Human papillomavirus: a strong case for vaccinating boys

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In the UK, human papilloma virus vaccination is restricted on the NHS to girls and only recently been recommended for men who have sex with men. The restriction is based largely on cost-effectiveness. In this article, Gillian Prue sets out the compelling case for vaccinating all boys. On page 10, Peter Baker describes HPV Action’s campaign for gender-neutral HPV vaccination.

Human papillomavirus (HPV) is one of the most common sexually transmitted infections worldwide, so predominant and so easily acquired that nearly all sexually active men and women will be exposed to the virus at some point in their lives. The rate of genital HPV infection is similar in males and females; however, males have a lower immune response to natural HPV infection than their female counterparts, meaning that there is not the same association between age and HPV prevalence in men as there is in women. In women, HPV prevalence peaks between 18–24 years and subsequently declines. In contrast, in men, there is a consistently higher prevalence of HPV.

There are many different types of HPV, and varying degrees of risk associated with persistent infection with each type. Many HPV infections are short-lived and clinically insignificant, but continual infection with certain types of HPV causes a considerable burden of disease in both sexes. Cervical cancer has been unequivocally linked to persistent infection with HPV, with two high-risk types, HPV 16 and 18, being linked to 70% of cases of cervical cancer worldwide. In addition, HPV has been linked to other cancers and non-cancerous conditions in both men and women, for example genital warts, oropharyngeal cancer (OPC), anal cancer or penile cancer. Estimates of the incidence of HPV-related cancers for 2008 has been calculated globally; of the estimated 12.7 million cancers, 610,000 could be...
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Australia, Austria, Canada, Israel, Switzerland and the USA recommend HPV vaccination for boys (© Dr P. Marazzi/Science Photo Library)

attributed to HPV infection. According to Stanley, in Europe around 23,250 cases of cervical cancer each year, plus vaginal and vulval cancer (3850 cases), several head and neck cancers (15,230 cases), as well as anal cancers (4630 cases) in both sexes and penile cancer (1090 cases) can be attributed to HPV. HPV also causes 614,700 cases of genital warts. In Europe, in men specifically, each year there are an estimated 15,490 new cases of HPV-related cancer and 325,700 new cases of genital warts.

Successful HPV vaccination in females, in combination with adequate screening programmes, has enabled remarkable progress in the reduction and prevention of cervical cancer; less progress has been made with other HPV-related cancers affecting both sexes. In the USA, it has been predicted that the number of HPV-related OPCs diagnosed in a year will soon surpass the annual number of cervical cancer cases. Anal cancer incidence has increased rapidly over the past 30 years in the UK in both sexes. Men who have sex with men (MSM) carry a disproportionate burden of anal cancer, similar to cervical cancer rates in females before the introduction of screening, and there is an increased incidence of anal cancer amongst MSM in comparison to heterosexual male population (over 15:1). Furthermore, HIV-positive MSM have an up to 80-fold estimated higher risk than HIV-negative men or women of developing anal cancer.

EFFECTIVE VACCINES
Two HPV vaccines are now licensed for use in the UK: a bivalent vaccine (Cervarix) which protects against two high-risk types of HPV (HPV 16/18) and a quadrivalent vaccine (Gardasil) protecting against the two high-risk HPV types and two low-risk types associated with genital warts (HPV 6/11/16/18). A new nonavalent vaccine has been developed to cover nine different types of HPV. In addition to HPV 6, 11, 16 and 18, it also includes protection against HPV 31, 33, 45, 52 and 58.

A decision on whether or not to vaccinate boys should not be made solely on the basis of cost-effectiveness

HPV vaccines have been shown to be effective in men. In a study of 4065 males aged 16–26, the quadrivalent HPV vaccine was shown to be effective in preventing genital warts, penile cancer and anal cancer. In addition, a meta-analysis of 29 studies (8360 men) that reported on HPV vaccine acceptability found a moderate level of acceptability in men, indicating that men would have the HPV vaccine if it was offered.

THE CASE FOR VACCINATING BOYS
The case for vaccinating boys with the HPV vaccine is summarised in Figure 1. Despite HPV’s impact on the health of both sexes and the availability of an effective vaccine for both adolescent males and females, only Australia, Austria, Canada, Israel, Switzerland and the USA recommend the vaccination of boys. Within country, HPV vaccination for boys is now also recommended in the German region of Saxony and the Italian regions of Emilia-Romagna and Sicily. Emilia-Romagna has recently introduced a vaccination programme for HIV-positive males under 26. Countries offering female-only vaccination believe males will be protected from HPV-related illness as a result of herd protection, i.e. a reduction in the risk of infection in males due to reduced exposure as a result of female vaccination. It is true that a high coverage in females may promote herd protection and there is some developing evidence that this is the case. An analysis of high-uptake female-only vaccination programmes in nine countries found a reduction of around one third in the number of boys with genital warts. However, even if herd protection is achieved with high female vaccination uptake, men are not protected as soon as they move outside of the ‘herd’. Men will live and work in other countries where females are not vaccinated and, as a result, likely become infected with HPV.

Female-only vaccination strategies do provide some degree of protection for men who have sex with women within the herd, but they offer no protection for MSM. Due to the higher incidence of anal cancer and the current lack of protection for MSM, the Joint Commission for Vaccinations and Immunisations (JCVI) in the UK announced in November 2015 that the current UK female-only vaccination policy be extended to MSM aged up to 45 years via a genitourinary medicine (GUM) or Human Immunodeficiency Virus (HIV) clinic, or opportunistic vaccination via GPs. Superficially, this may seem to be a suitable cost-effective answer, but a targeted MSM HPV vaccination programme would be difficult to implement. The vaccine offers most protection if it is given before exposure to HPV. It is totally inappropriate, impractical and unethical to ask adolescent boys if they are likely to have sex with another male when they are older and, if so, whether they would consider HPV vaccination.

The proposed solution suggested by the JCVI will most likely not protect the
The majority of MSM. Most MSM are likely to have had multiple sexual partners with increased risk of HPV acquisition before they attend a sexual health clinic, and many gay and bisexual men do not attend GUM clinics. There are also MSM who do not identify as gay or homosexual and will not disclose their sexual activity to a healthcare professional, meaning they will never be offered the vaccination. In addition, offering HPV vaccination to MSM up to the age of 45, if introduced, would present a further inequality, as women in the UK are not currently offered vaccination up to this age.

**QUESTIONS OF COST-EFFECTIVENESS**

The cost-effectiveness of a male vaccination programme is influenced by the degree of uptake of the vaccine in females. With a low uptake in girls, the cost-effectiveness of vaccinating boys is more easily demonstrated. The potential impact of a male vaccination programme has been estimated via various mathematical models, and a debate currently exists around their cost-effectiveness. Many models do not support the inclusion of men; however, MSM are frequently not included in the model, and the focus is largely on the impact of the vaccine in terms of cervical cancer outcome, and not predicting the impact on other HPV-related cancers.

A recent study provided a comprehensive health and economic assessment supporting the direct benefit of vaccinating boys along with girls against oncogenic HPV in the Netherlands. The analysis demonstrated that, with a 60% uptake in females, the burden of HPV related cancers in men reduced by approximately one third, and with a 90% uptake in females, the burden of HPV related cancers in men was reduced by 66%. However, anal cancer decreased by only one third. It was concluded that this was due to the disproportionate burden of anal cancer in MSM, who do not benefit from female-only vaccination strategies, and that the incremental benefit of including boys in vaccination programmes was driven by the prevention of anal cancer. These findings validate the importance of including MSM in cost-effectiveness modelling. The burden of genital warts is comparable to the burden of HPV-related cancers; the study did not assess the impact on genital warts, which could have led to an under-estimation of the impact of a universal vaccination strategy. The Dutch study is complemented by another recent cost-effectiveness analysis of male HPV vaccination in Canada, which suggested that HPV vaccination of adolescent boys may be a cost-effective strategy for the prevention of OPC.

**HUMAN COST**

The human cost of HPV-related diseases should be the primary consideration for including boys in HPV vaccination programmes. HPV-related lower genital tract lesions and genital warts significantly impair psychosocial wellbeing and health-related quality of life. Patients with head and neck cancer experience profound visible, functional and psychological consequences from their disease and treatment. A decision on whether or not to vaccinate boys should not be made solely on the basis of cost-effectiveness; the psychosocial impacts of HPV-related disease must be considered when calculating the benefit of male HPV vaccination.

Withholding a vaccine from any group of individuals at risk of developing a vaccine-preventable disease is unethical. It is also unfair for females to be expected to carry the responsibility for HPV prevention through vaccination, particularly when
HPV is a virus that is sexually transmitted and affects both sexes so prolifically. The burden of HPV-related diseases is now almost the same in men as in women. Unlike cervical cancer, there are no reliable and cost-effective screening methods to prevent cancers caused by HPV among men. A gender-neutral vaccination programme would achieve real herd immunity; without male vaccination, men who move outside of the herd, and especially MSM, remain at risk of HPV infection and life-threatening and life-altering HPV-related diseases.

REFERENCES

HPV vaccination: let’s have it for the boys too

PETER BAKER

HPV Action’s campaign for gender-neutral HPV vaccination is gaining ground. Peter Baker outlines the case, and describes what the campaign is doing and how readers can get involved.

The vaccination of boys as well as girls against human papillomavirus (HPV) in order to prevent a wide range of diseases in both sexes has become one of the most widely supported public health interventions not to have been implemented in the UK. As Gillian Prue notes in the previous article, it is now policy in many countries (Australia, Austria, the USA and others) and, in the UK, it has the support of the 43 professional, patient and other organisations that have come together as HPV Action to make the case for a change in policy.

Gender-neutral vaccination is also supported by the BMA, Jo’s Cervical Cancer Trust and over 100 individual experts who have signed a statement backing HPV Action’s goal. That list of experts is headed by Harald zur Hausen, Emeritus Professor at the German Cancer Research Centre in Heidelberg and winner of the Nobel Prize for Medicine in 2008 for discovering the link between HPV and cervical cancer. 83% of UK sexual health professionals believe both sexes should be vaccinated,1 as do a similar proportion of UK parents,2 according to recent studies.

Peter Baker, Campaign Director, HPV Action
It seems the only significant body not yet convinced of the case for gender-neutral vaccination is, unfortunately, also the one with the most influence – the government’s advisory body, the Joint Committee on Vaccination and Immunisation (JCVI). Its assessment as to whether boys should be vaccinated against HPV began in 2013. JCVI intended to make a decision in 2015, but this has been put back to 2017. The Independent Cancer Task Force has suggested that, even if the JCVI does decide that boys should be vaccinated, implementation would not begin until 2020. This is a very long timescale, particularly in light of the fact that, with each year that passes, 400,000 more boys are left unprotected against HPV.

The modelling on cost-effectiveness used by JCVI and others to assess whether or not boys should be vaccinated against HPV is very complex, but still excludes many variables (eg the cost of social care and cost to employers, as well as the risk of HPV infection to men who have sex with unvaccinated women from other countries). HPV Action estimates that the cost of vaccinating boys would be £20–22 million a year at most, a very modest sum when compared to the costs of treating HPV-related diseases. The cost of treating anogenital warts alone is an estimated £58.44 million a year in the UK.1

The JCVI’s recent decision to recommend the vaccination of men who have sex with men (MSM) up to the age of 45 via sexual health clinics is a welcome step, but an inadequate one. Most MSM will have been infected before they set foot in a clinic – the average age of first attendance is 28 years2 – and many do not attend at all or do not disclose their sexual identity. Moreover, as Gillian Prue points out, vaccinating MSM does nothing to protect men who have sex with unvaccinated women who may be from the UK (around 10% of UK girls are not vaccinated) or from countries that have no HPV vaccination programmes for girls or whose vaccination programmes have relatively low uptake.

HPV Action is seeking an acceleration of JCVI’s decision-making on the vaccination of boys from 2017 to 2016, and more importantly, a decision to vaccinate boys against HPV. To this end, we are seeking to influence the scientific debate about the issue through journal articles, conference presentations, informing politicians and policymakers, and alerting parents to the inequity of their daughters receiving protection but not their sons.

The only significant body not yet convinced of the case for gender-neutral vaccination is the one with the most influence

Progress is being made. For example, the chairs of several influential all-party groups in Parliament – those on cancer, sexual and reproductive health, dentistry, HIV/AIDS and men’s health – now support gender-neutral vaccination. There have been debates on the issue in both Houses of Parliament and an Early Day Motion has been tabled for both Houses by Danny Kinahan MP.3

HPV Action is now seeking support from clinicians, public health practitioners, policymakers, parents and others to:

- write to their MPs asking them to call for gender-neutral vaccination and to sign the Early Day Motion (no. 464, tabled by Danny Kinahan MP)4
- approach their professional organisations to ask for policy change, broadening and further strengthening the case for action
- support HPV Action through a donation: personal donations can be made online (and gift-aided) at www.justgiving.com/HPVAction.

To find out more about HPV Action, visit www.hpvaction.org.

Declaration of interests
Peter Baker is Campaign Director for HPV Action, which receives no commercial sponsorship.

REFERENCES

BLOG
Do you agree that HPV vaccination should be gender neutral? Let us know what you think about this debate: www.trendsinmenshealth.com/blog