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OPPORTUNISTIC HPV VACCINATION: AN EXPANDED VISION

SUMMARY POSITION

Human papillomavirus (HPV) infection is preventable—but not adequately prevented. At present, Canada has a robust school vaccination program deployed in all 13 provinces and territories. However, HPV vaccination uptake rates outside school-based programs remain disappointingly low. The lack of public funding for opportunistic HPV vaccination accounts for much of this gap, while missed opportunities for awareness and access may explain the rest. These opportunities translate to HPV-related cancers for too many Canadians.

Based on the available evidence and multiple stakeholder discussions, the Society of Gynecologic Oncology of Canada (GOC) recommends universal HPV vaccination in Canada. In line with this recommendation, we strongly encourage governments to fund opportunistic HPV vaccination, particularly in high-risk populations with the evidence of benefit. At the same time, our vision for increasing opportunistic uptake ranges far beyond government support; for example, we would strongly encourage employers to add coverage for HPV vaccination to their employees medical benefit packages. Our multipronged “Enroll, Engage, Empower” strategy can help the Canadian public overcome awareness and access gaps that hinder uptake. We are facilitating initiatives that align with these strategies and encourage other health care organizations to consider similar approaches.

BACKGROUND AND RATIONALE

HPV epidemiology

Human papillomavirus (HPV) infections are the most common sexually transmitted infections.¹ The overall prevalence of HPV infection in Canada ranges from 11% and 29%, with peak rates in people under age 25, particularly in the first 5 years after the onset of sexual activity.² A double-stranded DNA virus, HPV has more than 100 known variants, which divide broadly into low- and high-risk types.

Low-risk types may cause anogenital warts. High-risk types may lead to cervical and anogenital cancers, along with an increasing proportion of head and neck cancers.

The incidence of cervical cancer varies across the age span, with peaks in the 40s and after age 70.² About 70% of cervical cancers can be traced to HPV genotypes 16 and 18, with most of the remainder attributable to types 31, 33, 45, 52, and 58.¹ While HPV infection is necessary for the development of virtually all cervical cancers, lesions only become malignant after years of infection.

HPV vaccines

HPV vaccines available in Canada include:

- 2-valent: protects against HPV 16 and 18
- 4-valent: protects against HPV 6, 11, 16 and 18
- 9-valent: protects against HPV 6, 11, 16, 18, 31, 33, 45, 52, 58

HPV vaccination is recommended for both males and females between 9 and 26 years of age and available to females aged 26+ with no upper age limit. To date quadrivalent vaccine has been used in school-based programs, though most jurisdictions are likely to adopt the 9-valent vaccine in the near future.³

Evidence of efficacy

In pivotal clinical trials (involving younger women with no history of previous HPV infection), the 2-valent and 4-valent vaccines conferred close to 100% protection against persistent HPV 16/18 cervical infections and resultant changes, while the 9-valent vaccine had a 97% efficacy in preventing cervical, vulvar and vaginal cancers caused by the additional five HPV types in the formulation.⁴

In older women, efficacy drops slightly but remains high. In a study of women aged 24 to 45 years with no history of cervical disease, the 4-valent HPV vaccine had 91% efficacy, against the combined incidence of persistent infection.⁵ Long-term follow-up data indicate that, in women in the same age range, the vaccine's efficacy and safety persist through 6 years following administration.⁷

HPV vaccination does not appear to alter the course of existing HPV infections. In a study of women aged 18-25 years with carcinogenic HPV infections or treated precancerous cervical lesions, there was no evidence that HPV 16/18 vaccination had any effect on the outcome of detectable HPV infections, leading investigators to conclude that “vaccination does not protect against infections/lesions after treatment.”⁸ Perhaps for this reason, vaccination has been assumed to have little value in women with prevalent type-specific HPV infections or pre-existing lesions at the time of vaccination.⁹ However, an accumulating body of evidence suggests that vaccination stands to benefit not only PAP-test-negative and HPV-negative women, but those with a prior history of HPV infection and associated lesions^{9,10,15}.

Future Implications

High-grade cervical intraepithelial neoplasia (CIN2-3), considered a first step toward cervical cancer, can be eradicated with a loop electrosurgical excision procedure (LEEP) or other minimally invasive treatments, but residual/recurrent disease manifests itself in 5-10% of cases.¹⁰ In a study investigating 4-valent HPV vaccination post-LEEP, women who received the vaccine had a significantly lower risk ($p < 0.01$) of recurrent disease.¹⁰ Similarly, a post-hoc analysis of a randomized controlled trial found that women who underwent surgery for cervical lesions after receiving the HPV 16/18 vaccine may have a reduced risk of developing subsequent high-grade cervical cancer.⁹ Similar benefits may apply to HPV-related male cancers, though data are currently lacking.

Other potential benefits beyond cervical cancer prevention

Non-cervical HPV related cancers tend to occur later than cervical disease. It may be that vaccination in previously exposed women has the potential to reduce the risk of vulvar, anal and oropharyngeal disease. However, there is currently no evidence to show this other in vulvar dysplasia after cervical disease.¹⁵

Barriers and facilitators

According to available data on school-based HPV vaccination programs in Canada, vaccination uptake ranges between 46.7% and 93.9% in females and between 75.0% and 87.4% in males.³ Not surprisingly, uptake for opportunistic vaccination is dramatically lower. In a 2014 government audit, 8.3% of women aged 27 to 45 years received at least one dose of the vaccine.¹¹ Data from the private adult market indicate that uptake goes down with age, from 12% in the 27-31 range and just 2.7% in the 42-46 range.

These disappointing figures reflect such barriers as lack of knowledge and comfort among both physicians and the general public, out-of-pocket costs for patients without private coverage, dosing schedule, and the absence of a systemic framework to boost access and opportunity. Women beyond age 26 may not appreciate the value of vaccination in their age group¹² suggesting a gap in physician-patient communication and in physician education.

In a survey of primary care physicians, respondents cited on-site availability of vaccine, vaccine clinics, nurses to administer the vaccine, and information about the vaccine as facilitators to uptake.¹² Moreover, successful vaccination programs use well-coordinated communication campaigns, integrating traditional and social media to spread awareness.¹³ In general, communication of evidence supporting vaccine effectiveness had beneficial effects on the perception of the vaccine.¹³

GOC position

Following the introduction of the 9-valent HPV vaccine into the Canadian market, the National Advisory Committee on Immunization (NACI) issued updated recommendations on HPV vaccines, in which they recommend routine vaccination in people aged 9 to 26 years and support it in those beyond age 26. The Gynecologic Oncology Society of Canada (GOC) goes one step further: based on the available evidence and multiple stakeholder discussions, we actively recommend, rather than just support, universal HPV vaccination in Canada.

2018 GOC position	2016 NACI statement [paraphrased] ¹
<p>“Opportunistic HPV vaccination has the realistic potential to confer immunization to an extra 2-10 percent of the population and thus reduce the burden of anogenital and oropharyngeal cancers in the Canadian population. As such, health care systems, institutions and care providers should encourage opportunistic HPV vaccination by empowering patients with the information to make decisions for themselves through education, ease of access, and removal of financial barriers whenever possible.”</p>	<p>“HPV4 and HPV9 vaccines (and HPV2 in females) are recommended routinely in individuals aged 9 to less than 27 years and may be used in people 27 years of age or older who have not had or completed their HPV vaccination series.”</p>

PAP-negative women 25-45 are the highest priority as the greatest evidence of benefit exists for this group. Women who have already undergone treatment for related cervical cancer lesions represent a further high-risk group, having a 2-to-6-fold risk of subsequent cervical cancer compared to women with normal cytology.⁹ Other higher-risk populations include pre-transplant patients, men who have sex with men (MSM), immunocompromised individuals and patients in whom immunosuppressive medications are being considered.

Canada's smallest province, Prince Edward Island, has taken the lead in the promotion of opportunistic HPV immunization by providing free vaccines to such high-risk groups. GOC strongly encourages other provinces to follow suit. Criteria for "high risk" should be harmonized across the country and should include, at a minimum, immunocompromised and pre-transplant patients.

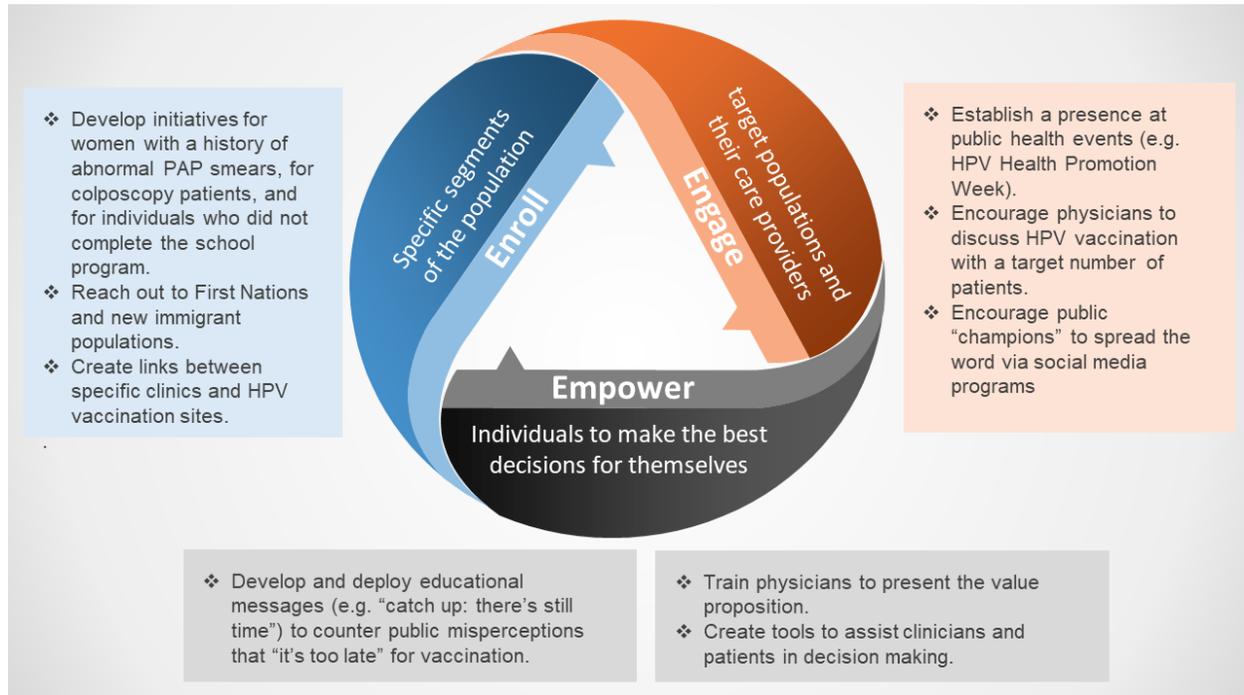
Concerns that opportunistic vaccination may reduce the motivation to undergo cervical cancer screening appear unfounded, based on data to date. In a Swedish study, for example, opportunistically vaccinated young women were *more* likely than their unvaccinated counterparts to attend cervical screening programs.¹⁴

GOC strategy

In consideration of the known uptake barriers and facilitators, GOC has developed a multi-year patient-focused strategy called "Enroll, Engage, Empower." The strategy seeks to:

- Reduce discrepancies in Canadians' awareness of the benefits and safety of HPV vaccination
- Establish a coalition of partners to implement projects to boost uptake of opportunistic HPV vaccination
- Enable and influence an infrastructure that facilitates delivery of HPV vaccination

GOC strategy in action



Conclusion

HPV vaccination gives us the means to prevent a significant number of cervical and other cancers. The school vaccination program has made an appreciable difference, but is not sufficient. Supporting and facilitating opportunistic access to the HPV vaccine will help protect more Canadians from HPV-related illnesses, thus reducing the individual and collective burden of suffering in our country. Our collective will and resources can help overcome many of the existing barriers to uptake.

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