GRADE Table 03. Duration of protection conferred by MenA conjugate vaccination in immunocompetent children (3 to 24 months of age) against serogroup A meningococcal disease

Population : Immunocompetent children aged 3–24 months
Intervention: One or two doses of MenA conjugate vaccine (5 µg dosage)
Comparison: No MenA vaccination
Outcome : Serogroup A meningococcal disease

What is the evidence of long-term protection against serogroup A meningococcal disease following vaccination with one or two doses of MenA conjugate vaccine in immunocompetent children aged 3–24 months?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		2/ RCT[1]	4
	Factors decreasing confidence	Limitation in study design	Very serious[2]	-2
		Inconsistency	None serious	0
		Indirectness	None serious[3]	0
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**2**
Summary of Findings	**Statement on quality of evidence**			We have limited confidence that the true effect is close to the estimated effect on health outcome. The true effect may be substantially different from the estimate of the effect.
	Conclusion			Our confidence in the duration of protection against serogroup A meningococcal disease conferred by MenA conjugate vaccine is low as no data are available on long-term protection beyond 27 months following vaccination with MenA conjugate vaccine in children aged 3–24 months.

[1] Two double blind, randomized clinical studies of MenA conjugate vaccine were conducted, PsA-TT-004 and PsA-TT-007. The MenA conjugate vaccine was co-administered with other vaccines routinely administered in this age group. In PsA-TT-007, 95.8% of vaccinees remained seropositive 7 months after one dose of MenAfriVac 5µg given at 9 months of age and 96.6% had antibody titres greater than or equal to 1:128. The PsA-TT-004 trial measured persistence of antibody until 24 months (12–15 months after last dose of vaccine) and until 36 months of age (18–27 months after last dose of vaccine). High levels of MenA rSBA were maintained until 36 months of age. In vaccinees who received two doses of MenAfriVac 5µg at 14 weeks and 9 months of age, 88.1% had antibody titres greater than or equal to 1:128 at age 36 months. The duration of protection beyond 27 months after vaccination is unknown. The conclusion reflects the lack of information on long-term protection.

[2] Downgrading since considered only protection up to 27 months after vaccination.

[3] In the two clinical trials, PsA-TT-004 and PsA-TT-007, immunogenicity was used instead of clinical endpoints. As the efficacy of MenAfriVac is well-established, the evaluation of efficacy in these trials was based on non-inferiority to bactericidal antibody levels produced by MenAfriVac. Serum capsular bactericidal antibodies correlate with protection and can be considered a valid surrogate marker of protection. Therefore, it was decided not to downgrade.

Reference List

1. PsA-TT-004 In Meningitis Vaccine Project and Partners. *Results from the MenA conjugate vaccine (PsA-TT) randomized controlled trials in infants and young children: Executive summary.* Geneva, World Health Organization, 2014 (http://www.who.int/immunization/sage/meetings/2014/october/3_MenA_vaccine_trials_SAGE_01Oct2014.pdf?ua=1, accessed November 2014).
2. PsA-TT-007 In Meningitis Vaccine Project and Partners. *Results from the MenA conjugate vaccine (PsA-TT) randomized controlled trials in infants and young children: Executive summary.* Geneva, World Health Organization, 2014 (http://www.who.int/immunization/sage/meetings/2014/october/3_MenA_vaccine_trials_SAGE_01Oct2014.pdf?ua=1, accessed November 2014).
3. Data to be published: Meningitis Vaccine Project. Protocol No. PsA-TT-004. Final version 1- 30 October 2007-Amendment 1- 15 May 2008- Amendment 2- 23 September 2010.
4. Data to be published: Meningitis Vaccine Project. Protocol No. PsA-TT-007. Final version 1- 20 October 2011-Amendment 1-8 December 2011.