

Pertussis vaccines: WHO position paper - October 1, 2010

Grading of scientific evidence in support of key recommendations

Table I: Protective efficacy/effectiveness of pertussis vaccines

Question: What is the scientific evidence that a primary series of wP or aP vaccine induces protection against severe pertussis* in infants?

Settings: Global

Conclusion: The scientific evidence demonstrates that a primary series of wP or aP vaccine induces protection against severe pertussis in infants. Further research is unlikely to change the estimated effect on health outcomes.

*severe pertussis is defined as ≥ 21 consecutive days of cough and confirmation of *B. pertussis* infection by culture, or by appropriate serology or epidemiology.

Quality Assessment						Summary of Findings	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Quality	
Protective efficacy/effectiveness of wP vaccines against strictly defined pertussis							
4	RCT	No serious	No serious	No serious	No serious	Further research is unlikely to change the estimated effect on health outcomes	Critical
Protective efficacy/effectiveness of aP vaccines against strictly defined pertussis							
5	RCT	No serious	No serious	No serious	No serious	Further research is unlikely to change the estimated effect on health outcomes	Critical

Significant heterogeneity across studies complicates comparisons of the vaccine efficacy/effectiveness (VE) of different types of pertussis vaccines. This grading is based on recent systematic reviews of selected trials, with emphasis on randomized controlled trials (RCTs).

The Jefferson review:

In the systematic review by *Jefferson T et al (2003)*, the 4 RCT studies *Greco D et al 1996*, (study population 14.751); *Gustafsson L et al 1996*, (study population 9.829); *Stehr K et al 1998*, (study population 10.271); and *Anonymous, 1951*, (study population 7558), were utilized for assessments of absolute efficacy of wP or combined DTwP vaccines. In all studies, wP-containing vaccines scored better than placebo against severe pertussis, but VE varied significantly. For DTwP vaccines VE

ranged from 46% (RR 0.54, 95% CI: 0.46 – 0.63) to 92% (RR 0.08, 95% CI: 0.05-0.13). VE for wP ranged from 61% (RR 0.39, 95% CI: 0.27-0.57) to 89% (RR 0.11, 95% CI: 0.08 – 0.15). *Jefferson et al* found 5 RCT studies eligible for absolute efficacy assessments of aP-containing vaccines (*Greco D et al 1996; Gustafsson L et al 1996; Stehr K et al 1998; Anonymous 1988*, (study population 3.901); *Trollfors B et al 1995*, (study population 3.450)). Pooled efficacy against severe pertussis was 73% (RR 0.27, 95% CI: 0.24-0.30). VE was 67-70% for 1- or 2-component aP vaccines, 84% for 3-component vaccines, 80% for 4-component vaccines, and 84% for 5-component aP vaccines.

The Cochrane review:

A recent Cochrane review (*Zhang L et al 2010*) included 4 RCTs (*Trollfors B et al 1995; Anonymous 1988, Greco D et al 1996; Gustafsson L et al 1996*) in the assessment of absolute efficacy of aP vaccines against severe pertussis in children. (In part, the same RCTs were also included in the systematic review by *Jefferson T et al*). *Zhang et al* concludes that all multi-component aPs provided high level of protection against pertussis: Thus, *Greco D et al (1996)* reported 84 % efficacy for both of the 3-component aP vaccines used; *Gustafsson L et al (1996)* found 44% efficacy for a 2-component vaccine, and 78% efficacy for a 5-component vaccine, whereas *Stehr K et al (1998)* reported 79% efficacy of a 4-component aP vaccine.

Observational studies (not included in the table¹):

Three relatively recent *observational* studies have shown similar results. *Gustafsson L et al 2006* (study population: Swedish birth cohorts), evaluated the effectiveness of aP vaccination that was introduced in Sweden in 1996. Immunization at 3, 5, and 12 months of age resulted in an overall reduction in the incidence of laboratory confirmed pertussis from 113 - 150 per 100,000 during 1992-1995 to 11 - 16 per 100,000 during 2001-2004. In areas of enhanced surveillance, the incidence of pertussis was 31 per 100,000 person-years after 2 doses and 19 per 100,000 person-years after the third dose received at 12 months of age. Based on a case-control study, *Bisgard KM et al 2005* (study population 1.072) assessed the VE of pertussis vaccines among US children 6 to 59 months of age. Any combination of ≥ 3 DTwP/DTaP vaccine was found to be highly protective against pertussis. As compared with 0 doses, the unadjusted VE estimate for 1 or 2 pertussis doses was 83.6%, for 3 doses 95.6%, and for ≥ 4 doses 97.7%. The VE estimate for 4 DTwP doses (96.7%) was not statistically different from the VE estimate for 4 DTaP doses (96.7%) or for a mixture of DTwP and DTaP doses (98.0%). *Preziosi MP et al 2003* (study population 1.190), assessing impact of vaccination on clinical severity of pertussis in Senegal according to a predefined scale, found that following 3 doses of the vaccine, a 67% reduction of disease severity was achieved by wP vaccine and a 32% reduction by a 2-component aP vaccine.

¹ Normally, observational studies carry less scientific weight than RCTs in the Grade system.

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