REVIEW

HPV vaccination for MSM: Synthesis of the evidence and recommendations from the Québec Immunization Committee

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ABSTRACT

Diseases associated with the human papilloma virus (HPV) are particularly common among men who have sex with men (MSM). Unlike heterosexual men, MSM do not benefit from the herd protection provided by the vaccination of girls. In this review, we synthesize the available evidence on HPV vaccination for MSM. We also present the recommendations of the Québec Immunization Committee (CIQ) in this regard, which are: to provide targeted vaccination for MSM up to 26 years of age and in-school vaccination of preadolescent boys since this is the best approach to take to have a real impact on the burden related to HPV in the MSM population and to provide direct protection for all men.

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Introduction

The burden of diseases associated with human papilloma virus (HPV) is particularly important among men who have sex with men (MSM). Unlike heterosexual men, MSM cannot count on the herd immunity provided by the vaccination of girls. The Québec Immunization Committee (CIQ) and several other advisory boards^{1–4} recommend vaccination of preadolescent boys, as the best approach to maximize the protection of men and particularly MSM. According to most analyses adding the vaccination of all preadolescent boys could produce benefits. However, given the current cost of the vaccine, the cost/utility ratio of boy vaccination would exceed commonly accepted threshold of \$40,000–50,000/Quality Adjusted Life Years (QALY), even with a 2-dose schedule. Introducing a free vaccination program for preadolescent boys may still be justified by political considerations or the desire for equity, to provide boys and especially MSM with direct protection.^{1,3,5,6}

The possibility of setting up a targeted vaccination program for MSM, which means, to offer the vaccine for free only to male who claim to have sex with men, was also envisioned by different advisory committees, particularly in areas where no HPV vaccination program for boys is in place. To our knowledge, this is the first review summarizing the data on HPV vaccination for MSM. The aim of this review is to synthesize the available evidence in this regard, presenting it according to the analytical framework generally used in Québec and elsewhere for decision making⁷ and to summarize the main recommendations of the CIQ that emerged from this analysis of the evidence.

Epidemiology and clinical burden of HPV among MSM

The HPV burden is particularly heavy in the MSM population. As a matter of fact, the prevalence of anal HPV infections is

high among MSM (>60%) and very high among those HIV positive (>80%).^{8–11} Sexual relations between men is strongly linked to the risk of developing anal cancer, with an odds ratio ranging from 3 to 17 (vs heterosexual men) depending on the study.^{12,13} In addition, genital warts are 2–3 times more common in MSM than in a group of heterosexual men the same age.¹⁴ Diseases associated with HPV are even more frequent in HIV positive MSM population.^{10,12,15}

In Canada and in the province of Québec, the percentage of MSM is estimated to be about 5%.^{16–18} Among those living in Québec, 18.3% have had anogenital warts sometime in their lives.¹⁹ The prevalence of HIV infection in the MSM population of all ages is reported to be about 14% in Québec and 15% in Canada.^{19,20}

The risk of contracting an HPV infection is present from the very first sexual relations. The prevalence of HPV infections rises quickly with an increasing number of partners.^{21,22} In Québec, the mean and median ages of the first sexual relations among men are estimated to be 18.3 and 17 years, respectively.¹⁹

Although many individuals in the MSM population have already been infected with HPV and may benefit from natural immunity, there is some evidence that a previous infection with one type of HPV does not necessarily protect against a new infection (or reinfection/reactivation) with the same type of HPV. Only 50 to 69% of women develop detectable antibodies after a recent infection with HPV.^{2,23} This percentage is even lower among men, with only 4–36% having detectable antibodies.²⁴ On the other hand, absence of detectable antibodies does not automatically mean susceptibility to infection and HPV related diseases, especially in previously vaccinated individuals.^{25–27}

Among the 7.6 million people living in Québec during the 2004–2007 period,²⁸ 464 new cases of cancers of the cervix, vagina, vulva, anus and oropharynx among women were

reported annually.²⁹ The burden was lower among men, with a yearly average of 246 new cases of cancers involving the anus, penis and oropharynx. A high percentage of these cancers, namely 89% among women and 69% among men, may be attributable to HPV. The exact percentage of these cancers occurring specifically in MSM is unknown. Considering the attributable fraction to HPV 16 and 18, each year 485 new cases of cancer in Québec (of which 154 among men) could be vaccine preventable.²⁹ According to the international literature, infection with HPV 6 and 11 is associated with approximately 85% of genital warts in both sexes.^{30,31}

HPV vaccination

Currently in Québec, the quadrivalent vaccine against HPV types 6, 11, 16 and 18 is offered free to the following populations: girls aged 9 to 17 years (included in the routine vaccination schedule since 2008), 18- to 26-year-old women who are immunosuppressed or living with HIV, and boys and men aged 9 to 26 who are immunosuppressed or HIV positive.³² In Québec, 2 doses 6 months apart are recommended for immunocompetent 9-13 year-old preadolescents (3 doses for those immunosuppressed or HIV positive with a 0, 6, 12 months schedule), and 3 doses (0, 2, 6 months) for those 14 years of age and up.³²

In pre-licensure clinical trials, vaccination against HPV has been shown to be efficacious in both men and women.^{14,33-38} In the MSM group, the efficacy of the vaccine in reducing the number of external genital lesions (warts and precancerous lesions) associated with HPV 6, 11, 16 and 18 was 79% in per-protocol analyses and 70% in the total cohort.¹⁴

Previous studies showed heterogeneous results regarding vaccine efficacy in preventing recurrences of anal lesions associated with HPV types to which MSM had been previously exposed.³⁹⁻⁴¹

Post-HPV program (girls-only) implementation studies showed not only a large decrease in genital warts among women in age cohorts to have been vaccinated, but also a statistically significant decrease in these lesions among heterosexual men (34%-80% in the under 20 or 21 age group after 3 or 4 years, depending on the studies). This herd effect was not observed in the MSM population.⁴²⁻⁴⁵

In conferences and congresses, some authors discussed the possibility to focus on male-only vaccination as a means to effectively reduce disease burden on both males and females. This option has been briefly discussed in Québec, but was not retained.

Acceptability, feasibility and ethical aspects of targeted vaccination for MSM

The targeted vaccination of MSM prior to infection is thought to lead to many barriers. First, young MSM must be aware that there is a free vaccine available for them. Second, they must consult a health professional to whom they will disclose their sexual practices either before or as soon as possible after sexual activity commences, in order to obtain the maximum vaccine efficacy. To address the issue of awareness, all means to inform young MSM that they are entitled to a free vaccine should be

identified. Regarding the disclosure of homosexual practices, evidence from the literature, mostly based on studies with MSM participants aged 20 years and older, indicates that MSM are willing to disclose their sexual orientation or homosexual practices but only a few years after sexual debut and after having had many different sexual partners.⁴⁶⁻⁴⁹ Studies on different age cohorts of MSM showed that young MSM (e.g. 16-20 years old) seem to be more willing to discuss their sexual activities with healthcare professionals than older MSM (e.g., 50 year-old MSM questioned in a study in 2011).⁴⁶ This information is encouraging in hoping to obtain some vaccine efficacy with young MSM immunization. Evidence also suggests that the majority of MSM considers HPV vaccination to be beneficial and important and is willing to be vaccinated.^{46,48,49}

Practically speaking, vaccination could be offered to young men in school. However, this strategy could also lead to barriers, since getting vaccination which is associated to MSM in a school setting might lead to stigmatization. Vaccination could also be offered in the healthcare setting, although the experience gained in 2008 when launching the catch-up vaccination program against HPV for girls aged 15 to 17 showed that the vaccine uptake was lower when offered outside schools (62% vs 83% in school vaccination).⁵⁰ It is also known that men, especially young men, rarely consult for health care.⁵¹

Previous evaluation of the implementation of a targeted vaccination program for MSM against hepatitis B suggests that targeted vaccination of this group of the population is acceptable and feasible, but that the impact on reducing the burden of the disease may be limited.⁵²⁻⁵⁵

The issue of targeted vaccination was also analyzed according to ethical principles. Any public health intervention targeting a particular population risks stigmatizing that population. Care must be taken to maximize beneficence, by protecting the health of the MSM population; non-maleficence, by minimizing the stigmatizing effects the intervention could have on this population; and justice, by offering a sub-population that does not currently benefit from public health interventions a prevention strategy designed to reduce the burden of diseases related to HPV. Although men who have relations exclusively with women should see their clinical burden of HPV infections gradually decline following the implementation of vaccination programs for girls, this indirect protection is not perfect and may leave some of them susceptible to these infections. Vaccinations that would be free only for MSM could, to some extent, result in inequity toward some heterosexual men. Some authors also argued that it is unethical to make females solely responsible for protective effect of both men and women.^{56,57} Furthermore, with respect to the general population, the concept of utility must also be considered, by maximizing the cost-effectiveness of the intervention. Putting in place a strategy that is not cost-effective could mean that large sums of money are not available for other interventions considered to be more efficient. Such a situation would also raise questions about equity and justice at a population level.

Economic aspects

Approximately 40,000 boys are born in Québec each year.⁵⁸ If a universal vaccination program for boys were delivered in

primary school (grade 4 in Québec), at the current cost of the vaccine (\$85 per dose, including administration expenses) and following the current recommendations to administer 2 doses at that age, the cost to offer the vaccine would be about \$6 million per age cohort vaccinated (40,000 9-year-old boys with a vaccine coverage of 80% $\times$ \$85 $\times$ 2 doses $\sim$ \$6 million per cohort). Cost-utility analyses done by a Québec team took account costs but also health savings and showed that at the current cost of the vaccine, adding a vaccination program for all preadolescent boys would exceed the generally accepted threshold for including an intervention in the public program (\$40,000-50,000/QALY), even with a 2-dose schedule.⁵⁹

If about 5% of boys are MSM, about 2000 of them per age cohort would be eligible for a targeted vaccination in Québec (40,000 $\times$ 5% = 2000). Since these boys would presumably get vaccinated after age 13, 3 doses would be considered necessary.³² Thus, if all MSM in a cohort (e.g., 15-year-olds) decided to take advantage of vaccination, which is unlikely, the cost to offer the vaccine would be \$510,000 per cohort (2000 boys $\times$ \$85 $\times$ 3 doses).

A cost-utility analysis done in the United States in 2010 showed that targeted vaccination for MSM (with 40% of men infected with HIV, as the base case scenario) would be cost-effective even for 26-year-old men, half of whom would have already been exposed to the types of HPV included in the vaccine.⁶⁰ Considering a lower prevalence of HIV infection (8%), targeted vaccination would still be cost-effective among those under the age of 26. Their vaccination would remain cost-effective even under the condition that up to 20% of them would have been previously exposed to one or more of HPV types included in the vaccine.⁶⁰

In summary, according to the available literature, doubling the vaccine cost by adding all young boys to the current girl-program would not be cost-effective, since immunization of girls contributes to reduce the burden of HPV infection among both men and women. However, adding to the current program a vaccination strategy targeting MSM only could be cost-effective, considering that MSM represent a relatively small proportion of the male population (few doses needed) but bear an important proportion of its HPV burden.

Conformity with other jurisdictions

Vaccination against HPV for all boys between 9 and 26 years of age and for all 9 year-old and older MSM is recommended by the Canadian National Advisory Committee on Immunization.⁶¹ In the United States, it is recommended for all boys aged 13 to 21 years, and for all MSM up to age 26.² Australia, Israel and 3 Canadian provinces have included or will include the vaccination of preadolescent boys in their public programs.⁶²⁻⁶⁶

The United Kingdom also recently took a position in favor of targeted vaccination for MSM from 16 to 40 years of age.³

Synthesis and recommendations from the Québec Immunization Committee

MSM are a high risk population for genital lesions and anogenital cancers associated with HPV. Although vaccination against HPV types 6, 11, 16 and 18 is currently offered to girls in

Québec, unlike heterosexual men, MSM derive little or no benefit from the herd protection that comes from girls vaccination.

A targeted HPV vaccination for MSM, although probably beneficial on an individual level, would not by itself solve the problem of the disproportionate burden of HPV infection among MSM, given the expected difficulty contacting MSM before they get infected.

Although the targeted approach alone seems to be more cost-effective than a universal vaccination strategy, the CIQ considers that in-school vaccination of preadolescent boys, especially for ethical reasons, is acceptable. As a matter of fact, this strategy would provide the best protection at the most opportune time, when they have not yet been exposed to HPV, to men and particularly men who will have sex with men. This universal approach is consistent with national and international authorities' recommendations.

Considering the evidence that MSM might benefit from HPV vaccination and given the fact that to this date, most MSM in Québec have not been vaccinated, a targeted approach for young MSM is still relevant.

Consequently, the CIQ has recommended the adoption of all 4 of these recommendations (not mutually exclusive) as the best way to reduce disease burden among men, especially MSM:

1. Introduction of a free in-school vaccination program for boys as it is for girls in grade 4 (in Québec). The committee believes this is the best strategy to have a real impact on the burden of HPV related diseases in MSM and to provide direct protection for all men.
2. Free vaccination for all MSM up to 26 years of age, as it is currently offered to immunosuppressed women and men.
3. Dissemination of information about the vaccine and the fact that it is free for the MSM population through schools during the vaccination period, in places where gay men socialize, and to healthcare professionals.
4. Evaluation of the implementation and impact of the selected vaccination strategy or strategies against HPV (e.g., vaccination coverage, assessment of the satisfaction and usefulness of the information tools developed, possible reduction in disease burden, etc.).

Conclusion

This synthesis of evidence and the recommendations from the advisory board are currently under review by the Québec ministry of health (MSSS) and its decision is expected soon.⁶⁷ With the current girl-only HPV vaccination program in Québec, the MSSS acknowledges that the implementation of these recommendations would benefit to men, especially to MSM. Historically, the MSSS usually endorses his advisory board's recommendations, but some delays between recommendation and implementation have been seen in the past depending on the government's ability to pay.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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