

Position paper on measles vaccines:

Grading of scientific evidence

I: Effectiveness

Settings: Global

Question 1: Are measles vaccines safe and effective in young children and adolescents?

Conclusion: Compared with no vaccination, measles vaccination is more effective at reducing the incidence of measles infection (Moderate level of scientific evidence).

Question 2: Are two doses of measles containing vaccine more effective than one dose in protecting against measles?

Conclusion: Two doses of measles containing vaccine are more effective than one dose in protecting against measles (Low level of scientific evidence)

Quality assessment						Summary of Findings	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Quality	
Effectiveness of measles vaccine for preventing measles in young children and adolescents							
1	RCT	Serious ¹	No serious	No serious	No serious	Moderate	Critical
Effectiveness of 1 versus 2 doses of MCV for the prevention of measles in young children and adolescents							
3	OBS	No serious	No serious	No serious	No serious	Low	Critical

1 Quasi-randomization, one RCT only

In the systematic review by *Elliman D et al, 2007*, grading of scientific evidence for protection against measles infection following immunization was based on the study by *Anonymous (1968)*, a quasi-randomized, controlled trial that followed 21.653 UK children aged 10 – 24 months for 2 years and 9 months after vaccination. The protective effects of live, monovalent vaccine was 94%.

The proven benefit of the vaccine makes it unethical to withhold vaccination in control groups and hence, randomized controlled trials in this field are scarce. However, numerous observational studies underline the high protective efficacy of measles vaccine. Since the literature search by *Elliman et al*, three observational studies have been published that include assessments of the effectiveness 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 the effectiveness of MMR vaccination in 72 households during a large outbreak on the Marshall Islands. The vaccine effectiveness 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 2 MCV-doses. VE was 98.1% (95% CI: 92-100%) in students with one and 99.4% (95% CI: 97-100%) with 2 MCV-doses.

Velicko I et al (2008) conducted a case-control study during a major measles epidemic in Ukraine. The two-dose vaccine effectiveness 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 vaccine effectiveness was 50.0% (95% CI: –57.4% (**check figure and wording!**) to 98.3%) when controls were matched by class and 63.0% (95% CI: –92.3% to 93.9%) when controls were matched by school/university.

II: Safety

Question: Are measles containing vaccines safe when used for preventing measles in young children and adolescents?

Settings: Global

Conclusion: Measles vaccine does not cause serious adverse events (Moderate level of scientific evidence)

Quality assessment						Summary of Findings	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Quality	
Risk of serious adverse event following MCV immunization							
2 ¹	RCTs	Serious ²	No serious	No serious	No serious	Moderate	Critical

¹ An overall adverse event grading by Demichele V et al, and an event-specific grading by Elliman D et al (see below)

² The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate.

In a Cochrane database systematic review in 2005 *Demicheli V et al*, reviewing 139 comparative prospective or retrospective trials published during the period 1985–2004, concluded that MMR was associated with a lower incidence of upper respiratory tract infections, a higher incidence of irritability, and a similar incidence of other adverse effects compared to placebo. The vaccine was likely to be associated with benign thrombocytopenic purpura, parotitis, joint and limb complaints, febrile convulsions within two weeks of vaccination and aseptic meningitis (mumps) using Urabe strain-containing MMR. Exposure to MMR was unlikely to be associated with Crohn’s disease, ulcerative colitis, autism or aseptic meningitis (mumps) using Jeryl-Lynn strain-containing MMR.

In the systematic review by *Elliman D et al, 2007*, the grading of scientific evidence related to different types of adverse events was as follows: As compared to control groups, MCV increases the incidence of acute fever and febrile seizures (moderate evidence): (*anonymous 1968; Virtanen M et al, 2000; Barlow WE et al, 2001; Vestergaard M et al, 2004*); does not seem to increase the risk of asthma and eczema (very low evidence) : (*Maher JE et al, 2004; McKeever TM et al, 2004*); does not

seem to cause aseptic meningitis (very low evidence): (*Dourado I, et al 2000; Ki M et al, 2003*); does not seem to increase the risk of development regression or autistic spectrum disorders (low evidence): (*DeStefano F et al, 2004; Madsen KM et al, 2002*); and does not seem to increase the risk of inflammatory bowel disease (*Patja A et al, 2000*).

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