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Human papillomavirus: the case for a gender-neutral vaccination programme

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Human papillomaviruses (HPV) are a large family of double-stranded DNA viruses that infect skin and mucosal cells [1]. Of the more than 100 recognised genotypes, at least 13 are considered to be oncogenic (or 'high-risk'). The two most common of these, i.e. type 16 and 18, are known to cause approximately 70 per cent of all cervical cancers. Oncogenic HPVs have also been implicated as the aetiological agents in squamous cell carcinoma of the anus, genitals and the head and neck. Current estimates suggest that human papillomaviruses are associated with around 5 per cent of all human cancers [2]. In addition, HPV type 6 and 11 are the causal agents of genital warts which are the commonest sexually-transmitted viral disease [3].

A previous decision made by the UK Joint Committee on Vaccination and Immunisation (JCVI) not to vaccinate boys against HPV has been received with widespread criticism by health bodies and campaigners [4]. In an interim statement released in July 2017, the independent expert advisory panel, which had been reviewing the vaccination programme, concluded that it would be 'highly unlikely to be cost-effective' to extend the existing scheme in order to include adolescent boys [5].

Under current regulations, all girls aged 12 to 13 years are routinely offered the HPV vaccine as part of the National Health Service (NHS) childhood immunisation programme with the aim of reducing the incidence of cervical cancer [6]. A pilot scheme providing the vaccine to men who have sex with men (MSM) and who attend sexual health clinics has recently been introduced in England [7]. A number of leading doctors and academics, however, have been urging the government to expand the current programme to cover school-aged boys also. In a letter to the UK Secretary of State for Health, a group of 13 clinicians - including Elizabeth Carlin, President of the British

Association for Sexual Health and HIV, and Saman Warnakulasuriya, Emeritus Professor of Oral Medicine and Experimental Pathology at King's College, London, called for the government to 'expedite a decision' on the issue [8].

The incidence of cervical cancer has been significantly reduced in economically-developed countries, primarily as a result of comprehensive screening programmes. Other cancers linked to the virus, on the other hand, are not amenable to screening and the incidence of these is rising in both men and women [9]. Oropharyngeal cancers, in particular, have caused a substantial shift in the landscape of HPV-related cancers [10]. The overall incidence of oropharyngeal cancer in high-income countries has increased substantially in recent years which correlates strongly with a rise in the proportion of HPV-positive oropharyngeal cancer. In the United States, the incidence of HPV-positive oropharyngeal cancer has been growing at an alarming rate, i.e. at 225 per cent over a period of less than two decades (from 0.8 cases per 100 000 people in 1988 to 2.6 cases per 100 000 people in 2004) [11]. The rise is greater, i.e. 2-3-fold, in men compared to women [12]. It is projected that the annual number of HPV-positive oropharyngeal cancer will surpass that of cervical cancer by the year 2020, with the majority occurring in men [11].

HPV vaccination has been shown to be effective in males [13]. In phase III clinical trials, similarly designed to those used in females, the quadrivalent vaccine which targets types 6, 11, 16, and 18 of the virus proved to be comparably immunogenic, efficacious, and safe in young men [14]. In a subgroup analysis of MSM, an 89 per cent reduction in genital warts and 75 per cent reduction in high-grade anal lesions was observed [15]. The vaccine was subsequently approved in October 2009 by the US Food and Drug Administration (FDA) for use in males aged 9 to 26 years [13].

Men will clearly benefit from HPV vaccination. Nevertheless, substantial debate continues to surround this issue. Despite the growing recognition of the virus' health impact on both sexes and the availability of effective vaccines for both females and males, existing immunisation programmes in the majority of countries remain exclusively for females [9]. Australia became the first country in the world to implement a publicly-funded programme for school-aged boys in 2012, with Canada and the USA following soon after [16].

Meanwhile, in the UK, a final decision on whether to recommend the HPV vaccine to boys is awaited. In its interim ruling, which is currently under consultation, the JCVI recognised that there were indeed advantages in vaccinating males. It argued, however, that the risk of infection in the male population had already been reduced by the existing programme for girls and that the resulting herd effect would continue to have an impact. It concluded that the incremental benefit gained from expanding the scheme to boys would not justify the cost [2].

High vaccine coverage in females could certainly offer a degree of protection to males and there is evidence that this is the case [17]. However, there are important limitations to reliance on female-only programmes. Even if high vaccine uptake among women is achieved, men are not protected as soon as they move outside of the 'herd'. Heterosexual men continue to be at risk of contracting HPV from unvaccinated women, either abroad or within the UK. An estimated 10 to 15 per cent of men aged 25 to 34 years have had at least one sexual partner from outside of the UK in the last 5 years [18]. In addition, annual figures show that 17 per cent of 12 to 13-year-old girls in England and 15 per cent of those in Scotland have not received the required number of doses of the vaccine [19, 20].

There are a number of economic models that support the routine vaccination of boys [21]. In logistical terms, the cost of expanding the programme to include boys is currently estimated at approximately £20 to £22 million a year [22]. This is a relatively modest sum when compared to the financial burden of treating HPV-related diseases. The cost of managing anogenital warts alone is approximately £58.44 million a year in the UK, a cohort of patients that is dominated by men [23]. Meanwhile, the secondary care cost associated with treating predominantly HPV-positive oropharyngeal cancers has risen sharply from an estimated £17.21 million a year in 2006/07 to £32 million in 2010/11 [24].

HPV-related cancers have become an increasingly important issue for men in high-income countries. The burden of disease among men is now comparable to that in women, with evidence suggesting a growing incidence of oropharyngeal cancers linked to HPV. In the absence of population-based methods of early detection and growing healthcare costs associated with treatment, primary prevention through vaccination becomes essential. A universal, gender-neutral immunisation programme would protect both females and males from infection, reduce transmission, increase herd immunity, and as a result, facilitate the eradication of HPV-related diseases in the general population.

The JCVI is expected to publish its final decision later this year.

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