed quadrivalent meningococcal ACWY conjugate vaccines, using serum bacterial antibody titer determined in the presence of rabbit complement (rSBA).

b. Seroresponse rate (defined as percentage of participants with a postvaccination SBA titer of at least 32 in those with a prevaccination titer of less than 8 or a titer that was at least four times as high as the prevaccination titer in those with a prevaccination titer of at least 8). The comparisons of immunogenicity between vaccine groups were performed with the use of a noninferiority method. Noninferiority was assessed by examining whether the lower limit of the 95% confidence interval for the between-group difference in percentages was above −10 percentage points (a commonly accepted noninferiority margin) for each serogroup (A, C, W, Y, and X).In this study, participants were assigned in a 2:2:1 ratio to receive nonadjuvanted NmCV-5 (commercial formulation), alum-adjuvanted NmCV-5, or the quadrivalent vaccine MenACWY-D, in two doses 12 weeks apart, according to the recommended immunization schedule for MenACWY-D. Immune responses to the nonadjuvanted and adjuvanted NmCV-5 formulations were similar. Immune responses for the four shared serogroups were higher in the NmCV-5 groups than in MenACWY-D, after the first dose of vaccine. Immune responses elicited after a single dose of NmCV-5 were similar to those after two doses of MenACWY-D. The lower boundaries of the 95% confidence intervals for differences in seroresponses (or in percentages of participants with SBA titers of at least 128) between groups (between each of the NmCV-5 groups and the MenACWY-D group) were above−10 percentage points. These results suggest the noninferiority of NmCV-5 to MenACWY-D regarding these endpoints.

c. This study documented additional safety data in children 12-16 months of age in the alum-adjuvanted NmCV-5 vaccine group, with 0/150 (0%) serious adverse effects reported.

Summary of Findings	**Statement on quality of evidence**	Protection against invasive meningococcal disease is mediated by bactericidal antibodies to meningococcal capsular polysaccharides or protein antigens in the presence of complement. This complement-dependent bactericidal activity is measured by use of a Serum Bactericidal Activity (SBA) assay with a rabbit (rSBA) or human (hSBA) complement source. SBA activity correlates with immunity to meningococcal disease and is well established as a correlate of protection. Therefore, it was decided not to downgrade.
	Conclusion	High scientific evidence that a single dose of NmCV-5 is safe and elicits a robust immune response in individuals as young as 12 months of age to prevent meningococcal disease. High certainty of evidence around the safety of the intervention.

References

1. Tapia MD, Sow SO, Naficy A, Diallo F, Haidara FC, Chaudari, A et al. Meningococcal serogroup ACWYX conjugate vaccine in Malian toddlers. N Engl J Med 2021; 384: 2115-23.
2. NmCV-5_2.5 Clinical Overview. 2023.
3. Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med 1969;129:1307–26. https://doi.org/10.1084/jem.129.6.1307
4. Borrow R, Balmer P, Miller E. Meningococcal surrogates of protection — serum bactericidal antibody activity. Vaccine 2005; 23: 2222-7.
5. Lucidarme J, Louth J, Townsend-Payne K, Borrow R. Meningococcal serogroup A, B, C, W, X, and Y serum bactericidal antibody assays. Methods Mol Biol 2019; 1969: 169-79.

Annex 3. GRADE table: Efficacy and safety of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5): 9-11 months of age

Author(s): Chen WH, Sow SO, Tapia M

Date of review: 3 September 2023

Population: Immunocompetent infants 9 to 11 months of age

Intervention: A single dose of Meningococcal Serogroup ACWYX Conjugate Vaccine (NmCV-5)

Comparison: A single dose of Meningococcal Serogroup ACWY-TT Conjugate Vaccine (MenACWY-TT), (Nimenrix, Pfizer)

Outcomes: Serogroup A, C, W, Y or X meningococcal disease

Question: What is the efficacy of a single dose of pentavalent meningococcal conjugate (ACWYX) vaccine, vs currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines in preventing meningococcal disease?

Quality assessment							No of patients (%)		Effect		
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other consi-derations**	**NmCV-5 28 days after a single dose for each serogroup A, C, W, Y and X[b,c]**	**MenACWY-TT 28 days after a single dose for each serogroup A, C, W and Y[b,c]**	**Relative Difference (95% CI)**	**Abso-lute**	**Quality**
Efficacy/effectiveness											
1	Randomised controlled trial[a]	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	A: 373/373 (100) C: 369/373 (98.9) W: 352/373 (94.4) Y: 360/373 (96.5) X: 371/372 (99.7)	A: 191/191 (100) C:190/191 (99.5) W: 186/191 (97.4) Y: 190/191 (99.5) X: 33/191 (17.3)	0.0 (-1.0, 2.0) -0.5 (-2.3, 1.9) -3.0 (-6.3, 0.8) -3.0 (-5.4, -0.4) 2.3 (0.3, 4.7)	-	⊕⊕⊕⊕ HIGH

Absence of serious adverse effects											
1	Randomised controlled trial	No serious risk of bias	No serious risk of inconsistency	No serious risk of indirectness	No serious risk of imprecision	-	0/400 (0%)	0/200 (0%)	-	-	⊕⊕⊕⊕ HIGH

a. In this clinical trial, immunogenicity is used instead of clinical endpoints. The evaluation of efficacy in this trial was based on non-inferiority to bactericidal antibody levels produced by licensed quadrivalent meningococcal ACWY conjugate vaccines, using serum bacterial antibody titer determined in the presence of rabbit complement (rSBA).

d. Seroprotective response rate response (defined as percentage of participants with a postvaccination SBA titer of at least 8). The noninferiority of NmCV-5 to MenACWY-TT was assessed on the basis of the difference in the percentage of participants with a seroprotective response (defined as prespecified titer; margin, lower limit of the 95% confidence interval [CI] above −10 percentage points). Serogroup X responses in the NmCV-5 group were compared with the lowest seroprotective response among the MenACWY-TT serogroups, after regulatory review. The estimated lower 95% confidence bound for the difference in seroprotective response (NmCV-5 minus MenACWY-TT) was greater than the non-inferiority margin of -10%. Thus, for the primary analysis for each meningitis serogroup A, C, W, and Y, the non-inferiority criterion was met for the NmCV-5 meningococcal vaccine. The serogroup X component of the NmCV-5 vaccine also generated A seroprotective response that met the prespecified noninferiority criteria, as well ²as the superiority criterion.

b. One of the secondary aims of this study was to demonstrate the non-inferiority of the immune responses to EPI vaccines (measles-rubella, yellow fever, measles-rubella second dose) when co-administered with NmCV-5 (at either 9 or 15 months of age) compared to the immune responses when co-administration with MenACWY-TT (at either 9 or 15 months). In the per protocol analysis set, the seropositive response rates for NmCV-5 and MenACWY-TT, respectively, were 100.0% (364/364) and 100.0% (187/187) for measles (difference 0.0 [95%CI, -1.0, 2.0]); 97.5% (355/364) and 99.5% (186/187) for yellow fever (difference -1.9 [95%CI, -4.2, 0.6]); and 80.8% (294/364) and 85.0% (159/187) for rubella (difference -4.3 [95%CI, -10.5, 2.6]). The non-inferiority criterion was met for measles and yellow fever. The non-inferiority criterion was not met for rubella because the lower limit of the confidence interval [95%CI] was not greater than the prespecified margin of −10 percentage points.

Summary of Findings	**Statement on quality of evidence**		Protection against invasive meningococcal disease is mediated by bactericidal antibodies to meningococcal capsular polysaccharides or protein antigens in the presence of complement. This complement-dependent bactericidal activity is measured by use of a Serum Bactericidal Activity (SBA) assay with a rabbit (rSBA) or human (hSBA) complement source. SBA activity correlates with immunity to meningococcal disease and is well established as a correlate of protection. Therefore, it was decided not to downgrade.
	Conclusion		High scientific evidence that a single dose of NmCV-5 is safe and elicits a robust immune response in individuals as young as 9 months of age to prevent meningococcal disease. High certainty of evidence around the safety of the intervention.

References

1. Wilbur H. Chen (Protocol Chair), Samba O. Sow (Site PI), Milagritos Tapia (Site Co-PI). A Phase 3 Trial to Evaluate the Safety, Immunogenicity, and Non-Interference with Concomitant Routine Vaccines, of a Meningococcal Serogroup ACYWX Conjugate Vaccine (NmCV-5) in Comparison with MenACWY-TT Conjugate Vaccine in Healthy Malian Infants. DMID Protocol 20-0024,Division of Microbiology and Infectious Diseases, NIAID/NIH, USA. ClinicalTrials.gov number, NCT05093829). Current results - Executive summary prepared for the SAGE, September 2023.
2. NmCV-5_2.5 Clinical Overview. 2023.
3. Goldschneider I, Gotschlich EC, Artenstein MS. Human immunity to the meningococcus. I. The role of humoral antibodies. J Exp Med 1969;129:1307–26. https://doi.org/10.1084/jem.129.6.1307
4. Borrow R, Balmer P, Miller E. Meningococcal surrogates of protection — serum bactericidal antibody activity. Vaccine 2005; 23: 2222-7.
5. Lucidarme J, Louth J, Townsend-Payne K, Borrow R. Meningococcal serogroup A, B, C, W, X, and Y serum bactericidal antibody assays. Methods Mol Biol 2019; 1969: 169-79.

Annex 4. SAGE evidence-to-recommendation framework: What is the efficacy of a single dose of pentavalent meningococcal conjugate (ACWYX) vaccine, vs currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines in preventing meningococcal disease?

Question:	What is the efficacy and safety of a single dose of pentavalent meningococcal conjugate (ACWYX) vaccine, vs currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines in preventing invasive meningococcal disease?
Population:	Children aged 9-23 months; children, adolescents and adults 2 years and older, living in the African meningitis belt
Intervention:	A single dose of pentavalent conjugate vaccine (NmCV-5)
Comparison(s):	Currently licensed quadrivalent meningococcal conjugate (ACWY) vaccines
Outcome:	Efficacy (immune correlate of protection through serum bactericidal activity [SBA]), Safety

Background:

For more than a century, meningococcus has been feared for its ability to cause epidemics in many parts of the world. The sub-Saharan African meningitis belt, which includes all or part of 26 countries, bears the heaviest burden of invasive meningococcal disease with marked seasonality combining annual outbreaks and large periodic epidemics that recur unpredictably. Serogroup A was the most common cause of endemic disease as well as large epidemics before the introduction of a monovalent meningococcal A conjugate vaccine from 2010 onward, through mass preventive campaigns associated with introduction into routine immunization programmes. Strains of other serogroups that are not currently targeted by preventive vaccination programmes continue to predominate and cause epidemics (1-6).

	CRITERIA	JUDGEMENTS				RESEARCH EVIDENCE	ADDITIONAL INFORMATION
PROBLEM	Is the problem a public health priority?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies by setting* ☐	Although serogroup A meningococcal disease has been virtually eliminated from the African meningitis belt, countries continue to experience high rates of disease due to other serogroups. Serogroups W, X and C have been predominating since 2011 though expansion and evolution of hypervirulent lineages and causing outbreak as well as large epidemics (4-13).	

BENEFITS & HARMS OF THE OPTIONS	Benefits of the intervention Are the desirable anticipated effects large?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐		There is no direct evidence of clinical effectiveness of a single dose of pentavalent meningococcal conjugate (ACWYX). But based on evidence bactericidal antibody levels correlating with protection, and on noninferiority of immune responses to two different licensed quadrivalent meningococcal conjugate vaccines (Annexes 1-3), which have been widely used and confirmed their effectiveness, this adds to the confidence level of the potential important effect (14-20).	
	Harms of the intervention Are the undesirable anticipated effects small?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐		The pentavalent meningococcal conjugate (ACWYX) has a safety profile similar to that of the comparator licensed vaccines (Annexes 1-3), meningococcal conjugate generally have an excellent safety profile (17).	
	Balance between benefits and harms	*Favours intervention* ☒	*Favours comparison* ☐	*Favours both* ☐	*Favours neither* ☐	Unclear ☐	The pentavalent meningococcal conjugate (ACWYX) is the first licensed vaccine with a serogroup X component, thus covering all disease- and epidemic-causing serogroups in the African meningitis belt.	
	What is the overall quality of this evidence for the critical outcomes?	**Effectiveness of the intervention** *No included studies* ☐	 *Very low* ☐	 *Low* ☒	 *Moderate* ☐	 *High* ☒	The quality of the evidence for efficacy and safety is high (Annexes1-3). Quality for effectiveness, duration of protection and efficacy on meningococcal carriage is low due to the lack of study results to date.	
		Safety of the intervention						

		No included studies ☐	*Very low* ☐	*Low* ☐	*Moderate* ☐	*High* ☒	Both Gambia and Mali where the vaccine was tested are in the meningitis belt.	
VALUES & PREFERENCES	How certain is the relative importance of the desirable and undesirable outcomes?	*Important uncertainty or variability* ☐	*Possibly important uncertainty or variability* ☐	*Probably no important uncertainty or variability* ☒	*No important uncertainty or variability* ☐	*No known undesirable outcomes* ☒	There does not seem to be any substantial item on the undesirable outcome. Hence, it is likely that the uncertainty/variability is not important.	
	Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?	*No* ☐	*Probably No* ☐	*Uncertain* ☐	*Probably Yes* ☐	*Yes* ☒	*Varies* ☐	Given the high remaining burden of disease and unpredictability of meningococcal meningitis, the desirable effect will be very large.	
RESOURCE USE	Are the resources required small?	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☒			The very limited supply and high prices of MMCVs have impeded a large deployment of these vaccines. The pentavalent meningococcal conjugate (ACWYX) can be produced in large quantities and marketed at a significantly lower price that other existing MMCVs. The Gavi alliance has been a key supporter and partner of countries in the African meningitis belt, and MMCVs are part of the current Gavi Vaccine Investment Strategy.	

	Cost-effectiveness	*No* ☐	*Uncertain* ☐	*Yes* ☒	*Varies* ☐		Studies indicate that expanding the coverage of a monovalent serogroup A to a multivalent vaccine would be cost-effective (21).	
EQUITY	What would be the impact on health inequities?	*Increased* ☐	*Uncertain* ☐	*Reduced* ☒	*Varies* ☐		The affected countries are largely low-income countries, the impact would be huge.	
ACCEPTABILITY	Which option is acceptable to key stakeholders (e.g. ministries of health, immunization managers)?	*Intervention* ☒	*Comparison* ☐	*Both* ☐	*Neither* ☐	*Un-clear* ☐	This is part of a broader WHO vision and strategy to significantly reduce the burden of meningococcal and other causes of meningitis by 2030. Elimination of meningitis epidemics is one of the three visionary goals of the Defeating meningitis by 2030 global road map, that has been approved by all 194 Member States of WHO during the Seventy-third session of the World Health Assembly (resolution WHA73.9). Strategic Goals 2 and 3 of the global road map include introducing effective and affordable new WHO prequalified vaccines targeting Neisseria meningitidis (Nm) and developing evidence-based policy on Nm vaccination strategies that result in optimal individual protection and, where possible, herd protection (22). Health authorities of countries in the African meningitis belt have been hoping for such a vaccine.	

	Which option is acceptable to target group?	*Intervention* ☒	*Comparison* ☐	*Both* ☐	*Neither* ☐	*Un-clear* ☐	Same as above.	
FEASIBILITY	Is the intervention feasible to implement?	*No* ☐	*Probably* No ☐	*Uncertain* ☐	*Probably* Yes ☐	*Yes* ☒	*Varies* ☐	The experience of the introduction of a monovalent meningococcal A conjugate vaccine in the same countries will be a great asset (3).	
BALANCE OF CONSEQUENCES		Undesirable consequences *clearly outweigh* desirable consequences in most settings ☐	Undesirable consequences *probably outweigh* desirable consequences in most settings ☐	The balance between desirable and undesirable consequences *is closely balanced or uncertain* ☐	Desirable consequences *probably outweigh* undesirable consequences in most settings ☐	Desirable consequences *clearly outweigh* undesirable consequences in most settings ☒		
TYPE OF RECOMMENDATION		We recommend the intervention ☒	We suggest considering recommendation of the intervention ☐ Only in the context of rigorous research ☐ Only with targeted monitoring and evaluation ☐ Only in specific contexts or specific (sub)populations	We recommend the comparison ☐	We recommend against the intervention and the comparison ☐			
RECOMMENDATION (TEXT)		Exact text to be finalized after the September 2023 SAGE session.						
IMPLEMENTATION CONSIDERATIONS		Exact text to be finalized after the September 2023 SAGE session.						

MONITORING, EVALUATION AND RESEARCH PRIORITIES	Exact text to be finalized after the September 2023 SAGE session.

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