

Human Papillomavirus: Cancer and Prevention, why doesn't everyone receive HPV vaccination?

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## Abstract

Human papillomavirus is a highly transmissible through skin to skin contact and has many strains, with strains HPV-16/18 being high-risk HPV, that is highly correlated with cervical, oropharyngeal, anal, and penile cancers. But these strains are highly preventable by using two of the available vaccines, Gardasil (2vHPV) and Gardasil 9 (9vHPV). Vaccination is between the ages of 9 to 26 years of age is recommended. But even with the advent of the vaccine, the vaccination rate in many countries remains low. Women and men who have sex with men are at higher risk for HPV-associated cancers. So why does not every eligible person receive the vaccination? Factors for apprehension include fear of early sexual behaviors, parental choice, and insufficient knowledge. But the greater good principle shows that since vaccination is for the greater good, it thus outweighs other moral objections to vaccination. It is recommended that all eligible for vaccination should receive it, regardless of sex, to add for a herd immunity and help lower HPV-associated cancer incidence.

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Human papillomavirus (HPV) is a highly contagious pathogen, DNA virus, of the epithelium that is readily transmitted via skin to skin contact. DNA viruses use the host cell's DNA to replicate and produce proteins that assist in infection and propagation. HPV has several different strains, variations of protein structure, which include those that assist in causing benign to malignant growths. Some strains are considered to be more aligned with sexually transmitted infections (STI) which include strains HPV-6,11,16,18,31,33,45,52,58. Of these strain, HPV-16 and HPV-18 are correlated to the development of neoplasm and cancers in the epithelium of the oropharynx, cervix, and anal tissues (Petrosky et al, 2015; Burd, 2003; Viens et al, 2016; Merck & Co., 2016). However, HPV alone is not the sole cause of these neoplasms or cancers but is one of the key factors in the proliferation of cancer cells (Kumar et al., 2013, p. 202). Unlike HPV-6 and HPV-11, the other strains, HPV-16,18,31,33,45,52, and 58, are relatively asymptomatic. The high-risk strains are transmitted more readily due to the infected not knowing they are carriers. HPV equally affects both men and women with a reported with the CDC (2017) reporting during 2013-2014 45.2% males and 39.9% of women had any HPV. The CDC (2017) further showed that the high-risk HPV affected 25.1% of males and 20.4% of females.

The high-risk HPV strains are RNA viruses that produce two genes, E6 and E7, that interfere with proto-oncogenes and tumor suppressor genes that are the pivotal reason of causing neoplasm and cancers (Kumar et al., 2013, p. 202; Markowitz et al., 2007). The high-risk HPV strains are known to be one of the aggregate causes of cervical, oropharyngeal, and anal cancers. It is through the E7 protein that stimulates the cells retinoblastoma protein (Rb) to initiate secretion of E2F transcription factors that are normally inhibited by Rb while also inhibiting cells that would attack viral components (Kumar et al., 2013, p. 202). This is one of the major

mechanisms of HPV carcinogenesis. The incidence of HPV-associated cancers in the USA was 123,172 for the years of 2008-2012 (Viens et al., 2016, p. 665). However, depending on the country of origin the incidence can be greater than this number. One such example is how Nicaragua has a higher incidence of HPV cancers compared to the US (Arbyn et al., 201, p. 2680). However, the numbers may have been greater in pre-vaccination era. Vaccination was introduced in the year 2007 with the first vaccine Cervarix. Subsequently, two newer HPV vaccines have been introduced which include Gardasil and Gardasil 9. With the introduction of vaccination, it is posited that the incidence and prevalence will continue to decline.

### Vaccination

Vaccination began with the work on Cervarix to help prevent HPV transmission and lower risk of cervical cancer. Cervarix, bivalent (2vHPV), is a now discontinued formulation that covered strains HPV-16 and HPV-18. The two vaccinations now available are Gardasil, quadrivalent (4vHPV), and Gardasil 9, 9-valent (9vHPV), with 4vHPV covering strains HPV-6, 11, 16, 18 and 9vHPV additionally covering HPV-31,33,45,52,58. 4vHPV dosing schedule can either be a 2 dose with initial and following dose 6 months from the initial or a 0, 2, and 6-month schedule (Harper et al., 2014). 9vHPV is dosed at 0 months, 2<sup>nd</sup> month, and 6<sup>th</sup> months to get coverage (Petrosky et al., 2015; Merck & Co., 2016). The vaccinations are recommended for adolescents aged 11 to 13 years of age with the youngest age for administration at 9 years old and maximal age of 26 of both sexes (Petrosky et al., 2015; Merck & Co., 2016; Markowitz et al., 2007). The vaccine is optimal in the those that have never had intercourse or any contact to others genitals. The 4vHPV and 9vHPV have the side effects of pain, swelling, and redness at the injection site with the possibility of a headache in females (Merck & Co., 2016). It has also been shown to be safe if coadministered with other vaccinations (Noronha, Markowitz, and Dunne,

2013). This attests to the relative safety of both 4vHPV and 9vHPV for the prevention of HPV and its associated cancers.

Vaccination has a high seropositive rate, where the body produces antibodies. Jach et al., (2016) had shown a decrease in HPV infection after initiation of vaccination in Australia from the years 2010-11 compared to years 2005-7 with 6.7% rate in 2010-11 and 28.7% for 2005-7. Hariri et al., (2015) also showed a decrease in cervical intraepithelial neoplasms from 53.6% in 2008 down to a 28.4% in 2012 in women who received one dose of one of the available vaccinations. This data was presented with low vaccination rates amongst the population being studied. Khatibi et al., (2014) showed a lifetime vaccine efficacy of 3 doses at 100%. Gichane et al., (2017) state that 9vHPV would have an estimated 90% chance of preventing cervical cancers. Amongst most of the clinical and scientific literature, it is seen that the coverage rates against HPV via vaccination approach 98%. The consensus amongst the literature is that the 4vHPV and 9vHPV worked to prevent greater than 90% of the population administered to with a seropositive coverage of greater than or equal to 98% (Jach et al., 2016; Chesson et al., 2013; Hariri et al., 2015; Rahman et al., 2016). There is no literature to refute this claim of protection against HPV and HPV-associated cancers. Vaccination is the only way for prevention of HPV and its associated cancers. As well, vaccination incurs a lower cost than the treatment of HPV-associated cancers. Due to its efficacy and cost, it would be recommended for those who are in the vaccination dosing window. But currently, the vaccination rates are low.

Current vaccination trends of either 4vHPV or 9vHPV are on a slight rise. Why are the numbers still low for a vaccine that could potentially protect and save lives from HPV-associated cancers? If cost is the issue, one should take into account that Gardasil 9 is a series of three shots costing around \$116.22 each, while treatment for cancer is around \$39,000 (Pendrith et al.,

2016). So, it is cost effective to get vaccinated in lieu of the future cost that one will incur. Seeing that it affects both sexes and that giving vaccination to boys will also give additive protection through herd immunity. Herd immunity is where many are vaccinated to help protect those who may not be due to those vaccinated will not be carriers of the disease. As well, men who have sex with men (MSM) are at higher risk of HPV-associated anal cancer than women and heterosexual male (Advisory Committee on Immunization Practices, 2011; Rahman et al., 2016 p. 12). All the research shows are that the 4vHPV or 9vHPV are very effective, 90% coverage, in the prevention of HPV and offer greater cost-effectiveness than any other option. The vaccine seems to have benefits that outweigh any risk associated and thus should be given to all those in the eligible population.

#### **Those most affected by HPV-associated cancers**

Women and Men who have sex with Men (MSM) are those that are most affected by HPV-associated cancers. Men are just as likely to be infected with high-risk HPV, especially MSM. However, the rate of vaccination is lowest amongst this group with less than 2% vaccination rate (Advisory Committee on Immunization Practices, 2011). Many males are unaware or do not believe that they are at a risk for HPV. This translates even into the MSM community, especially as it is seen more as a female problem due to the majority of coverage being on its correlation with cervical cancers. But even among physicians where 72% found it necessary only recommended it to 33% of their eligible male patients (Allison et al., 2013). Due to physicians not recommending, many males continue to have inadequate knowledge on their HPV risk.

It was shown that many African-American college-aged males who are at high risk had false beliefs or inadequate knowledge on HPV and the HPV vaccination. Fontenot et al., (2014)

that in 2009 the FDA approved the vaccinations for male use most of those in their study thought the vaccine was only for women and not for men. Males were less likely to have heard of HPV or the HPV vaccine than their female counterparts, a 23.9% difference (Bynum et al., 2011, p. 299). This shows how an in-bias of how males were unaffected by HPV leads to a higher risk and greater chance of spreading. But, as the high-risk HPV are asymptomatic most infected individuals do not know of their infection. As most males perceived that the vaccine was for their female counterparts they felt that they didn't need to worry about it and continued their sexual habits as before. Bynum et al., (2011) also showed that 33% of participants reported not using condoms at times during sex. This further leads to more risk of transmission of HPV to other sexual partners, either male or female.

There is an in-group bias of males not having a risk for HPV or their associated cancers. This hurts a part of this in-group, MSM, as they hold some of the same beliefs as their counterparts. Even though MSM are in-group with other males, they are also an out-group by other members of the male in-group. The in-group bias is however perpetuated throughout their community. This plays on Hofstede's masculinity versus femininity, due to males being shown superior in the current culture. Being male on its own makes one more resistant to disease and thus tougher. MSM is also in a high-risk category for HIV which furthers the risk of HPV as they are often concomitant infections. It is recommended that MSM and MSM with HIV under 26 years of age receive HPV vaccination (Petrosky et al., 2015). Yet, females are another out group that is heavily affected by the male in-group bias of low risk and insufficient knowledge of HPV.

Females are another high-risk group that affected by HPV. Females have a tendency to have more knowledge of the risk of HPV, HPV cancers, and vaccination than males. This is where the in-group bias is more advantageous due to it raising awareness. Yet, at the same time,

it is detrimental to the cause due to males not being included which, if included, would lower risk of HPV. But have women treated differently for their high-risk of HPV-associated cancers? The simple answer is yes, they are. They are viewed by out-group members and in-group members as being the indulgent side of Hofstede's theory. It is seen that those who are infected with HPV are promiscuous due to HPV being classified as a sexually transmitted infection (STI). Christian, Christian, and Hopenhayn (2009) that many correlate vaccination to encourage sexual behaviors in adolescent girls. This lowers the rate of vaccination due to an apprehension of females becoming or being considered promiscuity, which in a masculine society is seen as a negative. The outgroup's perceptions of it being negative, and some in-group, continues the practice denying protection against a life-threatening and costly disease. Women are suffering from this inequality of sexual expression and the vaccine should not be correlated to sexual behaviors.

MSM and women should be exposed to more education on HPV and its associated cancers. MSM and all males should be educated how important vaccination is to help out both the female and MSM communities. The inequalities faced by females due to stigmatizing HPV vaccination as being for the promiscuous. As well, a push for the male vaccination will offer herd immunity to help out these communities that are most affected by HPV-associated cancers.

### **Apprehensions of vaccinating.**

Many parents are uneasy about allowing their child to receive an HPV vaccination. The main cause of worry for parents is that the vaccination will lead to encouragement of early sexual behaviors (Gichane et al., 2016). Even though the CDC has shown that risk for STI, such as HIV, do not deter sexual behaviors in adolescents or young adults (Aguanno, 2008, p. 645). But many



parents feel that mandating a vaccination associated with sexual activity goes against their rights of free choice (Aguanno, 2008). Is it right for parents to make this decision that will affect their children as adults? The parent should look out for what is in the best interest in their child's health, which would include 4vHPV or 9vHPV. But what about the greater good principle, which vaccination would be for the greater good. Since vaccination does not correlate to increase sexual behaviors and is for the greater good it is a social responsibility to vaccinate. But in most cases, it is mandatory that a girl is educated on the HPV vaccine but not their male counterparts. But as it stands, just educating is not sufficient for our greater good through a herd immunity.

Merck & Co. have also had issues with the quick release and push for their Gardasil vaccines. This comes after their Vioxx drug causing severe complications and death in arthritis sufferers. This raised many concerns of patients as to the safety of the vaccination. This was further perpetuated by Texas state Governor Rick Perry instituting a state executive mandating Gardasil for those entering the 6<sup>th</sup> grade (Aguanno, 2008). Gov. Perry along with Women in Government receiving money from Merck & Co. seen as kick-backs or bribes (Aguanno, 2008). This showed a vested interest from these parties to unethically push for vaccination. This correlation harmed the reception for some of Gardasil. As those in government have a social contract with the people they serve to protect them. The mandatory vaccination requirement was overwritten by the state's Congress with this and parental concerns taken into consideration, even if it were to create more risk of HPV cancers.

The issues faced with apprehension are that of choice and what is for the greater good. The parent's responsibility to protect their children's health versus a misconception of engagement in sexual activity as their reasoning for choice. Then the social responsibility of those in governance to make adequate and appropriate choices in health policy without bribery

from corporations. The question is who is more correct, parent's decision or the greater good of a society? Did money given by Merck & Co. lead to rash and unsafe decisions by those in government?

***Vaccination for all.***

Women and MSM are at times villainized and shown to be sexually uninhibited. Since HPV is categorized as an STI, it tends to stigmatize these groups further. It is necessary that these groups are included in any education on HPV vaccination and work within their groups to promote better sexual health. Men should also receive the vaccine to protect these two groups as they tend to be the ones spreading the disease. Anecdotally, there was a woman who had only one sexual partner, her husband, who gave her HPV which led to her cervical cancer. It is important that everyone works to get everyone eligible for vaccination to be vaccinated. As well, it is warranted for a shift in the paradigm of a masculine culture to a more neutral one and away from indulgence judgments. Indulgence and masculinity only show to propagate more risk with lessening those exposed to vaccination.

Vaccination programs are necessary for the protection of our society from HPV-associated cancers. As they are 90% effective against HPV, they are for the greater good due to herd immunity and protection against HPV (Jach et al., 2016; Chesson et al., 2013; Hariri et al., 2015; Rahman et al., 2016). This proves how vaccination is for the greater good. The greater good is a better reasoning than that of personal choice. Another argument is that the child in question should be allowed the vaccination for as an adult their possible choice would have been to receive the vaccination. The main reason parents choose not to vaccinate is the correlation to sexual behavior even though evidence from the CDC shows to the contrary (Aguanno, 2008). In Christian et al., (2009) showed that 66 to 75% would consider giving their daughters the vaccine.

Vaccination should be mandatory for both male and female adolescents to alleviate the HPV-associated cancers, even if parents are against it.

It should also be looked into possible problems with government regulation on the amount that corporations can give to those who hold office. The incident with Gov. Perry has led to questioning of health policy, which was good in hindsight (Aguanno, 2008). The vaccine through all the literature and previous research show its effectiveness and appropriateness. There have been no major reported incidents related to Gardasil or Gardasil 9. Holding those in office to a higher standard of ethics is required and have ethics boards review the actions taken by our officials.

*Conclusion.*

Vaccination for the prevention of HPV works. HPV can lead to serious complications that can cost an individual money, time, and health. It has been shown to be more cost-effective than treating cancer. Those who have been neglected are MSM and women by not educating men of their necessity to get vaccinated along with females. It is the most ethical recourse to get your child vaccinated. It is thus most important for the protection of our society to make vaccination of HPV mandatory for male and female adolescents aged 11-13 years of age.

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