

PE1477/B

Professor Heather A Cubie

PE1477 Gender Neutral HPV immunisation

What is your view on the petitioners' call to extend the HPV immunisation programme to boys in Scotland?

When a national programme of HPV immunisation was introduced across the UK in 2008, the bivalent vaccine, Cervarix® (active against HPV 16 and HPV 18) was selected. As this vaccine is licensed only for prevention of cervical cancer, there was no question of immunising boys. I believe use of Cervarix® at this time was wise because it allowed messages about cancer prevention to remain 'uncontaminated' by the concepts that HPV is a sexually transmitted infection. I also believe this could have contributed to the high uptake of vaccine in schoolgirls, with sustained coverage over 4 years around 90% of 12 year olds in Scotland, a record of which Scotland can be proud.

It should be noted however that HPV is not a sexually transmitted *disease*. Other factors are important, of which the most relevant is difficulty in clearing virus from the cervix in some women. Persistence of virus provides opportunities for progression to cancer. HPV is common in men as well as women, but is much less likely to persist. Indeed HPV infection is so common that it is considered that around 80% of men and women who are sexually active will experience an HPV infection at some point in their lives.....but they will not know about it because there will be no clinical signs and the virus will be cleared within 1-2 years.

JCVI recommended a change of vaccine to the quadrivalent vaccine, Gardasil® (active against HPV 6,11,16 and 18) and this was introduced from September 2012. HPV 6 and 11 are responsible for around 90% of genital warts, the most common viral STI diagnosed in the UK. The number of genital warts in the UK has continuously risen since records began in 1971, with a 30% increase between 2000-2009 to approx. 80,000 cases in men and 60,000 in women, split almost equally between new cases and recurrences. The highest rates of new cases are in 20-24 year old men and 16-19 year old women (PHE data, 2011). The change of vaccine has provided an opportunity to consider vaccination of men and boys to prevent genital warts. It is essential that we practice evidence based medicine and evidence is beginning to accumulate that some protection against HPV infection is demonstrable in unvaccinated cohorts. Herd immunity was first demonstrated in Australia in Sexual Health Clinics where males of the same age as girls who had been vaccinated with qHPV showed a lower incidence of genital warts while older men and men who had sex with men showed no such decrease^{1,2} In October 2011, the Centres for Disease Control in the US recommended HPV vaccine for boys and girls³. More recently Australia has provided federal funds for a programme which includes boys⁴. The financial burden of treating genital warts in western societies is considerable. ***As the cost of HPV vaccine reduces, then universal immunisation of pre-teens looks increasingly attractive.***

HPV causes other cancers besides cervical cancer and these affect men as well as women. It is estimated that most anal cancers, and up to 50% of penile and vulval cancers are due to persistent HPV, most frequently HPV16, the prime target of both HPV vaccines. Data from the Scottish Cancer Registry show an increase in all of these cancers between 2001-2010.

Oropharyngeal cancers used to be considered a disease of older men who smoked and drank alcohol. However the increase is largely in HPV associated tumours in younger non-smoking men and women and may reflect increasing sexual freedoms associated with oral sex. In a retrospective study of Scottish patients, Junor and colleagues⁵ showed a significant increase in HPV-positive oropharyngeal cancers between 2000 and 2005, rising from 67% to 81% in men and 50% to 85 % in women. Oral base of tongue and tonsillar cancers are also increasing in the UK⁶ and assumed to be HPV associated. Oral and oropharyngeal cancers have a high morbidity with unpleasant and disfiguring treatment regimes. ***The reduction in burden of disease and associated costs of treatment and care for both men and women with any HPV associated cancer through immunisation of both boys and girls at age 12 could offset the cost of vaccine.***

A recent JCVI consultation asked for comments on the acceptability and feasibility of targeted HPV immunisation for MSM. Certainly MSM, particularly those who are HIV positive, carry a disproportionate burden of HPV infection e.g the prevalence of HPV 16 in HIV positive MSM in a small Australian cohort is almost three times higher than in HIV negative men⁷; MSM over 18 showed 56% carried anal HR-HPV, most frequently HPV 16⁸ and there is some evidence that HPV vaccine can reduce rates of AIN in MSM⁹. Kim et al (2010)¹⁰, using decision-analytic models, concluded that HPV vaccination of MSM up to age 26 was likely to be a cost-effective intervention for the prevention of genital warts and anal cancer. However, at what age should targeted population-based immunisation be offered to MSM, especially when the most effective strategy is through a schools programme?

There are therefore increasingly strong arguments for universal immunisation of boys and girls around the age of 12, rather than targeted programmes which require dissemination of complex messages. I believe the Petition is timely but further changes to the national HPV immunisation programme should await the outcome of updated UK modelling.

What are your views on the issues raised in the petition and during the discussion on the petition at the meeting on 11 June 2013?

Many of the issues raised in the petition are cogent. With the vaccine change from Cervarix® to Gardasil®, the argument that the current policy is discriminatory against boys is certainly stronger. With Cervarix® as explained above, the vaccine is marketed as a prevention measure for cervical cancer and appropriate therefore only for girls. However, there is early evidence that herd immunity in the UK is real and this might offer some protection to boys from HPV-associated diseases.

The potential sexual exposure scenarios presented are much more about life-style choices. Population-wide immunisation of boys in case they have a sexual contact with someone who has not been vaccinated, or to counteract potential future sexual

encounters in those who travel to unvaccinated communities are not legitimate arguments for an NHS programme intervention. I disagree that there is evidence for a prophylactic effect from vaccine. For efficacy at the population level, vaccine requires to be given before sexual debut, supporting the hypothesis that targeted immunisation of MSM is unlikely to be clinically effective. There is now a significant case for universal immunisation around aged 12. Availability of vaccine for other ages, whether male or female, is very restricted. Many doctors have had their sons immunised privately in mid/late teens. I think greater availability, in the same way that travel vaccines can be accessed for those who wish to pay, would be helpful.

The vaccine is expensive and there is as yet insufficient evidence to show that immunisation of other groups, whether all boys aged 12 or targeted groups such as MSM, could be cost effective overall. Nevertheless, the human cost of morbid, debilitating and disfiguring treatments which would be avoided by immunisation at a pre-sexual stage should not be forgotten. While it is true that modelling studies have not to date taken into account the steep rises in several HPV-associated cancers in recent years, modelling through JCVI and in other countries is currently being updated.

One aspect which could be explored is whether a 2 dose rather than 3 dose schedule of immunisation is effective. In the 4 years of the national programme in Scotland, over 215,000 girls received 2 doses of vaccine (ISD Scotland), between 2008 -2011. Attempts should be made to follow some of these girls for long term protection, most simply through direct linkage to Scottish Cervical Call and Recall System (SCCRS), but also through direct enrolment in a long-term follow-up study. In a Costa Rican study the same level of protection after 4 years of follow-up against persistent infection with HPV 16/ 18 was found in girls receiving 2 doses¹¹.

Scotland has invested heavily in prevention of HPV-related disease, through national roll-out of LBC sampling and development of national databases for cervical screening and treatment (SCCRS and NCCIAS), sustained delivery of HPV immunisation to >90% of 12 year olds, establishment of a national HPV Reference Laboratory associated with a 12-year programme of HPV surveillance, and robust support for translational and health services research through CSO and Health protection Scotland (Scottish HPV Investigators' Network; www.shine.mvm.ed.ac.uk). This includes a new study of oral HPV carriage (HOPScotch) which will provide baseline prevalence against which vaccine impact can be measured. Evidence is already accumulating for a reduction in HPV prevalence in HPV types 16/18 and also in other closely related HPV types. Latest figures also show a reduction in the incidence of precancerous cervical disease in young women.

Please note that the views expressed within this response are my own.

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