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IFMSA Policy Document HPV Vaccines

Proposed by LeMSIC-Lebanon and SfGH-United Kingdom

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Policy Statement

Introduction:

Human papillomavirus (HPV) is a sexually transmitted infection that leads to a range of conditions, including the development of secondary non-communicable diseases such as cervical, throat and anal cancers. It is responsible for 4.5% of the worldwide cancer burden, and 7.5% of all female cancer deaths. HPV vaccination, along with early detection and treatment of HPV-associated disease, could prevent almost all cervical cancer cases, and eventually lead to the elimination of HPV. Many countries have introduced vaccination programmes with varying access and coverage, but are often faced with cultural, social, financial and political barriers.

IFMSA position:

As the leading cause of cervical cancer, and a significant cause of many others, attention given to the supply and administration of HPV vaccines is insufficient. IFMSA believes that young people of all genders must be vaccinated, which will reduce population HPV prevalence and therefore the incidence of HPV related diseases. Increased access to vaccination through fair pricing is essential to allow all WHO member states to reduce preventable deaths and morbidity.

Call to Action:

Therefore, IFMSA calls on:

WHO Member States to:

1. Ensure that their entire population has access to HPV vaccination at a young age
2. Add HPV to the regular vaccination schedule for children
3. Promote HPV vaccination in conjunction with cervical screening programmes and recognise the importance of these combined public health initiatives in reducing the burden of HPV-associated diseases
4. Employ routine cervical cancer screening for the general population via Pap smears and utilising HPV DNA co-testing to increase cost-effectiveness and improve patient outcomes
5. Utilise health promotion campaigns to alert the public to risk factors and reduce vaccination hesitancy, encouraging increased uptake of the vaccine

International Organisations and NGOs to:

1. Utilise health promotion campaigns to alert the public to risk factors and reduce vaccination hesitancy, encouraging increased uptake of the vaccine
2. Create campaigns that focus on the deconstruction of the stigma surrounding HPV vaccinations and gender-neutral vaccinations



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3. Conduct post-marketing surveillance of vaccine efficacy and adverse events, using independent monitoring, addressing potential conflicts of interest and ensuring this information is made readily available

IFMSA National Member Organisations and medical students to:

1. Promote education on appropriate HPV vaccination practices to medical students and other healthcare professionals, as well as the general public
2. Work to deconstruct the stigma surrounding HPV vaccination
3. Collaborate with relevant stakeholders to work towards adequate access to vaccinations, particularly in resource-limited settings
4. Support and encourage participation in cancer screening programmes alongside vaccine implementation
5. Advocate for independent monitoring of vaccination efficacy and reporting of adverse effects



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POSITION PAPER

Background information:

The Human Papilloma Virus (HPV) is a sexually transmitted pathogen associated with the development of several diseases. The acquisition and persistence of a viral infection with HPV types 16 or 18 causes ~70% of cases of cervical cancer worldwide. HPV types 31, 33, 45, 52 and 58 are responsible for a further 20% of cases. Effective and safe vaccinations are currently in use that protect against acquisition of HPV and hence its sequelae.

Discussion:

Global Burden of HPV-associated disease

The Human Papilloma Virus (HPV) is a sexually transmitted pathogen associated with the development of several diseases. HPV infection has been well established as a causative agent in six types of cancer: cervical, vulvar, vaginal, anal, oropharyngeal and penile cancer. Nearly all types of cervical cancer are attributed to HPV infection (1), while the estimated proportion of HPV-associated cancers is 90% of anal cancer, 70% of vaginal cancer, 23-49% of vulvar cancer (2, 3), 35-40% of penile (4) and 70-80% of oropharyngeal (5, 6). The viral infection has also been implicated in the development of the benign conditions recurrent respiratory papillomatosis and genital warts. Of all the HPV-related diseases, cervical cancer carries the highest global burden of disease (7).

The global prevalence of HPV infection is estimated at 11.7%, as determined by a comprehensive meta-analysis of studies conducted from 1995 to 2009. The regions with the highest prevalence were found to be – Sub-Saharan Africa (24.0%), Eastern Europe (21.4%), and Latin America (16.1%) (8). The high rates of HPV infection in the pre-vaccination era give an indication of disease burden and are matched by the high incidence of HPV-driven cancers. From the 12.7 million known diagnoses of cancer globally in 2008, 700 000 occurred at HPV-associated sites and 610 000 of these were attributed to infection with HPV (9).

Oropharyngeal cancer can be HPV driven or non-HPV-associated. Generally, HPV-associated cancers occur in younger populations, while non-HPV-associated cancers are attributed to smoking. Recently there has been a rise in the incidence HPV-associated oropharyngeal cancers and a decrease in the incidence of cancers in the latter group (10).

Current vaccine recommendations

There are three different vaccines currently available, which offer protection against different strains of HPV. All the available vaccinations cover the high-risk types 16 and 18. It is recommended that these vaccines are given to children around the age of 11-13, as they are mostly effective if given prior to first exposure to HPV. The available vaccines include:

- a. Quadrivalent HPV vaccine (Gardasil) targets HPV types 6, 11, 16 and 18
- b. 9-valent vaccine (Gardasil 9) also targets the HPV types 6, 11, 16 and 18 as well as types 31, 33, 45, 52 and 58
- c. Cervarix - Bivalent vaccine (Cervarix) targets HPV types 16 and 18

While vaccination was initially offered to females to protect against cervical cancer, recently there has been a shift towards providing full population coverage. It is already routine practice



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in Australia, the UK, the United States (11), and several other countries to vaccinate both males and females. HPV vaccination has a direct benefit to males through protecting against development of HPV-driven cancers and other conditions associated with HPV infection. Furthermore, it has been demonstrated in high risk groups such as Men who have sex with men (MSM) that HPV vaccination is likely to be a cost effective initiative (12). However, the largest population benefit of vaccinating males is the herd immunity conferred to females and the resultant reduction in incidence of cervical cancer. It has been demonstrated that vaccinating men and women is more effective in reducing cervical cancer than vaccinating women alone (13).

The reported adverse effects associated with the vaccine are limited, particularly in the context of their significant public health benefit (14). Studies have identified that the most commonly reported adverse effects include fatigue, pain and swelling at the injection site, headaches and gastrointestinal symptoms (15). Other severe adverse effects including autoimmune responses have been associated with HPV vaccination, however further investigation has failed to establish a clear causative link (14).

Gender Neutral Vaccinations

Since its introduction to the routine vaccination in 2006, the HPV vaccine was only recommended for females in the US (16). It was only until 2011, that male HPV vaccination was first considered recommended as part of the routine vaccination (17). Feminization of HPV vaccination has played a big role in increasing the disparity between the sexes in prevention of HPV-related cancers (18) and has led to having no countries in Africa for example who offer this vaccine to men (19) despite the fact that the number of HPV attributed cases of Oropharyngeal Cancer are now higher for male than females in all African countries that have introduced HPV vaccination for females only (19). This result goes back to the fact that herd immunity which was hypothesized to protect males by adequate rates of female vaccination (20), is not efficient enough solely to eradicate the virus (18). Low vaccines rate among females was an important factor behind the the lower efficiency. There are other major factors to this that include disregarding key populations like MSM who are completely unprotected by girls-only vaccination programs. Offering the HPV vaccine to MSM only will not be practical since the effective administration age that starts on 11-12 years is earlier than the sexual 'debut'. Additionally, offering it to questioning boys is unreliable and unethical on different levels. And that is whether by asking boys to disclose their sexuality at a young age, or by taking the action of vaccination solely based on their disclosure. It's important to take into consideration the incidence of anal cancer in this group that is estimated to be similar to that of cervical cancer in an unscreened population of women (21). On the other hand, both social and gender inequality issues are raised when HPV vaccination is not gender neutral. This can be apparent first when more informed and financially capable families tend to privately vaccinate their male children, thus exacerbating existing inequalities in cancer incidence between richer and poorer social groups (21, 22). The concept of vaccinating girls only adds support to the patriarchal systems by upholding the sexist belief that women and girls should be the ones responsible of health and prevention. And even on a deeper meaning makes girls believe that they are the ones spreading HPV and this is why they should be the ones getting vaccinated. Whereas, health prevention is the responsibility of all individuals regardless of their gender (21) especially that HPV infection is actually non-specific for a gender and that males experience a longer duration of genital warts, thus, necessitate greater treatment costs than women (23). As for evidence of cost-effectiveness based on research conducted in many countries like Austria, the US, Canada, Kenya, Uganda, Italy, Mexico, UK, Brazil, Denmark, Vietnam, Taiwan, Norway, Hungary, China, Ireland, Netherlands, and Japan, the inclusion of adolescent boys in vaccination program was found to be efficient if vaccine price and coverage was low and in countries where less than 75% of girls were vaccinated (24).

Vaccines as a part of a wider preventative strategy



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Both as a preventive method from HPV infection and a preventive method from HPV-related cancer or genital warts, HPV vaccination should be part of bigger preventive measures. Although condoms are not as protective from HPV transmission as they are from other STIs, their recommended usage, in addition to vaccination and other safe sexual behavior like lowering the number of sexual partners can decrease the risk of transmission (25, 26). Since HPV vaccination might decrease the positive predictive value of cervical Pap smears other screening tools like HPV DNA testing are also recommended (27). Additionally, despite the fact that routine screening for the general population regarding other types of HPV-related cancers like anal cancer and oropharyngeal cancer is not recommended due to the low prevalence and lack of research information, (28) routine screening of selected populations at high risk using tools like anorectal exams, anal Pap smears, and anoscopy might be important (29). On another hand, primary prevention that includes awareness related to HPV, STIs and sexual health in general, has positive outcome by increasing vaccination rates and safe sexual behavior (30).

Stigma surrounding HPV

While myths used to claim that HPV vaccination was more likely to increase inconsistent condoms use among adolescents, many research abstracts have proven how HPV vaccine was unlikely to increase risky sexual behaviors in general including STI testing, condoms use and the number of partners (31, 32). Despite this, stigma and taboo surrounding HPV play a big role in the parent's acceptance of HPV vaccination both whether they were well informed or not about HPV (33, 34). This is why educational approach regarding HPV vaccination should also be extremely cautious since it might create more fear, anxiety, and thus more stigma surrounding HPV and vaccination (35).

Therapeutic vaccines

Increasing population immunity to high-risk strains of HPV through use of prophylactic vaccines is the best strategy for reducing the incidence of HPV-associated cancers. However, these vaccines are ineffective at clearing already established HPV infections. There is therefore a need for continued development of HPV therapeutic vaccines, which are designed to trigger cell-mediated immune responses to clear established HPV infection. These vaccines would be particularly beneficial to individuals with HPV-related cancer (36).

HPV-related proteins E6 and E7 have been shown to be essential for the both the establishment and maintenance of malignancy, making them ideal targets that could be used to induce tumour regression. Therapeutic vaccines that target these proteins are currently in Phase 2 Clinical Trials and will likely be commercially available within the next few years. However, there is significant concern that when these vaccines do become available, the high costs will make them inaccessible to patients in developing countries, where the highest incidences of HPV-associated cancers occur (36).

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