

HPV vaccination in boys — will the UK join the fight?

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The UK Joint Committee on Vaccination and Immunization recently announced a further delay before considering the subject of widespread human papillomavirus (HPV) vaccination in teenage boys, thereby excluding an estimated 2.9 million boys from receiving an effective treatment in this interim period. Vaccination of boys can offer significant clinical, economic and ethical advantages.

Refers to Pratt, A. & Barber, S. UK Government strategy on male HPV vaccination. *parliament.uk* [online] <http://researchbriefings.parliament.uk/ResearchBriefing/Summary/CDP-2016-0117#fullreport> (2016)

The human papillomavirus (HPV) group comprises >100 viral subtypes that can affect the skin and mucous membranes. As well as being associated with cervical cancer, certain HPV strains are associated with a range of other cancers, including those of the head and neck, vulva, vagina, penis and anus. Infection with HPV16 and/or HPV18 (the high-risk subtypes) account for >90% of cases of HPV-related cancer, while infection with HPV6 and HPV11 (the low-risk subtypes) is primarily associated with genital warts. In the past, demographic profiling suggested a greater burden of HPV-related disease among females than males; however, this distribution is changing in developed countries owing to the implementation of effective cervical cancer screening programmes and the rising incidence of other HPV-associated cancers, such as HPV-associated oropharyngeal cancer, which affects at least three times more men than women. In the USA, the annual incidence of oropharyngeal cancer is projected to overtake that of cervical cancer within the next decade. In Europe, the annual incidence of HPV-related diseases in 2012 was ~700,000; the majority of these cases being genital warts with a similar overall distribution between both sexes¹ (FIG. 1).

HPV vaccination has been offered to teenage girls in most developed countries since 2006. Vaccination is now also recommended for boys in Australia, Austria, Brazil, Canada,

Germany, Israel, Italy, Switzerland and the USA². However, most vaccination programmes, worldwide, do not include boys, primarily owing to costs and a lack of recognition of the emerging epidemic of HPV-associated cancers in men. Initially, the UK female HPV immunization programme used Cervarix, a bivalent vaccine that confers protection from HPV16 and HPV18 infection. In 2012, the immunization programme changed to use of Gardasil, a quadrivalent vaccine, which confers additional protection against HPV6 and HPV11 infection. In 2014, FDA approval was granted for Gardasil-9, a nonavalent vaccine offering additional protection against infection with other HPV strains (HPV31, 33, 45, 52 and 58) that can result in either malignant or benign HPV-related disease. Protection against the targeted HPV types has been found to last for at least 9 years with Cervarix, and for at least 8 years with Gardasil³. The duration of protection with Gardasil-9 has not been determined, and various ongoing studies are attempting to do so; this vaccine is not yet available within the UK.

In June 2016, the UK Joint Committee on Vaccination and Immunization established a pilot HPV vaccination trial specifically for men who have sex with men (MSM)⁴. Men in this group have a higher lifetime incidence of HPV than heterosexual men because neither they, nor their partners are likely to have immunity against HPV. We note that, since

2013, the programme has been subject to considerable delays and reports on the outcomes will not become available until 2017. As a consequence, any potential extension of HPV vaccination to include all teenage boys could be postponed until 2020 (REF. 4). The cumulative effect of this delay is that an estimated 2.9 million boys are likely to be excluded from receiving HPV vaccination during this period⁵.

If introduced to the UK health-care system, vaccination of all teenage boys can offer considerable clinical, economic and ethical advantages. The potential benefits include: protection of men who have sex with unvaccinated women from the UK or elsewhere; protection of more females from HPV-related disease than is currently achieved through vaccination of females alone; provision of enhanced protection for MSM; less reliance on cancer screening protocols; reduced costs of treating HPV-related disease; reduced reliance on 'herd immunity'; and improved access to treatment, regardless of gender.

An estimated 10–15% of 25–34-year-old males have had at least one sexual partner from outside of the UK in the past 5 years — many of whom originate from countries with ineffective HPV vaccination programmes⁶. Furthermore, an estimated one in ten women in the UK do not participate in the current vaccination programme^{4,7}. This limitation might relate to the fact that, despite various campaigns to increase knowledge of

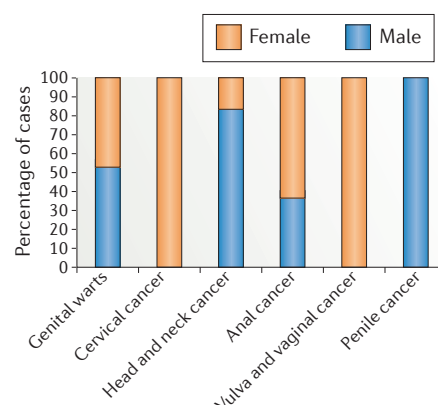


Figure 1 | Estimated annual percentages of new cases of HPV-associated cancers and genital warts, by gender, in Europe¹. Modified with permission from Springer Nature © Stanley M. *Nature* 488 (Suppl.), S10 (2012).

“...vaccination of all teenage boys can offer considerable clinical, economic and ethical advantages”

HPV-related disease, a lack of understanding of the effects of vaccines or diseases caused by HPV infections persists among the general public^{7,8}. Research has also shown that parents are more likely to refuse HPV vaccination of their children than they are to refuse other vaccines, owing to cultural or religious factors⁸. Broadening HPV vaccination programmes, particularly through inclusion of boys, would counter many of these deficits and ensure increased protection of the population from HPV infection.

With regard to HPV vaccination of MSM, the current pilot scheme in the UK only recruits MSM who attend sexual health clinics; however, we note the average age at first attendance of such clinics is 28 years⁶. This observation means that the overwhelming majority of MSM will not receive protection from HPV-related infections before becoming sexually active. In our opinion, the best way to sufficiently protect this group is to vaccinate all males in their teenage years.

Importantly, although effective cervical cancer screening programmes exist and are carried out formally in most developed countries, no validated screening strategies exist for early-stage oropharyngeal or anal cancer. Hence, many patients with oropharyngeal or anal cancers present with advanced-stage disease. In the absence of effective secondary prevention programmes for many HPV-associated cancers, a focus on the implementation of available primary prevention strategies should be considered a priority.

The annual cost to the UK National Health Service (NHS) of treating HPV16-infection-associated oropharyngeal cancer is estimated

at UK£30 million, and treatment of anogenital warts costs a further ~£60 million⁴. By contrast, HPV Action (a patient-oriented charity group) estimate that the yearly cost of vaccinating boys in the UK will range between £12–22 million⁴. However, any cost-effectiveness calculation is dependent on the type of vaccine selected and its price — which might be negotiable, owing to the availability of a number of competing manufacturers.

Data from most health-economic models suggest that vaccination of boys is not a cost-effective approach when female vaccination coverage is high: ~70% of the female population, assuming a 99% vaccine efficacy rate for ~20 years. This lack of cost-effectiveness reflects a ‘herd immunity’ effect, whereby the risks of HPV exposure are minimized owing to widespread, but not uniform immunity⁹. Herd immunity is an argument often quoted by governments in order to justify a lack of funding of male vaccination trials. Unfortunately, only a few vaccination programmes have established the high female coverage rate required for adequate herd immunity¹.

In addition to the points raised above, UK national statistics suggest that HPV causes >2,000 cases of cancer and 48,000 cases of genital warts per year in males, and ~5,000 cases of cancer and 39,000 cases of genital warts per year in females^{4,7}. Therefore, seeing as the burden of HPV-related disease is similar, a strong ethical argument exists for both genders to be treated equally.

In summary, HPV immunization of boys can be cost-effective if the vaccine is priced appropriately⁷. We strongly urge the Department of Health to use economies of scale to facilitate access to an intervention with proven benefits, irrespective of a patient’s gender. The UK has an opportunity to be part of an international effort to eradicate and/or significantly reduce the incidence of HPV-related disease... will we ever join the fight?

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Competing interests statement

The authors declare no competing interests.