Table II a. Efficacy of MenC conjugate vaccines. Do conjugated MC group C-vaccines protect children aged ≥2 months to <5 years against invasive meningococcal disease?				
			Rating	Adjustment to level
Quality Assessment	No of Studies/Quality starting level		1 RCT	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	Serious[1]	-1
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Mitigated bias and confounding	Not applicable	0
	Final rating of quality of evidence			3
Summary of Findings	Statement on quality of evidence			We are moderately confident in the estimate of effect on the health outcome
	Conclusion			Conjugated MC group C-vaccines protects children aged ≥2 months to <5 years against meningococcal disease.

[1]Immunogenicity rather than clinical protection is used as an endpoint. Serum bactericidal activity at titres ≥1:4 (tests using human complement, hSBA) or 1:8 (tests using rabbit complement, rSBA) are considered reliable immunologic correlates of protection. References providing the rationale for this conclusion include *Borrow RP et al 2005; Adrews NR et al 2003*; and *Goldschneider IEC 1969.*

Table II b. Efficacy of MenC conjugate vaccines. Do conjugated MC group C-vaccines protect individuals aged ≥5 years against invasive meningococcal disease?				
			Rating	Adjustment to level
Quality Assessment	No of Studies/Starting quality starting level		2 RCTs	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	Serious[1]	-1
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Mitigated bias and confounding	Not applicable	0
	Final rating of quality of evidence			3
Summary of Findings	Statement on quality of evidence			We are moderately confident in the estimate of effect on the health outcome
	Conclusion			Conjugated MC group C-vaccines protect individuals aged ≥5 years against meningococcal disease.

[1]Immunogenicity rather than clinical protection is used as an endpoint. Serum bactericidal activity (SBA) at titres ≥1:4 (tests using human complement, hSBA) or 1:8 (tests using rabbit complement, rSBA) are considered reliable immunologic correlates of protection. (For references providing the rationale for this conclusion, see Table IIIa).

Randomised Controlled Trials on Immunogenicity

Table II a. Individuals aged >2 months to <5 years:

A single-center, double-blind, randomized controlled trial conducted in UK by *MacLennan et al* in 1995-96 included 182 health infants. Participants were randomly assigned to receive vaccination with doses of 1 of 2 lots of meningococcal C conjugate vaccine (groups 1 and 2; n=60 in each group) or a hepatitis B control vaccine (group 3; n=62), administered with routine immunizations at 2, 3, and 4 months of age. Approximately half of each group received meningococcal C conjugate vaccine and half received plain meningococcal polysaccharide vaccine (MPS) at 12 months of age. After 3 doses, children in groups 1

and 2 achieved significantly higher meningococcal C IgG geometric mean concentrations and SBA titers (629 and 420, respectively, vs 4.1) than controls. At 12 months, antibody concentrations had decreased in all groups but remained significantly higher in children vaccinated with meningococcal C conjugate vaccine (SBA, 24 and 16 in groups 1 and 2, respectively, versus 4.2 in group 3). Following vaccination with MPS at 12 months of age, SBA in the meningococcal C conjugate vaccine group was significantly higher than in controls (SBA, 789 versus 4.5).

Table II b. Individuals aged ≥5 years:

Schondorf et al conducted a Phase IV, stratified-randomized, double-blind, multi-center study in Canada to investigate the safety and immunogenicity of a single dose of the conjugated meningococcal Group C vaccine, Menjugate®, stored for 6 months at room temperature (25 ± 2 °C, Group W: $N = 250$) or at 2–8 °C (Group C: $N = 250$) when administered to 500 healthy toddlers aged 12-23 months. Blood draws for determination of anti-meningococcal C titers were taken prior to immunization on Day 1 and 28 days thereafter (i.e. Day 29 of the study). Immunogenicity was assessed by BCA (assay for bactericidal antibodies), using rabbit complement (rBCA), using standardized protocols as described elsewhere. A rBCA titer ≥1:8 was reached by 87.7 and 87.4% of subjects in Groups W and C, respectively.

Choo et al (1999) conducted a study which included healthy male and female adolescents aged 15-17 years. Subjects were randomised to one of two groups; group 1 received one dose of a group C meningococcal conjugate vaccine (MenC) containing meningococcal serogroup C oligosaccharide conjugated to diphtheria toxin. Group 2 subjects received one dose of a group A+C meningococcal polysaccharide vaccine (MenPS) containing 50 µg each of meningococcal groups A and C polysaccharides (Mengivac (A+C)®. SBA GMTs were significantly higher in the MenC group than the MenPS group 1 month after vaccination (87.3 versus 20.1). 85% of MenC recipients achieved bactericidal titres of ≥1:8 at 1 month compared with 68% of MenPS recipients. SBA GMTs remained significantly higher in the MenC group than the MenPS group 12 months after immunisation (81.0 versus 20.2). The proportion of subjects achieving bactericidal titres of ≥1:8 at 12 months was also significantly higher in the MenC group than the MenPS group.

References:

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2. Choo S, Zuckerman J, Goilav C, Hatzmann E, Everard J, Finn A. Immunogenicity and reactogenicity of a group C meningococcal conjugate vaccine compared with a group A+C meningococcal polysaccharide vaccine in adolescents in a randomised observer-blind controlled trial. Vaccine. 2000 Jun 1;18(24):2686-92.

3. Schondorf I, Banzhoff A, Nicolay U, Diaz-Mitoma F. Overcoming the need for a cold chain with conjugated meningococcal Group C vaccine: A controlled, randomized, double-blind study in toddlers on the safety and immunogenicity of Menjugate, stored at room temperature for 6 months. Vaccine. 2007 Jan 26;25(7):1175-82.

Observational studies on vaccine effectiveness

In addition to the evidence provided by randomized, controlled efficacy studies, the effectiveness of conjugated MenC vaccines has been clearly demonstrated in observational studies in England and Wales, where the incidence of MenC infection was reduced by 97% during the period 1998-2009 *(Campbell 2010)*. Similar results have been seen in many other countries, for example in the Netherlands and Australia *(De Greeff SC et al 2006; Patel MS, 2007)*.

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Goldschneider, I., E. C. Gotschlich, and M. S. Artenstein. "Human Immunity to the Meningococcus. I. The Role of Humoral Antibodies." J Exp Med 129, no. 6 (1969): 1307-26.