

## Measles vaccines: WHO position paper – 28 April 2017

### Grading of scientific evidence in support of key recommendations

**Table Ia: Effectiveness of measles vaccine in young children and adolescents**

**Population** : Immunocompetent young children and adolescents

**Intervention:** Measles (-containing) vaccination (any dose)

**Comparison** : No vaccination

**Outcome** : Cases of measles

PICO Question: Are measles vaccines effective in young children and adolescents compared to no vaccination?				
		Rating	Adjustment to rating	
Quality Assessment	No of studies/starting rating		1 RCT / 5 observational studies <sup>1</sup>	4
	Factors decreasing confidence	Limitation in study design	Serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	Not applicable	0
	Factors increasing confidence	Strength of association/ large effect	Applicable <sup>2</sup>	+2
		Dose-response	Not applicable	0
		Antagonistic /mitigated bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			4 <sup>3</sup>
Summary of Findings	Statement on quality of evidence		Evidence supports a high level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome.	
	Conclusion		Compared with no vaccination, any dose of measles (-containing) vaccination is highly effective at reducing the incidence of measles infection (high level of scientific evidence).	

<sup>1</sup>In the systematic review by *Elliman D et al* (2007), grading of scientific evidence for vaccine effectiveness (VE) based on the study by Anonymous (1968), a quasi-randomized, controlled trial that followed 21,653 UK children. VE was 94%. Numerous observational studies underline the high VE. Since the literature search by *Elliman D et al* (2007), three observational studies have been published that include assessments of VE of measles containing vaccine. These three studies also allow a comparison between the levels of protection induced by one versus two doses of the vaccine. *Marin M et al* (2006) studied VE of MMR vaccination during a large outbreak. The VE was 92% (95% confidence interval [CI], 67-98%) for 1 dose and 95% (95% CI, 82-98%) for 2 doses. *Wichmann O et al* (2007) investigated vaccine effectiveness based on a large outbreak of measles in a German public school. Among 1098 students the attack rate was 53% in unvaccinated individuals, 1.0% in students with one, and 0.4% in those with two MCV-doses. VE was 98.1% (95% CI: 92-100%) in students with one and 99.4% (95% CI: 97-100%) with two MCV-doses. *Velicko I et al* (2008) conducted a case-control study during a major measles epidemic in Ukraine. The two-dose VE was 93.1% (95% CI: 80.5-98.0%) when controls were matched by class and 92.0% (95% CI: 79.4-97.2%) when controls were matched by school/university. One-dose VE was 50.0% (-57.4-98.3) (Corrected from manuscript through personal communication by the author) when controls were matched by class and 63.0% (-92.3-93.9%) when controls were matched by school/university, but the authors highlight the wide confidence intervals and note the small number of cases and controls with one dose of vaccine, predicting one-dose VE to be significantly higher. In 2012, Demicheli conducted a systematic review on the effectiveness of MMR vaccination. Effectiveness against measles was investigated in three cohort studies (Marin 2006 (see above); Marolla 1998; Ong 2007). Marolla et al evaluated the vaccine effectiveness (one dose) to be 97% (95% (CI) 88- 99). Vaccine effectiveness (VE = 97%) was calculated from Ong et al in Orenstein 1985.

<sup>2</sup>The quality of evidence was upgraded to "high" based on evidence of a very strong association (>90% VE seen across multiple studies)

<sup>3</sup> Based on the GRADE criteria, 4 represents the highest possible score.

## References

1. Anonymous. Vaccination against measles: clinical trial of live measles vaccine given alone and live vaccine preceded by killed vaccine. Second report to the medical research council by the measles vaccines committee. *BMJ* 1968;2:449-452.
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8. Orenstein WA, Bernier RH, Dondero TJ, Hinman AR, Marks JS, Bart KJ, et al. Field evaluation of vaccine efficacy. *Bulletin of the World Health Organization* 1985;63(6):1055-68.
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**Table 1b: Effectiveness of two doses of measles vaccine in young children and adolescents**

**Population** : Immunocompetent young children and adolescents

**Intervention**: Two doses of vaccine

**Comparison** : One dose of vaccine

**Outcome** : Cases of measles

<b>PICO Question:</b> Are two doses of measles containing vaccine more effective than one dose in protecting against measles?				
			Rating	Adjustment to rating
<b>Quality Assessment</b>	No of studies/starting rating		3 observational <sup>4</sup>	2
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	None serious	0
		Imprecision	None serious	0
		Publication bias	Not applicable	0
	Factors increasing confidence	Strength of association/ large effect	Not applicable	0
		Dose-response	Applicable <sup>5</sup>	+2
		Antagonistic /mitigated bias and confounding	Not applicable	0
	<b>Final numerical rating of quality of evidence</b>			<b>4</b>
<b>Summary of Findings</b>	<b>Statement on quality of evidence</b>		Evidence supports a high level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome.	
	<b>Conclusion</b>		Two doses of measles containing vaccine are more effective than one dose in protecting against measles (moderate level of scientific evidence).	

<sup>4</sup> *Marin M et al* (2006) studied VE of MMR vaccination during a large outbreak. The VE was 92% (95% confidence interval [CI], 67-98%) for 1 dose and 95% (95% CI, 82-98%) for 2 doses. *Wichmann O et al* (2007) investigated vaccine effectiveness based on a large outbreak of measles in a German public school. Among 1098 students the attack rate was 53% in unvaccinated individuals, 1.0% in students with one, and 0.4% in those with two MCV-doses. VE was 98.1% (95% CI: 92-100%) in students with one and 99.4% (95% CI: 97-100%) with two MCV-doses. *Velicko I et al* (2008) conducted a case-control study during a major measles epidemic in Ukraine. The two-dose VE was 93.1% (95% CI: 80.5-98.0%) when controls were matched by class and 92.0% (95% CI: 79.4-97.2%) when controls were matched by school/university. One-dose VE was 50.0% (-57.4-98.3) (Corrected from manuscript through personal communication by the author) when controls were matched by class and 63.0% (-92.3-93.9%) when controls were matched by school/university, but the authors highlight the wide confidence intervals and note the small number of cases and controls with one dose of vaccine, predicting one-dose VE to be significantly higher.

<sup>5</sup> The quality of evidence was upgraded to "High" based on evidence of a very strong association (97% of children who did not develop neutralizing antibody after one dose of measles vaccine seroconverted after the second dose). Although immunogenicity is a surrogate marker for vaccine effectiveness, no downgrading is applied due to indirectness since the surrogate marker is well-established.

## References

1. Marin M, Nguyen HQ, Langidrik JR, Edwards R, Briand K, Papania MJ, Seward JF, LeBaron CW. Measles transmission and vaccine effectiveness during a large outbreak on a densely populated island: implications for vaccination policy. *Clin Infect Dis*. 2006 Feb 1;42(3):315-9.
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