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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,[1] 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.[2]. In contrast, in men, there is a consistently higher prevalence of HPV.[3]

There 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,[4] with two high-risk types, HPV 16 and 18, being linked to 70% of the cases of cervical cancer worldwide.[5] In addition to cervical cancer, 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 attributed to HPV infection.[6] According to Stanley, in Europe around 23 250 cases of cervical cancer each year plus vaginal and vulval cancer (3,850 cases), several head and neck (15 230 cases) as well as anal cancers (4630 cases) in both sexes and penile cancer (1090 cases) can be attributed to HPV.[7] 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 in men and 325 700 new cases of genital warts.

Successful HPV vaccination in females in combination with adequate screening programmes has made 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 soon the number of HPV-related OPCs diagnosed in a year will surpass the annual number of cervical cancer cases.[8] 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 many countries; a bivalent vaccine which protects against two high-risk types of HPV (HPV 16/18) and a quadrivalent vaccine 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.

HPV vaccines have been shown to be effective in men. In a study of 4065 males aged 16–26 years old, the quadrivalent HPV vaccine was shown to be effective in preventing genital warts, penile cancer and anal cancer.[1,9] In addition, a meta-analysis of 29 studies (8360 men) that reported on HPV vaccine acceptability found a moderate level of acceptability in men,[10] indicating that men would have the HPV vaccine if it was offered.

THE CASE FOR VACCINATING BOYS

Despite HPV's impact on the health of both sexes and the availability of an effective vaccine for both adolescent males and females, Australia, Austria, Canada, Israel, Switzerland and 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 program 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 *ie* a reduction in the risk of infection in males due to reduced exposure as a result of female vaccination.[11] It is true that a high coverage in females may promote this 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.[12] 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 to the person 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, would they consider HPV vaccination. The proposed solution suggested by the JCVI will most likely not protect 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.[13] Also, 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

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, but frequently MSM are 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.[14]

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.[15] The analysis demonstrated that with a 60% uptake in females the burden of vaccine-preventable cancers in men reduced by approximately one third, 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 owing to the disproportionate burden of anal cancer in MSM and who do not benefit from female only vaccination strategies. It was concluded that the incremental benefit of including boys in vaccination programmes was driven by the prevention of anal cancer. This validates the importance of including MSM in cost-effectiveness modelling. The burden of genital warts is comparable to the burden of HPV-related cancers; the Dutch 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 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.[16]

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.[17] 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 solely be made 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 that 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

1. Giuliano AR, Palefsky JM, Goldstone S, et al. Efficacy of quadrivalent HPV Vaccine against HPV infection and disease in males. N Engl J Med 2011;364:401-411
2. Burchell AN, Winer RL, de Sanjose S, Franco EL. Chapter 6: Epidemiology and transmission dynamics of genital HPV infection. Vaccine. 2006;24(Suppl 3):S3/52–61
3. Anic GM, Giuliano AR 2011 Genital HPV infection and related lesions in men Prev Med. 2011 October ; 53(Suppl 1): S36–S41. doi:10.1016/j.ypmed.2011.08.002.
4. Bosch FX, Lorincz A, Munoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. J Clin Pathol 2002;55(4):244–65.
5. de Sanjose S, Quint WG, Alemany L et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Lancet Oncol 2010;11(11):1048–56.
6. Forman D, de Martel C, Lacey CJ, et al. Global burden of human papillomavirus and related diseases. Vaccine 2012; 30: F12 – 23.
7. Stanley M. Vaccinate boys too. Nature 2012; 488:S10.
8. Chaturvedi A, Engels E, Pfeiffer R, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol 2011;29;4294-301.
9. Palefsky JM, Giuliano AR, Goldstone S, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. N Engl J Med 2011;365:1576–85.
10. Newman PA, Logie CH, Doukas N, Asakura K. HPV vaccine acceptability among men: a systematic review and meta-analysis. Sex Transm Infect 2013;89:568-574
11. Brisson M, de Velde N, Franco EL, Drolet M, Boily M-C. Incremental impact of adding boys to current human papillomavirus vaccination programs: role of herd immunity. J Infect Dis 2011;204:372-376.
12. Drolet M, Benard E, Boily M-C, et al. Population level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis. The Lancet Infectious Diseases 2015;15:565-580.
13. Zou H, Tabrizi SN, Grulich AE, et al. Early acquisition of anogenital human papillomavirus among teenage men who have sex with men. J Infect Dis 2014; 209:642-651.
14. Marty R, Roze S, Bresse X, Largeron N, Smith-Palmer J. Estimating the clinical benefits of vaccinating boys and girls against HPV-related diseases in Europe. BMC Cancer 2013;13:10
15. Bogaards JA, Wallinga J, Brakenhoff RH, Meijer CJLM, Berkhof J. Direct benefit of vaccinating boys along with girls against oncogenic human papillomavirus: Bayesian evidence synthesis. BMJ 2015;350:h2016.
16. Graham DM, Isaranuwatchai W, Habbous S, et al. A cost-effectiveness analysis of human papillomavirus vaccination of boys for the prevention of oropharyngeal cancer. Cancer 2015; Online First.
17. Dominiak-Felden G, Cohet C, Atrux-Tallau S, Gilet H, Tristram A, Fiander A. Impact of human papillomavirus-related genital diseases on quality of life and psychosocial wellbeing: results of an observational, health-related quality of life study in the UK. BMC Public Health 2013; 13: 1065.