

HPV Vaccinations for Boys



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Abstract

In this mini-review successful human papillomavirus (HPV) vaccination programmes for boys and cost-effective analyses of these programmes are discussed. HPV-related oropharyngeal cancer incidence is rapidly increasing in the Western world. Cost-effective analyses have shown direct health and economic benefits for universal HPV vaccination programmes. Successful universal HPV vaccination programmes are running now in Australia, the U.S., Austria and hopefully soon in the U.K but take off has been slow. The barriers to HPV vaccine introduction are the greatest in low-income countries that have also the greatest burden of HPV-related cancers. The argument that a single girls' vaccination programme provides sufficient herd immunity for boys is false, as herd immunity is no longer a realistic target.

Introduction

HPV-related oropharyngeal cancer is the cancer with the fast-growing incidence in the U.K. and will soon be more common than cervical cancer in the U.S.A. [1]. HPV vaccination programmes have greatly reduced the prevalence of human papillomavirus (HPV) in young women, leading to a future reduction in cervical cancer [2]. An increasing number of countries as e.g. Australia, Bermuda, Brazil, Canada, Germany, Israel, Italy, Lichtenstein, New Zealand, Serbia and the U.S.A. vaccinate boys as well as girls. Recently, they were joined by the U.K. that postponed HPV vaccination from 2013 until now. The Joint Committee on Vaccination and Immunization (JCVI) has advised an universal vaccination strategy, vaccinating boys 12 and 13 years, too [3]. Why do not all countries vaccinate boys in their teens? Flawed cost-benefit analyses and austerity seem to be the main reasons. To justify this it is often stated that the girl's vaccination programme will provide sufficient herd immunity for boys. However, this is only possible if the uptake by girls is > 80%. Vaccination coverage rates are rapidly declining worldwide for various reasons, with a growing anonymous anti-vaxxers movement in the frontline. Therefore, herd immunity is no longer a realistic target, because countries as Ireland (51% uptake) and the Netherlands (45% uptake) show extremely low coverage rates for HPV vaccination in girls [4]. In this mini-review successful HPV vaccination programmes for boys are discussed as well as real cost-effective analyses.

Successful Universal HPV Vaccination Programmes

The Australian HPV vaccination programme has been extremely successful. Free HPV vaccination programmes were started for girls in 2007 and in 2013 the programme was extended to boys. 12 and 13 years old. Girls and boys older than 12-13 years can get catch-up vaccinations between the age of 14-19 years outside the programme. In 2016, 78,6% of 15-year

old girls and 72,9% of 15-year old boys had been vaccinated. Immunization rates have risen further since 2015. As a result the HPV rate among women aged 18-24 dropped from 22,7% to 1,1%. HPV is a sexually transmitted infection that causes 99,9% of cervical cancers. With the present coverage rates herd immunity is reached and Australia can be the first country where cervical cancer will nearly be eradicated in 40 years, projecting present figures to the future [5]. The incidence of genital warts in girls and boys dropped in their early twenties, even before they were included in the vaccination programme.

A new vaccine prevents persistent infection and precancerous cervical lesions and is associated with nine different HPV types instead of the 2-4 most occurring types now and will be included soon.

The current vaccines protect against about 70% of cervical cancers, 70% of vaginal cancers and up to 50% of vulvar cancer cases [6]. HPV is the most commonly sexually transmitted infection in the U.S. [7]. HPV can spread through direct sexual contact to genital areas, as well as the mouth and throat. Oral HPV is transmitted to the mouth by oral sex, or possibly in other ways. Many people are exposed to oral HPV in their life. About 10% of men and 3,6% of women have oral HPV and oral HPV infection is more common with older age. Most people clear HPV within one to two years, but HPV infection persists in some people [7]. HPV can infect the mouth and throat and cause cancers of the oropharynx. HPV is thought to cause 70% of oropharyngeal cancer and the incidence of this cancer is rapidly rising in the U.S. [1]. It usually takes years after being infected with HPV for cancer to develop. It is unclear if having HPV alone is enough to cause oropharyngeal cancer or if smoking and alcohol interact with HPV to cause these cancers. HPV is not known to cause other head and

neck cancers. Symptoms may include a long-lasting sore throat, earaches, hoarseness, swollen lymph nodes, pain when swallowing and unexplained weight loss. Some people have no symptoms. Although the HPV vaccine was developed to prevent cervical and other cancers of the reproductive system, the vaccine protects against the types of HPV that can cause oropharyngeal cancers, so it might also prevent oropharyngeal cancers but studies have not been done to show this [7]. HPV vaccination is also recommended for men who have sex with men (MSM) outside the programme of vaccinating 12-13 years old boys. Two HPV vaccines are now licensed for use in the U.K.; a bivalent vaccine (Cevaxix) which protects against high-risk HPV 16/18 and a quadrivalent vaccine (Gardasil) protecting against the two high risk and two low-risk types associated genital warts. (HPV6/11/16/18). A new nonvalent vaccine has been developed to cover nine different types of HPV. In addition, to HPV 6,11,16 and 18 it also includes protection of HPV 31,33,45,52 and 58 There are some 100 HPV serotypes identified [7]. HPV vaccines have been shown to be effective in men. In a study of 4065 males aged 16-26 years, the quadrivalent HPV vaccine was shown to be effective in preventing genital warts, penile cancer and anal cancer [8,9].

A meta-analysis of 29 studies (8360) men that reported HPV vaccine acceptability in men found a moderate level of acceptability in men, indicating that men would have the HPV vaccine when it was offered [10]. HPV-uptake in the U.S. has been increasing as more children are up to date on HPV vaccination. In 2017, roughly half (49%) of adolescents are up to date on the HPV vaccine and 66% of adolescents ages 13-17 years received the first dose to start the vaccine series. On average the percentage who started the HPV vaccine series increased by 5 percentage points each year over the past 5 years (2013-2017)-[11]. There is some delay in uptake by males mainly because it is believed a girl's affair and is not always offered. Coverage for males is not bad and, on the rise, but still far from the 2020 goal [12]. In addition, to Australia and the U.S., Scotland has reached > 80% of targeted girls with the full schedule [13]. Boys' HPV vaccination in Scotland will be started soon according to the 2018 JCVI advice[3]. During the last 12 years over 80 countries have introduced national HPV vaccination programmes. The majority of these countries are high or upper-middle income countries. The barriers to HPV vaccine introduction remain greatest in those countries with the highest burden of cervical cancer and the most need for vaccination. Innovation and global leadership is required to increase and sustain introductions in low-income and lower-middle -income countries [14].

Cost-Effectiveness Analyses

Cost effective analysis of HPV vaccination programmes is dependent i.e. on the mathematical models used, HPV transmission rate, vaccine type, number of doses ,uptake of the programme, vaccine price and not at least if MSM males are included, as well as the income status of the country. One-dose regimen; Although guidelines for prophylactic HPV vaccination recommend two doses for girls 9-14 years old, several studies

suggest similar protection with one dose. Burger et al. studied cost-effectiveness of routine one-dose HPV vaccination (bivalent) of 9 year-old girls in Uganda using a three-tiered hybrid modelling approach that captured HPV transmission, cervical carcinogenesis and population demographics, assuming 80% efficacy against HPV 16/18. [15]. Routine one-dose HPV vaccination of 9-year old girls required substantial upfront investment but was cost-saving compared to no vaccination when accounting for the cost-offsets from future cancers averted. Forty years after initiating routine vaccination and depending on vaccine waning, one dose HPV vaccination with equivalent coverage (70%) averted 15-16% of cervical cancers versus 21% with two dose vaccination, but required only half the upfront economic investment. Vaccination with two doses had an attractive cost-effectiveness profile except if one dose vaccination enabled higher coverage (90% vs 75%) and did not wane. The authors conclude that one dose HPV vaccination is cost-saving compared to no vaccination and could be cost-effective compared to two dose vaccination if protection is longstanding and higher coverage can be achieved [15].

Cost-effectiveness HPV vaccination for boys

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 [16]. The analysis demonstrated that with a 60% uptake in females, the burden of vaccine-preventable cancers in men was reduced by 66%. However, anal cancer decreased by only 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 [16]. These findings validate the importance of including MSM in cost-effective 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 an universal vaccination strategy. Unfortunately, the HPV uptake by girls is at a historical low (45%) in the Netherlands [4]. and there is still no HPV vaccination programme for boys pending an advice of the Gezondheidsraad (National Health Council). Austerity, politics and a forceful anonymous anti-vaxxers movement complicate the decision making process further [17]. The Dutch study is complemented by another recent cost-effective 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 oropharyngeal cancer (OPC)-[18]. At the moment successful HPV vaccination programmes for boys are running in Australia ,the U.S., Austria and hopefully soon in the U.K [3].

Conclusion

HPV vaccination programmes for boys primarily aimed at reducing HPV-related cancers in men in the upcoming forty years have been slow to take off. Flawed cost-benefit analyses, austerity, and a growing anonymous anti-vaxxers movement are main reasons. To justify these lazy politics, it is often stated

that the girl's HPV vaccination programme will provide sufficient protection for boys. Because herd immunity is no longer a realistic target when vaccination coverage is rapidly declining worldwide these arguments must be considered false [4]. HPV-related oropharyngeal cancer (OPC) is the cancer with the fast-growing incidence in the U.K and will soon be more common than cervical cancer in the U.S. [1]. Cost-effective analyses have shown direct health and economic benefits for boys 'vaccination programmes along with girls 'vaccination programmes, so called universal vaccination [16,17]. Successful universal HPV vaccination programmes are now running in Australia, the U.S., Austria and hopefully soon in the U.K. [3]. The barriers to HPV vaccine introduction are the greatest in those countries with the highest burden of HPV-related cancers [14]. Strong leadership and innovation is required to overcome these barriers.

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