

## HPV PP: grading of scientific evidence (Anogenital Warts)

**Question:** Is there evidence to support administration of the currently licensed quadrivalent HPV vaccine\* to young adolescent girls to substantially reduce their risk of developing anogenital warts later in life?

**Settings:** Global

**Conclusions:** Moderate quality of scientific evidence to support administration of quadrivalent HPV vaccine to young adolescent girls to prevent anogenital warts later in life.

Quality assessment							Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations		
<b>Efficacy of vaccination of young adolescent girls with quadrivalent HPV vaccine to prevent anogenital warts</b>								
2+2+1 <sup>1</sup>	RCTs	no serious	no serious	serious <sup>2</sup>	no serious	none	⊕⊕⊕O MODERATE	CRITICAL
<b>Risk of severe adverse reactions following HPV immunization</b>								
2 <sup>3</sup>	RCTs	no serious	no serious	no serious	no serious	none	⊕⊕⊕⊕ HIGH	CRITICAL

<sup>1</sup>The evidence that this vaccine prevents anogenital warts is based on the outcome of two efficacy studies, two immunogenicity studies, and on one immunobridging study comparing young adolescent girls and young females in terms of observed vaccine immunogenicity.

*Garland SM et al* evaluated quadrivalent vaccine efficacy against anogenital warts in 2261 females and 2279 controls aged 16-24 years at enrolment. Among females naive to HPV 6 or HPV 11 through to 1 month following the 3rd vaccine dose, protection against such lesions due to the HPV type or types for which the subject was naive at enrolment was 100% (95% CI 94-100%) after a mean follow-up of 3 years. In an analysis of combined data from three phase II or III studies, *Dillner J et al* found 99% (95% CI 95-100%) protection against HPV 6/11/16/18-related anogenital warts in a per protocol study population of 15,799 females aged 16-26 years who were naive to these HPV types at baseline and who had received 3 doses of the vaccine.

*Reisinger KS et al* found ≥99.5% seroconversion rates following 3-doses of the quadrivalent vaccine in girls (and boys) aged 9-15 years. Similarly, based on a study of 12,343 individuals aged 9-26 years, *Giuliano AR et al* investigated possible effects of baseline characteristics such as age of the vaccines on immunogenicity of the quadrivalent HPV vaccine. Following 3 vaccine doses, the geometric mean antibody titres against HPV 6, 11, 16, and 18 were each found to be inversely proportional to the participants' age at vaccination.

In an immunobridging study, *Block SL et al* compared the quadrivalent vaccine in females aged 10-15 years and 16-23 years. Following 3 vaccine doses, both groups showed ≥ 99% seroconversion against the 4 genotypes, with higher geometric mean titres (GMTs) in the younger age group.

<sup>2</sup>There is only indirect evidence that quadrivalent HPV vaccination of young adolescent girls will prevent the development of anogenital warts later in life. Young adolescent girls under 15 years of age are considered the primary target group for large-scale HPV vaccination programmes, but were not included in efficacy trials due to concerns about cervical sampling in this age group. The demonstration that the immune response in young adolescent females was stronger than that of females aged 15-26 years in whom the vaccine has been proven to be efficacious, supports the assumption that the vaccine will also be efficacious in young adolescent girls, but also adds to the indirectness of the scientific evidence. Finally, long-term immunogenicity and/or clinical protection is important to vaccine efficacy because females who are vaccinated as girls may not be exposed to HPV types associated with anogenital warts until years to decades later. As of early 2009 immunogenicity and efficacy studies have followed cohorts for only 5 years.

<sup>3</sup>Two RCTs investigated safety and reactogenicity of the quadrivalent HPV-vaccine in females aged 9-15 years (*Block SL et al* and *Reisinger KS et al*). Compared with placebo recipients, vaccinees were more likely to have local injection-site reactions, but were not more likely to have severe adverse events. These findings are consistent with large safety studies in older adolescent females and women (See Background Paper for references).

\*The bivalent HPV vaccine is not designed to protect against anogenital warts

### Bibliography

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