Public perception
A significant challenge in the battle against HPV

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ABSTRACT
HPV accounts for 5.2% of the worldwide cancer burden, including all cervical cancers, 50% of penile cancers and 88% of anal cancers. Two vaccines have recently been developed and licensed to target specific oncogenic and non-oncogenic types of HPV. In 2006, the Canadian government supported a vaccination program for girls aged 9 to 13 and female vaccination rates in this population in Canada now range from 50% in Alberta to 86% in Quebec. There are compelling reasons to include boys in the vaccination campaign as well. Two provinces have recently stated their intention to do so. Perceptions of individuals and parents are important in vaccine acceptance. Understanding how their decisions are made will help design measures to improve vaccine uptake.

Key words
HPV vaccine, cervical cancer, vaccine safety, public perception.

Viral and bacterial infections are the third leading causes of cancer, after tobacco and diet. Approximately 16% of cancers worldwide are known to have an infectious cause, of which 95% are attributed to hepatitis B and C, helicobacter pylori and the human papillomavirus (HPV). HPV accounts for 5.2% of the worldwide cancer burden and is the most common sexually transmitted infection (STI). HPV affects 3 out of 4 sexually active individuals at some point in their lives, but many may not be aware that they have the virus since HPV is often asymptomatic. Approximately 70% of HPV infections spontaneously resolve within the first year of contracting the virus and 90% spontaneously resolve within 2 years. HPV infection can be spread by skin-to-skin contact (via the genital area), and thus condoms do not fully protect against the virus.

There are over 100 different strains (designated as genotypes according to taxonomic guidelines, or types, for short) of HPV, of which four are among the most prevalent (types 6, 11, 16 and 18). HPV is implicated in all cases of cervical cancer, which is responsible for more than 275,000 deaths per year worldwide, of which 87% occur in the developing world. Oncogenic types (such as HPV 16 and 18) are also causally implicated in an estimated 70% of vaginal cancers, 43% of vulvar cancers, 50% of penile cancers, 88% of anal cancers and 13-56% of oropharyngeal cancers. Non-oncogenic, low-risk types of HPV (such as HPV 6 and 11) are responsible for 90% of anogenital warts.

SCREENING AND EARLY DETECTION
Two preventive measures are in place to detect precancerous lesions and infection: Pap screening and the HPV test. Pap screening can detect abnormal cervical cells, often before they become cancerous. The specificity of the procedure is very high (96.8%), but the sensitivity to detect abnormal cervical cells is just slightly better than a coin flip, at only 55%. This means that Pap screening has a 45% chance of producing false negative results. Pap screening guidelines have recently changed in Canada and, as of January 2013, it is recommended that women 25 years of age and older be screened every 3 years and no routine screening for those under 25. (The recommendation was based on cervical cancer data from 2002 to 2006 showing that the incidence and mortality rate of cervical cancer in women younger than 25 was 1.3 and 0.2 [per 100,000] respectively.)

The HPV test is another method of detection, whereby the DNA of high-risk (oncogenic) HPV types can be detected from vaginal and epithelial cells (around the genital area). It is much more sensitive than Pap screening (94.6%), though slightly less specific (94.1%). HPV testing is only recommended for women 30 years of age or older and/or for women who test positive for abnormal cervical cells. Unfortunately, the HPV test is not yet routine or standard and is currently not available for men (except in clinical research settings). Moreover, in Canada, 15% of women have never had a Pap smear and 30% have not been screened in the last 3 years. Due to these limitations, the Pap and HPV test cannot be exclusively relied upon to detect infection and/or cancer.

HPV VACCINES
In recent years, two vaccines (Gardasil® and Cervarix™) have been developed and licensed to target specific oncogenic
and non-oncogenic types of HPV. Gardasil™ is effective in preventing HPV types 6, 11, 16 and 18, while Cervarix™ is effective in preventing HPV types 16 and 18 only.5,22,23 There is in fact evidence to suggest that the vaccine offers some cross-protection against other HPV types,44 although the long-term efficacy of this protection is still under investigation. The vaccine is given in a three-dose regimen (at 0, 2 and 6 months).3,25 Recent studies have found that 2 doses are just as effective as 3, although long-term trials are still needed.26,27 Efficacy studies of these vaccines have shown high antibody titres and good tolerability.28-34 Long-term prospective trials are still in progress, though some studies have reported 100% efficacy against specific HPV types and precancerous lesions up to 8.4 and 8.5 years post vaccination.3,35-37 Because both vaccines have a prophylactic and not therapeutic effect, they are recommended for administration prior to inception of sexual activity.29,38,39 Predictive mathematical modelling studies of vaccine efficacy suggest that when uptake rates are high, important reductions in morbidity and mortality can be achieved.40 As a result, policy makers in both Western and developing countries are currently implementing vaccine programs, with the hopes that vaccination will reduce morbidity and mortality related to HPV infection, as well as reduce healthcare costs in the long term.41 To date, more than 65 million doses of the vaccine have been safely administered worldwide.41

**CANADA’S HPV VACCINATION PROGRAM**

In 2006, the Canadian government allocated $300 million to support provincial universal vaccination programs for girls aged 9–16.42,43 All of Canada’s provinces now have publicly funded immunization strategies in place for girls through school-based programs. Some of the provinces offer catch-up programs for female high school students (Grade 7–9) and young women as well.4 However, female vaccination rates in Canada vary by region, with uptake rates as low as 50% in Alberta and as high as 86% in Quebec.3,44 Vaccination programs seek to be cost-effective by attaining a level of population coverage that not only protects vaccinated individuals, but also induces a “herd” immunity to prevent transmission to their potentially unvaccinated partners.

In January 2012, the National Advisory Committee on Immunization (NACI) extended its HPV vaccine recommendation to include Canadian males aged 9 to 26.7 This policy is consistent with those of many other jurisdictions, including the United States, Australia and the UK.17,44,45 Despite the almost universal recommendation that both girls and boys should be vaccinated, publicly funded programs are still exclusively offered to girls, with the exception of Prince Edward Island and Alberta, which have plans to implement vaccination programs for boys in the near future.6,16 The Society of Obstetricians and Gynecologists of Canada (SOGC) is encouraging other provinces and territories to follow PEI’s and Alberta’s initiative to include males in school-based vaccination programs.52,68

**VACCINE DECISION MAKING**

Over the last decade, there has been a proliferation of studies attempting to identify factors correlated with vaccination intentions and uptake of the HPV vaccine.57-64 Study populations include adolescents, college students and parents of children. It is known that a continuous interplay of individual (cognitive, attitudinal) and social factors (doctor’s recommendation, the impact of the media, social norms) may influence an individual’s decision. Attitudes toward vaccines in general are relevant; worries about vaccine side effects are weighed against fears of disease.

Our own research group at the Lady Davis Institute for Medical Research and the Louise Granofsky Psychosocial Oncology Program, Jewish General Hospital and McGill University, aims to understand what factors play a role in motivating individuals to receive the HPV vaccine. In a recent study, published in *Health Psychology*, we found that among female college students in Montreal, “negative health consequences of the vaccine, physician’s recommendation, positive attitudes toward the vaccine, and subjective norms were significant correlates of vaccination intentions… [while] physician’s recommendation, subjective norms, and perceived susceptibility to HPV were unique correlates of [vaccine] uptake.”70 In another published study, we examined knowledge of HPV and the HPV vaccine among male college students, and discovered that perceived knowledge (what one thinks they know) may be a separate construct from objective (factual) knowledge when intending to get the HPV vaccine.71 This suggests that other factors such as confidence, attitudes/beliefs about HPV and even self-efficacy may be at play when considering vaccination.

**THE ROLE OF PARENTS**

Since HPV is an STI, vaccination is most effective if administered to children before their sexual debut. HPV vaccine

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**Figure 1. Reasons to vaccinate males**

There has been much debate about whether to include males in vaccination programs, partly because most clinical trials for the vaccines were conducted only in women, but also because some feel that any additional government efforts should be directed towards increasing vaccine coverage rates in females. Nonetheless, including males may be an effective way to obtain the highest coverage for the population, especially since control of HPV infection among females requires vaccination coverage rates of 85% or more.72 Additionally, since both men and women suffer from HPV morbidity, these provide compelling reasons for a gender-neutral approach to HPV vaccination.73-75

- **Past experience indicates that universal, gender-neutral vaccination policies have been more effective, less confusing to the public and more equitable.**
- **Vaccinating males would protect men who have sex with men (MSM), who are at increased risk of HPV-associated diseases.**
- **In males, genital warts and HPV-related cancers are costly and burdensome conditions that warrant medical intervention.** By receiving the HPV vaccine, males can reduce their own risk of contracting HPV and diminish the risk of anal intraepithelial neoplasia, anal, penile cancer and head and neck cancers, as well as genital warts.
- **Although Pap and HPV tests are available for cervical cancer screening, screening tests for other HPV-related cancers (e.g. anal, penile) are not yet routinely administered.**
- **Some cultures may perceive it as more acceptable to vaccinate males than females.**
- **Vaccinating males ensures the greatest protection for females.** When males are included in vaccination programs, cervical cancer incidence and genital warts are further reduced in females. This is particularly important when lower than optimal female vaccination rates exist.
is routinely administered to girls aged 9–13 years old, and thus parental consent is critical to ensure optimal vaccination rates. It is important to understand the reasons underlying parents’ acceptance or refusal of the HPV vaccine. Consistent with other studies, we have found that the issue of safety (fears and worries about vaccine side effects) is one of the most prominent concerns of parents when considering the HPV vaccine for their child.72,73 Importantly, a health care professional’s (HCP) recommendation has also been shown to be one of the primary reasons for vaccine acceptance.74,75

Other factors that may influence parents’ decision to have their child vaccinated include: beliefs about the susceptibility to/severity of HPV/cancer; whether their child is of appropriate age to receive the vaccine; attitudes toward vaccines in general; accessibility (both financial and proximal); one’s personal experience with HPV/cancer and the opinions/messages of the media, organizations and friends and family.

Although there has been extensive research concerning parents’ acceptance/refusal of the HPV vaccine for their daughters, very few Canadian studies have examined these factors with respect to sons.76,77 From the few studies that compare vaccine attitudes, beliefs and knowledge among parents of sons and parents of daughters, it is clear that reasons regarding HPV vaccination differ depending on the gender of the child.78,79 In line with this reasoning, we are about to launch a Canadian Institutes for Health Research (CIHR)-funded study, which involves a longitudinal, Canada-wide survey targeting parents of boys, designed to more closely examine the factors that guide parental decisions regarding the HPV vaccine. The findings from this study will complement our previous research concerning parents of girls and the data will be the first to provide estimates of national uptake rates of the HPV vaccine for boys in Canada.

**“I don’t want to take a risk, but unfortunately, I don’t have enough information to justify my decision.”** – MOTHER, 47

**CONFRONTING MISCONCEPTIONS**

In a world of fast-advancing technology, information is more easily shared and is readily accessible and available. The disadvantage of technology is that messages can be publicized by anyone (in the form of blogs, tweets, YouTube videos and the like), without any verification of the information being disseminated. Accessibility does not translate into accuracy. Biased reporting can hinder public understanding even when accurate information becomes available. Content analysis studies specifically about the media’s representation of the HPV vaccine demonstrate that the tone is very inconsistent. One study examining YouTube videos about the HPV vaccine found the majority of articles to be negative,82 while another found online news content related to the vaccine to be neutral in tone,83 and yet another study in the blogosphere found the predominant tone to be positive.84 An additional study about the HPV vaccine in the media found that risk messages (focus on threatening illness or injury) associated with the vaccine were prevalent. With an overload of conflicting information instantly available, navigating the decision-making process becomes more complex.

Parents have legitimate questions and concerns about vaccine safety and efficacy. The media tends to sensationalize these concerns, and common misconceptions about HPV and the HPV vaccine become further salient. Some of the most commonly mentioned fears include: 1) fear of vaccine side effects; 2) fear of the “newness” of the HPV vaccine; and 3) fear that the HPV vaccine will provoke early sexual promiscuity.

This information may be highly complex and difficult for the average parents to understand, leading to broad generalizations and unwarranted fears. One example is the misunderstanding and/or misreporting of Vaccine Adverse Event Reporting System (VAERS) data. In a recent newspaper article, the author reported that there were “more than 600 adverse reactions to the (HPV) vaccine, including 22 hospitalizations and one death.”85 The report does not establish a causal link between adverse event/hospitalization/death and vaccination, nor does it specify the severity or duration of adverse effects. The most frequently reported adverse side effects of the HPV vaccine include pain at injection site, fever and dizziness, which are in line with other childhood vaccines.86-89 Further, several controlled trials about the efficacy of the HPV vaccine have shown that adverse events (e.g. pain at the injection site) are not only reported by participants who have received the HPV vaccine, but also by those who have received a placebo.90,91 Other parents have reported that the novelty of the vaccine raises suspicion about its safety when in fact, there are now up to 10 years of efficacy trials to support vaccination.92,93

The media has also raised the concern that vaccinating young females will cause an increase in early sexual promiscuity and sexual disinhibition (also known as risk compensation). Several studies found that this was rarely cited by parents as a genuine concern.94,95 Two recent peer-reviewed scientific studies published in *Pediatrics* and the American Journal of Preventive Medicine found that the HPV vaccine is not linked to an increase in sexual promiscuity. On the contrary, it has been shown that the HPV vaccine is actually associated with responsible sexual health behaviours (e.g. condom use, regular Pap screening, seeking gynecologic exams, etc.).96,97

It seems that cherry-picking the statistics on side effects and then reporting only the associations with vaccination is a typical strategy by anti-vaccine activists. With literally hundreds of conditions, by chance alone, one is bound to see at least 5% (the level of significance) of them associated significantly with vaccination. If winning the lottery had been reportable as a side effect, who knows, it might also be associated with vaccination.

There has been publicity surrounding the 32 supposed deaths related to the HPV vaccine among girls/women in the US.98 The Centers for Disease Control and Prevention (CDC) estimated that “from June 1, 2006, through December 31, 2008, there were 23,051,336 doses of the quadrivalent HPV vaccine distributed in the United States. Based on a 6-week window of biologic plausibility after immunization, this
gives a total of 2,650,667 person-years at risk.” If we assume that age distributions among vaccines were 50% for 10–14, 30% for 15–19, and 20% for 20–24 year-old groups and then apply the observed death rates for the US population in 2006 for females in these age groups, we obtain a total of 728 deaths, which is the expected number for a cohort comparable in size, age and gender to those so far vaccinated.

**THE CHALLENGE OF PUBLIC TRUST**

The HPV vaccines are an exciting breakthrough that will enable us to prevent HPV-related cancers in future generations. However, experience in Canada demonstrates that there remain obstacles to vaccine acceptance, even when the vaccine is offered free of charge and there is ample study evidence of safety and efficacy. Our challenge is to understand how to dispel myths and appropriately address misconceptions. As Larson and colleagues have affirmed, “The vaccine community demands rigorous evidence on vaccine efficacy and safety and technical and operational feasibility when introducing a new vaccine, but has been negligent in demanding equally rigorous research to understand the psychological, social, and political factors that affect public trust in vaccines.” The efforts of research groups (including ours) to understand these processes better will hopefully lead to clearer messaging, better understanding and rational decision-making.

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