



HPV Questions and Answers
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## **1.0 HUMAN PAPILLOMAVIRUS (HPV)**

### **1.1 What is HPV?**

HPV is a very common, highly transmissible virus primarily acquired through sexual contact. In Canada, it is one of the most common sexually transmitted infections (STIs). Estimates are that 75% of sexually active women will have at least one HPV infection in their lifetime. Within 2 to 5 years of initiating sexual activity, 70% of females will acquire one type of the 15 oncogenic HPV types.

At least 40 HPV types are able to infect the genital tract. Of these, 15, including HPV types 16 and 18 are called high-risk (HR-HPV) types, as they are known to cause cervical cancer. HPV 16 and 18 contribute to 70% of cervical cancer. While high-risk HPV types must be present to cause cervical cancer, infection with HR-HPV types alone does not necessarily lead to cervical cancer. That is, an individual cannot develop cervical cancer without contracting HPV, but an infection with HPV does not necessarily mean an individual will develop cervical cancer. Other co-factors, such as age of sexual debut, smoking, other STIs, long term oral contraceptive use, and cervical trauma may contribute to cervical cancer.

In addition to the HR types, there are other HPV types that are low risk for causing cancer, but cause the majority of genital warts. It is estimated that low risk (LR) HPV types 6 and 11 cause 90% of genital warts. It has also been reported that 20% to 50% of genital wart lesions contain HR HPV co-infections.

Most people spontaneously clear HPV infection within two years of becoming infected.

About 10% of women do not clear their HPV infection and are at risk for developing persistent HPV infections and potentially pre-cancerous cervical lesions which may then progress to cervical cancer if not treated.

### **1.2 How do people get HPV?**

Although most genital HPV infections are caused by sexual intercourse, anyone (males and females) who has any kind of sexual activity involving genital contact with an infected person can get HPV – intercourse isn't necessary.

Many people who have HPV may not show any signs or symptoms, so they can pass the virus on without even knowing it.

HPV infections are transmitted sexually by direct epithelial (skin or mucosa) to epithelial contact and vertically to an infant exposed to the virus in the maternal genital tract. As well, transmission from oral mucosal contact in head and neck infections is likely.

A recent US study showed that infection with HPV happens very commonly with the first sexual partner. About 30% of women between the ages of 19 – 26 years became infected with HPV within one year after the first time they had sexual intercourse. Almost 50% of these women were infected within 3 years of starting sexual activity.

### **1.3 What diseases are associated with HPV?**

Persistent infection with high-risk types of HPV is associated with almost all cervical cancers.

In addition to cervical cancer, HR-HPV types are also associated with vaginal, vulvar, penile, anal, and oro-pharyngeal cancers.

Genital HPV infection with low-risk types of HPV is associated with genital warts in men and women. Genital warts are typically warty projections that can occur anywhere in the genital skin surface but primarily on the vulva, penis and perianal skin. They are usually self-limited lesions in immunocompetent individuals, resolving typically in 12 to 24 months.

Rarely, perinatal transmission of low-risk HPV infections can result in upper respiratory tract warts or papillomas in infants and children, a condition known as recurrent respiratory papillomatosis (RRP). It is a rare condition, given the relatively ubiquitous nature of HPV in the female genital tract. Almost all cases of RRP are linked to HPV 6 and 11.

### **1.4 What is the immunology of HPV?**

HPV has adapted over the years to avoid detection by the body's immune system. The virus often does not induce an inflammatory response, and there is little tissue destruction associated with HPV infection. There is often no blood borne phase of the infection. In clinical assessments, many women who develop cervical HPV infections do not develop measurable antibody responses within 18 months of infection.

Once an individual demonstrates a protective antibody response to one HPV type, they likely will not be re-infected with that same type in the future.

### **1.5 What is the epidemiology of HPV?**

HPV is not a nationally notifiable disease in Canada and, to date, no population-based studies have been published. Estimates of HPV infection and associated disease burden are based on Canadian prevalence and incidence studies in select populations. These populations have included patients in routine cervical screening clinics, family planning clinics, STI/HIV clinics, and university health clinics.

Within Canada, HPV prevalence appears to vary with age, place of residence and ethnicity. These differences in reported prevalence of HPV may be partly attributed to laboratory detection methods and the refinements occurring in the technology for both polymerase chain reaction (PCR) amplification and detection of the PCR products.

All published Canadian studies have been conducted in women. The overall prevalence of HPV (any type) ranges from 10.8% to 29% and varies greatly within different age groups, ranging from 3.4% to 42%. The peak prevalence tends to occur in adolescents and young adults  $\leq 25$  years of age with a subsequent decrease with age.

Risk factors that contribute to this pattern of prevalence include:

- In younger females, trauma to the cervix occurs more frequently during intercourse
- Younger females are more likely to chose older sexual partners who have a greater likelihood of already being infected with HPV
- The transformational zone of the cervix of younger females is more anatomically vulnerable to infection
- Older women tend to have fewer sexual partners are they are more likely to be in monogamous relationships.

### 1.6 What are the risk factors for HPV?

Among females, the following factors are associated with both prevalent and incident HPV infections:

- an increasing number of sexual partners, both lifetime and within the previous year
- both current and past use of tobacco
- marijuana use
- previous infection with an STI, specifically chlamydia and herpes simplex virus
- history of sexual abuse
- early age of first sexual intercourse
- immune suppression; HIV.

As well, the following are indicators for other risk factors (such as serial monogamy):

- having never married
- not living with a sexual partner
- having never been pregnant or having been pregnant but never having delivered a child

The risk factors for HPV infection in males have not been studied to the extent of those in females. An increasing number of previous sexual partners in the male has been identified as a risk, both lifetime as well as recent. Being uncircumcised was also found to be a risk in some studies.

## 2.0 THE VACCINE

### 2.1 What Human Papillomavirus (HPV) vaccines are available in Canada?

Currently, the only licensed HPV vaccine in Canada is GARDASIL™, manufactured by Merck Frosst. GARDASIL™ protects against infection caused by HPV types 6, 11, 16 and 18, and against diseases associated with these HPV types. These diseases include cervical cancer, vulvar and vaginal cancer, genital warts, cervical intraepithelial neoplasias (CIN 2/3), vulvar intraepithelial neoplasia (VIN 2/3), vaginal intraepithelial neoplasia (VaIN 2/3), and cervical adenocarcinoma *in situ*.

Gardasil™ consists of the L1 capsid protein of each of the four HPV strains. A gene encoding the L1 protein of each type is expressed in the yeast *Saccharomyces cerevisiae*. The protein product self-assembles into a non-infectious virus-like particle (VLP) that is identical in shape and size to the natural virus. The VLPs of each type are purified and adsorbed onto an aluminum-containing adjuvant (amorphous aluminum hydroxyphosphate sulfate 225 µg). The formulation also includes sodium chloride, L-histidine, polysorbate 80, and sodium borate. The product does not contain preservative or antibiotics, and the packaging is latex-free.

Cervarix, manufactured by GSK, is not yet licensed in Canada. It will protect against HPV types 16 and 18.

### 2.2 What evidence is there for GARDASIL™ immunogenicity and efficacy?

The Gardasil™ Phase II and Phase III clinical trials demonstrated vaccine immunogenicity and efficacy for women aged 16 to 26 years. Type specific competitive radioimmunoassay was used to determine immunogenicity to each vaccine subtype. The overall seroconversion rates to subtypes contained in the vaccine was over 98% within one month after the third dose. Antibody response peaked at Month 7, declined through Month 18, and then appeared to stabilize through to 60 months. The antibody response generated in vaccine recipients was between 10 to 100 times greater than the antibody response found in naturally acquired infection. The antibody response was well above that found in women who had naturally acquired type 11 and 16 infections, but close to those who had naturally acquired type 6 and 18 infections.

In addition, the antibody responses induced by vaccines were higher in males and females aged 10-15 years than those observed in 16 to 23 year olds.

#### **Efficacy**

Gardasil™ was 100% effective in preventing CIN 2/3 due to HPV types 6, 11, 16, and 18. In addition, the vaccine was 100% protective against HPV 6, 11, 16, and 18 - related VIN2/3 and VaIN 2/3.

### 2.3 What evidence is there for the efficacy of GARDASIL™ in girls as young as 9 years of age?

The recommendation for vaccine use in girls as young as 9 years of age is based on “bridging” immunogenicity and safety studies. Bridging studies attempt to determine whether the vaccine immunogenicity is the same in a particular group of individuals as in the group for which both immunogenicity and efficacy data are available. For the latter group, prior evidence of HPV vaccine immunogenicity and efficacy was determined from four Gardasil™ Phase II and Phase III trials that included 20,541 women 16 to 26 years of age. Clinical efficacy was assessed by studying the ability of the vaccine to prevent the precursors to cervical cancer in women who stayed within the study protocol. Pelvic examinations were performed on women in the study group and clinical specimens were taken. Over the 5 years of the clinical trials, the vaccine had close to 100% efficacy in preventing pre-cancer lesions in women who received all three doses and had not yet been infected with any of the four HPV types contained in the vaccine.

Studies demonstrating the efficacy of HPV vaccines against disease endpoints in 9 – 15 year olds were not feasible given legal and ethical issues regarding evaluations of sexual activity (pelvic exams) in this population and the relatively low rate of exposure to the virus at this age. Accordingly, bridging studies for Gardasil™ were used to infer **efficacy** for the 9 to 15 year old age group in which only immunogenicity studies had been conducted.

One month after the third dose in the series, almost all ( $\geq 99.5\%$ ) of the 1,100 study participants 9 to 15 years of age seroconverted to all four of the vaccine HPV types. The final antibody titres against all four vaccine HPV types were each 10 to 100 times higher than corresponding antibodies produced by natural infection. The bridging studies revealed that cLIA anti-HPV GMTs in adolescent boys and girls (9 to 15 years of age) were 2 to 3 fold higher than the GMTs in adults. This finding allowed the researchers to conclude that the **efficacy** of the vaccine is comparable between the two age groups of 9 to 15 year olds and 16 – 26 year olds. The data also predict well for persistence of protection over time, and provide support for vaccination at an earlier age.

### 2.4 Is there evidence of a therapeutic effect with the vaccine?

Because participants were enrolled into the clinical trials even if they were HPV DNA or antibody positive, it was possible to evaluate vaccine efficacy against cervical cancer surrogate CIN 2/3 in women already infected with a vaccine type at the time of vaccination. At baseline, 27% of participants in the clinical trials had evidence of past or current infection with a vaccine HPV type.

The trials demonstrated no clear evidence that the vaccine protected against disease caused by HPV types for which the subjects were already seropositive and/or HPV DNA positive. In short, the vaccine does not prevent the consequences of current HPV infection.

However, if women are only infected with one of the HPV subtypes contained in the vaccine, the vaccine will likely prevent acquisition of other HPV types.

## 2.5 How do we know the vaccine is safe, and how will it be monitored in Canada?

There was no difference in reports of serious or severe adverse effects between the placebo and vaccine arms of the Gardasil™ clinical trials. Also, there was no evidence of an increase in adverse events in women already infected with HPV subtypes contained in vaccine.

In June 2007, the World Health Organization's Advisory Committee on Vaccine Safety reviewed all available data that address the safety of HPV vaccines, including post-marketing reports, and expressed no concerns regarding the vaccine's safety to date.

Health Canada conducts rigorous scientific reviews about a vaccine's safety, efficacy, and quality prior to granting approval for use in Canada. Post-marketing vaccine surveillance also is in place. Provinces/territories and manufacturers report adverse events following immunization to the Public Health Agency of Canada (PHAC) on an ongoing basis.

## 2.6 How long does vaccine protection last? Will a booster be needed?

A subset of participants ( $n = 241$ ) in the Gardasil™ Phase II trial has been followed for 60 months after dose 1 with high sustained vaccine efficacy and no evidence of waning immunity. There is no data on duration of immune response beyond 60 months. At a five year follow up, a strong anamnestic response to antigen challenge was found, with a fourth dose resulting in an 11 to 40 fold increase in anti-HPV antibody titres.

It is also known that the trajectory of the immune titers is consistent with the immune titers of other vaccine antibody responses that are lifelong. There is sufficient data implying that these titers will be sustained for at least 15 years, if not lifelong.

The issue of duration of protection is important to program decision-making regarding the age cohort for vaccine administration. It is known that within the first few years of sexual activity, most young women acquire the virus, so it is critical to give it to women pre sexual debut. Vaccine administration at 9, 10, 11, or 12 years old will have the greatest preventative impact.

Starting vaccination at age 12 (pre-sexual debut) vs age 15 vs age 18 would result in a greater number of HPV related cases prevented (70% vs 50%) by year 2050.

Duration of protection will be monitored closely and the need for booster doses will be assessed.

## 2.7 Why is GARDASIL™ only licensed for females $\geq 9$ years to $\leq 26$ years?

Immunogenicity, efficacy, and duration of protection are not known for females  $< 9$  years of age.

Studies of GARDASIL™ use in females  $> 26$  years are ongoing. At this time, no recommendations can be made for vaccine use in females  $> 26$  years of age.

On an individual level, a clinician could make the decision to immunize a woman over the age of 26.

## 2.8 Why is the vaccine NOT being recommended for males?

There isn't data on the clinical efficacy of the HPV vaccine in males. At this time Merck has 2 studies underway and it is likely that results will be available by the end of 2008. One study is examining the efficacy of the HPV vaccine in heterosexual men, and the other in men who have sex with men (MSM).

The basis for these trials is the determination of vaccine efficacy in men. Experience with the herpes vaccine showed it was effective in women but not effective in men because of the histologically different milieus where the infections occur. The areas for HPV infection in men (the penis, scrotum and the glans) are keratinized squamous epithelium. It will be important to determine if a highly robust antibody response seen in men translates in clinical protection against genital HPV acquisition.

## 2.9 Why is the vaccine being recommended for girls as young as 9?

It is important to vaccinate young women **before** infection in order to maximize protection. This would be before sexual debut, when most females still have not been infected with HPV.

Additionally, data from the bridging studies provide support for vaccination at an earlier age. Girls 9 – 15 years old were found to have antibody titres 2 to 3 times higher than those of the 16 to 26 year olds.

## 2.10 Can the vaccine be given to females that are already sexually active?

The vaccine is safe for women who are already sexually active. However, within 2 years of being sexually active, 70% of women will acquire one type of the 15 oncogenic HPV types. So the vaccine will not be as effective in women who are already sexually active.

There is no harm in women who have already been infected with an HPV subtype receiving the vaccine.

### **2.11 Is there testing available to determine if the vaccine will be effective in sexually active women?**

No. There are two methods of looking for evidence of HPV infection. One is a molecular test [either polymerase chain reaction (PCR) or hybrid capture technique] that is performed like a Pap smear, and determines whether a woman currently has a cervical HPV infection. The other method is to perform serology for HPV antibodies, to determine if a woman has been previously exposed to HPV.

Molecular testing only provides evidence of current infection and not past infection. This means that if a test came back negative, it doesn't necessarily indicate that the woman hasn't been infected with the HPV in the past, and it also doesn't show if she has had an immunologic response. This method of testing is not currently performed routinely in British Columbia. Serological testing for HPV antibodies is not available commercially, and some women may have undetectable antibody levels which may be sufficient to offer protection against future genital HPV infections.

### **2.12 What is the route, dose, and schedule for administration of the vaccine?**

The vaccine is administered intramuscularly in three 0.5 mL doses, preferably given at 0, 2, and 6 months. If the schedule is interrupted, the vaccine series does not need to be restarted. If the series is interrupted after the first dose, the second dose should be given as soon as possible. If only the third dose is delayed, it should be administered as soon as possible.

The minimum interval between the first and second dose is 4 weeks and between the second and third dose is 12 weeks.

The minimum interval schedule of 0 – 1 – 4 months should not be followed on a routine basis. It should only be used at the client-specific level based on health care provider assessment. The preferred schedule for a school-based program is 0 - 2 - 6 months.

### **2.13 Can the vaccine be given at the same time as other vaccines?**

The vaccine can be administered at the same visit as all age-appropriate vaccines (e.g., Tdap, Td, meningococcal conjugates, hepatitis B, and varicella).

### **2.14 What are the contraindications to the receipt of HPV vaccine?**

Gardasil™ vaccine is contraindicated for persons with a history of anaphylactic reaction to a previous dose of any HPV vaccine, yeast, or to any vaccine component [amorphous aluminum hydroxyphosphate sulfate (as the adjuvant), sodium chloride, L-histidine, polysorbate 80, and sodium borate].

Gardasil™ vaccine is not recommended for use in pregnancy. Although the vaccine has not been causally associated with adverse outcomes of pregnancy or adverse events to the developing fetus, the data are limited. Until further information is available, initiation of the vaccine series should be delayed until after completion of the pregnancy. If a woman is found to be pregnant after initiating the series, completion of the three-dose regimen should be delayed until after pregnancy. If a vaccine dose has been administered during pregnancy, there is no indication for any intervention.

### **2.15 Can immunocompromised persons receive the vaccine?**

Because Gardasil™ is a sub-unit (inactivated) vaccine, it can be administered to persons who are immunosuppressed as a result of disease or medications. However, the immunogenicity and efficacy in this population are not known. The immune response might be less than that in persons who are immunocompetent.

### **2.16 What are the possible adverse events following immunization with HPV vaccine?**

In clinical trials, Gardasil™ was safe and well tolerated. There were 102 serious adverse events, with no difference reported between placebo and vaccine groups. There was an increase in rates of injection site events in vaccine vs placebo, including pain, redness and swelling, but similar types and rates of systemic adverse events. There were ten deaths reported in the vaccine group and 7 reported in placebo group, but none were reported to be vaccine related. Deaths were consistent with events expected in the enrolled age groups, including motor vehicle accidents, overdose and pulmonary embolus. Other causes were sepsis, pancreatic cancer, arrhythmia and asphyxia.

Since Gardasil™ was licensed, there have been 13 reports of Guillain-Barre syndrome (GBS) among vaccine recipients. Investigators at the US CDC are in the process of confirming GBS. Of the 13 reports, six individuals received Gardasil™ alone, five received Gardasil™ and Menactra®, one received Gardasil™, Menactra®, and Hepatitis A vaccine, and one received Gardasil™ and Pneumococcal polysaccharide vaccine given within 30 days of one another.

Because GBS occurs at a rate of 1-2 per 100,000 person years during the second decade of life, some cases will occur by coincidence following vaccination, but not due to vaccination. To date, the number of cases of GBS reported in the US are below the expected naturally occurring background rate.

In Canada, to date, there have been no reports of GBS in Gardasil™ vaccine recipients.

### **2.17 Will other non-vaccine HPV types become more prevalent with widespread HPV immunization programs?**

The threat that other oncogenic HPV types will replace HPV 16 and 18 is more of a theoretical concern than a barrier to implementing a vaccination program based on the known virology, natural history, and epidemiology of HPV. As with evaluating the long-term duration of protection, post-vaccine surveillance will evaluate the theoretical risk for type replacement.

### 3.0 THE HPV VACCINE PROGRAM

#### 3.1 Why are we giving a vaccine for a cancer that only 150 BC women develop per year?

That number is misleading because it only reflects the number of women who actually develop cervical cancer. Many women undergo significant interventions that result in the statistic of 150 women with cervical cancer per year in BC.

Each year in BC, over 750,000 women are screened for cervical cancer. Of these 750,000 smears, 30,000 are abnormal and there are 5000 women that develop high-grade pre-cancerous lesions. Those women need to be treated with significant interventions to prevent these lesions developing into cervical cancer. For example, over 13,000 colposcopies are conducted as part of cervical lesion diagnosis and treatment programs.

As well as the burden of disease for women who need to undergo repeat screening, colposcopy and treatment, these abnormal Pap smears represent a significant cost to the health care system.

In the recent HPV prevalence study conducted in BC, prevalence of HPV 16 and HPV 18 was 35.3% and 5.8% respectively in CIN 2 lesions and 52.3% and 22.2% respectively in CIN 3 lesions. Thus, in addition to reducing the number of cases of invasive cervical cancer in the province, another important benefit of the HPV vaccine program will be to decrease the number of mild, moderate and severe atypias in the province. It is estimated that the HPV vaccine, alone, will prevent about 60% of the 5000 lesions per year.

From another perspective, the primary purpose of health care is prevention. It would be irresponsible and unethical to dismiss prevention and instead emphasize significant intervention.

#### 3.2 So, should there be an HPV vaccine program?

**YES!** The HPV vaccine is highly efficacious and has few side effects. An HPV vaccine program offers a significant opportunity to decrease cervical cancer and HPV related diseases in the province. While the vaccine won't eliminate the disease, it will reduce the emotional costs of a precancer diagnosis and the financial costs of early treatment.

Although the burden of cervical cancer itself is relatively small as a result of the comprehensive Pap screening program, the burden of cervical cancer precursors of CIN 2 and CIN3 is significant in the province of BC and the role of HPV types 16 and 18 in those lesions is significant. As such, it is expected that the HPV vaccine would significantly reduce the number of CIN2/3 lesions in British Columbia. In addition, the quadrivalent vaccine offers protection against HPV 6 and 11 associated genital warts and cytological abnormalities associated with infection with low risk subtypes.

### 3.3 Why is the program going to be offered in grade six to girls aged 12 yrs and to girls in grade 9, aged 14 years?

The majority of females become infected with at least one subtype of HPV within 2-5 years of initiating sexual activity. In British Columbia, 3% of girls aged 12 or younger have already had sexual intercourse, and over 30% are sexually active by age 16. Because this is a prophylactic vaccine, it should optimally be administered to young women prior to sexual debut and exposure to HPV types. In addition, the best immune response to HPV vaccine was found at younger ages. Also, school based programs have demonstrated increased vaccine uptake for adolescents compared to clinic-based programs. Since the introduction of the school based Hepatitis B Vaccine (HBV) program in BC in Grade 6, there has been a very good uptake rate of ~ 90% each year.

### 3.4 Why can't we rely on Pap screening alone to catch cervical cancer early, instead of investing in a new vaccine program?

Although Pap smears remain an important element in cervical cancer prevention, there are some limitations with Pap testing. Firstly, Pap tests are not 100% accurate: there is about a 15% false negative rate. Also, despite efforts to increase the number of Canadian women who do get a Pap test, the rate has plateaued at about 80%. So women don't always get their Pap tests or get them on time. Finally, Pap testing identifies pre-cancerous lesions, but does not prevent them. While cervical cancer progresses slowly, a missed early diagnosis puts women at considerable risk of allowing a cancer to progress. In women with impaired immune systems, that cancer can progress very rapidly.

### 3.5 So - will Pap testing still be necessary?

Vaccinated women will need to continue with regular cervical cancer screening for three reasons:

- (a) The vaccine will NOT provide protection against all types of HPV that cause cervical cancer. The two strains of HPV that cause 70 per cent of cervical cancers (HPV 16 and 18) are present in GARDASIL™. Annual pap smears will still be necessary to screen women against the effects of the other 30 per cent of the HPV viruses that are implicated in cervical cancer.
- (b) Women may not receive the full benefits of the vaccine if they do not complete the vaccine series.
- (c) Women may not receive the full benefits of the vaccine if they receive the vaccine after they have already acquired a vaccine HPV type.

Pap testing should be started at age 18 as part of a routine health examination, or earlier—as soon as one becomes sexually active.

Cervical cancer screening programs may need to be adapted in a highly vaccinated population in order to efficiently achieve goals of the program. The screening programs may be modified in either type and/or frequency of screening.

This is an area requiring careful research and surveillance before guidelines can change.

**For this reason, it is a necessity to have easily accessible documentation of vaccine receipt via a client-specific immunization registry.**

### **3.6 How can we implement an HPV vaccine program when the duration of vaccine immunity is not known?**

When any new vaccine is approved for use it is not unusual that there are a number of unanswered questions. These can include such questions as the duration of protection and whether a different vaccination schedule may be equally effective. Many successful vaccination programs have been routinely implemented without obtaining long-term efficacy data (e.g. hepatitis B vaccine program). The pneumococcal conjugate vaccine program was introduced without complete knowledge of the number of doses needed for long-term protection.

Clinical trials have shown that Gardasil™ is safe and effective for at least five years. Why deny protection today and for at least the next 5 years? Surveillance and research on the duration of efficacy and the potential need for boosters will continue. For the time being, the vaccine gives women much-needed protection.

### **3.7 Will parents give this vaccine to their daughters given that it is for a sexually transmitted infection?**

Because the HPV vaccine is a vaccine for a sexually acquired infection, concern exists regarding parental acceptability. In 2006 - 2007, BCCDC conducted a random digit dialing survey in BC. The survey looked at parental acceptance of the vaccine with the parameters of delivery in a school based program to 11 and 12 year old girls and “piggy-backed” on the Hep B program. Sixty-five percent of 400 parent respondents agreed with the statement that they intended to vaccinate their daughters against HPV, and 89.9% were either neutral or agreed with the statement. Over 90% of parents stated that if the vaccine was paid for, but made available through physician’s offices and public health units, they would vaccinate their daughters.

Parents were much more likely to indicate they were willing to vaccinate their child against HPV if they thought vaccines were good and their children had received all the childhood vaccines. If parents thought that vaccines were harmful, they were significantly less likely to vaccinate their children against HPV.

So, the strongest predictor of parents being against the vaccine was their overall attitude about vaccines. It had very little to do with concerns over sexual activity.

**3.8 There has been a concern presented in the media that receipt of HPV vaccine will promote earlier onset of sexual activity.**

There were similar concerns in 1992 when BC introduced the hepatitis B vaccine program for grade 6 students. There has been no rise in earlier sexual activity since then (i.e. the McCreary study).

There are many factors that influence young peoples' decisions about early sexual activity. These include peer pressure, self-image, sex education, and impact of the media. There is no evidence that being vaccinated against HPV influences a young girl's decision regarding earlier sexual activity.

#### 4.0 REFERENCES

1. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis.* 1996;174:679–689.
2. Castellsagué X, Muñoz N. *J Natl Cancer Inst Monogr.* 2003;31:20–28.
3. Castle PE. *J Low Genital Tract Dis.* 2004;8:224–230.
4. Carter JJ, Koutsky LA, Hughes JP, et al. *J Infect Dis.* 2000;181:1911–1919.
5. Fairley CK, Gay NJ, Forbes A, Abramson M, Garland SM. *Epidemiol Infect.* 1995;115:169–176.
6. Ferenczy A, Bergeron C, Richart RM. *Obstet Gynecol.* 1989;74:950–954.
7. Franco et al. *Vaccine.* 2005; 23:2388  
Mariani. <http://www.medscape.com/viewarticle/458995>
8. Herrero R, Castellsague X, Pawlita M, et al. *J Natl Cancer Inst.* 2003;95:1772–1783.
9. Hildesheim A, Schiffman MH, Gravitt PE, et al. *J Infect Dis.* 1994;169:235–240.
10. Ho GYF, Burk RD, Klein S, et al. *J Natl Cancer Inst.* 1995;87:1365–1371.
11. Ho GYF, Bierman R, Beardsley L, Chang CJ, Burk RD. *N Engl J Med.* 1998;338:423–428.
12. Insinga RP, Dasbach EF, Myers ER. *Clin Infect Dis.* 2003;36:1397–1403.
13. Kahn JA. *Curr Opin Pediatr.* 2001;13:303–309.
14. Kjaer SK, Chackerian B, van den Brule AJC, et al. *Cancer Epidemiol Biomarkers Prev.* 2001;10:101–106.
15. Kobayashi A, Greenblatt RM, Anastos K, et al. *Cancer Res.* 2004;64:6766–6774.
16. McCreary Centre Society, Adolescent Health Survey III, 2003
17. Meijer CJLM, Helmerhorst TJM, Rozendaal L, van der Linden JC, Voorhorst FJ, Walboomers JMM. *Histopathology.* 1998;33:83–86.
18. Moore R, et al. (2005). Prevalence of HPV in a Population Based Sample in British Columbia, Canada
19. Murthy NS, Mathew A. *Eur J Cancer Prev.* 2000;9:5–14. 4.

20. NACI Statement.

Available at: <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/07pdf/acs33-02.pdf>

21. Nakagawa M, Viscidi R, Deshmukh I, et al. *Clin Diagn Lab Immunol.* 2002;9:877–882.

22. Ogilvie GS et al. Parental intention to have daughters receive the human papillomavirus vaccine. (2007). *CMAJ.* 177 (12).

23. Rager KM, Kahn JA. *Curr Women Health Rep.* 2002;2:468–475.

24. Roden RBS, Lowy DR, Schiller JT. *J Infect Dis.* 1997;176:1076–1079.

25. Schiffman M, Castle PE. *Arch Pathol Lab Med.* 2003;127:930–934.

26. Schiffman M, Kjaer SK. *J Natl Cancer Inst Monogr.* 2003;31:14–19.

27. Smith EM, Ritchie JM, Yankowitz J, et al. *Sex Transm Dis.* 2004;31:57–62.

28. Svare EI, Kjaer SK, Worm AM, Osterlind A, Meijer CJLM, van den Brule AJ. *Sex Transm Infect.* 2002;78:215–218.

29. Stanley M. *J Natl Cancer Inst Monogr.* 2003;31:117–124.

30. Pinto AP, Crum CP. *Clin Obstet Gynecol.* 2000;43:352–362.

31. Walboomers JMM, Jacobs MV, Manos MM, et al. *J Pathol.* 1999;189:12–19.  
Bosch FX, Lorincz A, Muñoz N, Meijer CJLM, Shah KV. *J Clin Pathol.* 2002;55:244–265.

32. Wang SS, Hildesheim A. *J Natl Cancer Inst Monogr.* 2003;31:35–40.

33. Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. *Am J Epidemiol.* 2003;157:218–226.

34. Winer R. et al. *Journal of Infectious Disease.* 2008,137:279 – 282.