Grading of scientific evidence (Males)*

*September 2014: This table will be updated as soon as a current systematic review on the topic is finalized.

HPV vaccination of males to reduce incidence of cervical cancer in females

Population : Immunocompetent males
Intervention: HPV vaccination
Comparison: Placebo/ no vaccination
Outcome : Cervical cancer in females

What is the scientific evidence to support vaccination of males with current HPV vaccines to substantially reduce incidence of cervical cancer in females?				
			Rating	Adjustment to rating
Quality Assessment	No. of studies/starting rating		5/ RCT[1]	4
	Factors decreasing confidence	Limitation in study design	None serious	0
		Inconsistency	None serious	0
		Indirectness	Serious[3]	-2
		Imprecision	None serious	0
		Publication bias	None serious	0
	Factors increasing confidence	Large effect	Not applicable	0
		Dose-response	Not applicable	0
		Antagonistic bias and confounding	Not applicable	0
	Final numerical rating of quality of evidence			**2**
Summary of Findings	**Statement on quality of evidence**			**Our confidence in the estimate of the effect on the health outcome is limited**
	Conclusion			**We have limited confidence in the quality of scientific evidence in support of vaccination of young males to reduce incidence of female cervical cancer, though evidence suggest that vaccinating young males prevents these from HPV infection and disease (genital warts, AIN 2/3 and anal cancer).**

[1] Immunogenicity studies by *Block SL et al* and *Reisinger KS et al* (quadrivalent vaccine) as well as by *Lehtinen M et al* (bivalent vaccine) show that both HPV vaccines are as immunogenic and safe in young adolescent males as they are in young adolescent females. Recent reports by *Palefsky J et al* and by *Giuliano A et al* show that the quadrivalent HPV vaccine decreases the incidence anal infections and lesions (Palefsky et al) and infection and external genital lesions (as a combined outcome of anogenital warts and anogenital intraepithelial neoplasia) (Giuliano et al) due to HPV types 6/11/16/18 in a population of young men aged 16-26 years. In the per protocol population, the efficacy of the vaccine for the prevention of HPV 6, 11, 16 and 18-related genital warts was 89.4%, and the efficacy for the prevention of HPV 6, 11, 16 and 18-related AIN 2/3 was 74.9%. Data are not available on clinical efficacy of the bivalent vaccine in males immunogenicity, though data are available on the immunogenicity (Petaja et al. and Block et al.).

[3] There are no studies that currently demonstrate that HPV vaccination of males will result in less sexual transmission of these vaccine related HPV types from males to females and in reduced incidence of cervical cancer. Although recent studies support the assumption that HPV vaccination also protects against vaccine related HPV type infection and disease in males, *Barnabas*

RV et al modelled vaccinating boys with a HPV 16 vaccine at either low or high coverage levels, in addition to vaccinating adolescent girls in Finland and found that vaccination of both genders added little benefit over vaccinating adolescent girls alone. Predictions are based on modelling. *Taira AV et al* predicted that adding vaccination of adolescent boys with a HPV 16/18 vaccine to a vaccination programme for girls would further reduce cervical cancer cases by 2% in the US. *Ebasha EH et al*, in model studies on the quadrivalent vaccine, predicted that vaccination of males in addition to girls aged < 12 years could further reduce the incidence of cervical cancer from 79% to 91%, compared to vaccinating girls alone at low to moderate coverage levels currently seen in the US. *Insinga RP et al* who examined the potential outcomes of various vaccination strategies using the quadrivalent HPV vaccine in Mexico found that vaccination of 12-year-olds, plus a temporary 12-24-year-old catch-up program covering both sexes was most effective, reducing by 84-98% the HPV 6/11/16/18-related cervical cancer, high-grade cervical precancererous lesions, and genital wart incidence during year 50 following vaccine introduction. *Kim JJ et al,* modelling transmission of HPV types 16 and 18 infection between males and females found that at 90% coverage, vaccinating girls with a HPV 16/18 vaccine reduced cancer risk due to these HPV types by 63%; including boys at this coverage level provided only 4% further cancer reduction. *Kulasingam S et al* found adding HPV 16/18 vaccination of males was not cost-effective for cervical cancer prevention compared with the current policy of vaccinating 12 year old females in Australia. Information is still insufficient or missing on a number of key issues required for precise modelling of the possible impact of male vaccination on the incidence of female cervical cancer.

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