Rapid Review

Eligibility and Outof-Pocket Costs for HPV Vaccines Across Canada

Prepared for the Public Health Physicians of Canada

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December 2022



This work was commissioned by Public Health Physicians of Canada (PHPC). Production of this report has been made possible through collaboration and financial support from the Canadian Partnership Against Cancer Corporation and Health Canada. PHPC has also worked with the Urban Public Health Network (UPHN) on aspects of this work. The views expressed herein do not necessarily represent the views of CPAC, Health Canada, or the other organizations above.



Acknowledgements

We are grateful to the Canadian Partnership Against Cancer, Scott Halperin, Sarah Wilson, Chantal Sauvageau and Sarai Racey for their review of earlier versions of this report. We also thank Patrick Farrell for copyediting support.

Suggested citation

Umar, I., Albert, M., Roerig, M., Saragosa, M., & Allin, S. (2022). Eligibility and out-of-pocket cost for HPV vaccines across Canada. Toronto: North American Observatory on Health Systems and Policies. *Rapid Review* (No. 36).

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List of Abbreviations

GBMSM	Gay, bisexual, and other men who have sex with men
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
MSM	Men who have sex with men
NACI	National Advisory Committee on Immunization
OOP	Out-of-pocket
РТ	Province and Territory



Executive Summary

Human papillomavirus (HPV) is the most common sexually transmitted infection in Canada and causes 3,800 new cases of cancer annually. Vaccines to prevent high-risk types of HPV have been available for use in Canada since 2006, with publicly funded school-based immunization programs (2007–2010 for girls and expanded to include boys from 2013–2018) rolled out across all provinces and territories (PTs). Publicly funded HPV vaccines outside of school-based programs are available, but population eligibility criteria vary greatly across PTs. Individuals who are not eligible for publicly funded HPV vaccines face out-of-pocket (OOP) costs for the vaccine series, an amount that exceeds \$600 in many PTs for a three-dose schedule. This rapid review provides a snapshot of population eligibility gaps across HPV vaccination policies and related OOP costs, and draws attention to the impacts of these gaps to inform efforts aimed at improving catch-up immunization and access to the HPV vaccine across populations.

We conducted a rapid review of academic and grey literature to identify population eligibility criteria for publicly funded HPV immunization programs, OOP costs to obtain the HPV vaccine, and populations that are impacted by current policies. Our findings highlighted the non-uniformity of HPV vaccination policies across PTs based on an individual's age, gender, sexual orientation and sexual behaviour, and other categories considered higher risk for contracting HPV. Costs (both direct and indirect) for HPV immunization were reported in the literature as prohibitive for vaccine uptake by many populations. Examples of populations that were found in the academic literature to be impacted by costs in certain PTs included low-income populations, all genders older than 26, gay, bisexual, and other men who have sex with men (GBMSM) living with HIV over 26, and recent immigrant and refugee populations.

Derived from the reviewed literature, five key considerations were identified to aid in improving access to HPV vaccines across Canada:

- 1. Continue to expand eligibility criteria for publicly funded HPV vaccine programs
- 2. Improve public awareness regarding eligibility and OOP costs of the HPV vaccine
- 3. Ensure convenient access to HPV vaccinations
- Support healthcare provider recommendations and education of the HPV vaccine, especially for populations considered higher risk for HPV; and
- 5. Strengthen HPV immunization record systems.



Introduction & Background

Human papillomavirus (HPV) is the most common sexually transmitted infection in Canada, with more than 70% of all sexually active Canadians estimated to contract an infection at some point in their lifetime if they are not immunized (1). There are over 100 types of HPV, but only select types can cause cancer (considered high-risk HPV) and anal/genital warts (considered low-risk HPV) (2). As many HPV infections are asymptomatic, individuals can be unaware if they have the virus (3). Although HPV infections may resolve on their own, some types of HPV can linger and cause genital warts and cancers in all genders, with HPV attributed to cause 3,800 new cases of cancer annually (4). Specifically, HPV is implicated in almost all cervical cancers (over 90%) and anal cancers (80–90%), 40% of vaginal and vulvar cancers, 40–50% of penile cancers, and 70% of oropharyngeal cancers (5,6). Since 2020, the World Health Assembly formalized a global strategy to eliminate cervical cancer; the strategy consists of targets related to treatment, screening, and vaccination coverage that all countries should achieve by 2030 (7). As part of the *National Immunization Strategy objectives for 2016-2021* to eliminate cervical and other cancers caused by HPV, Canada's vaccine coverage goals aim for 90% HPV vaccination coverage for all adolescents by age 17 by the year 2025 (8).

To lower the burden of cancer in the population, HPV vaccines offer effective protection against numerous high-risk HPV types. Many studies have reported on the safety and efficacy of the vaccines to prevent HPV-related cancers and infections (9,10). Three vaccines to prevent certain types of HPV have been authorized for use in Canada: *Gardasil*® (authorized in 2006 for females and 2010 for males for protection against four types), *Cervarix*® (authorized in 2010 for protection against two types for females only), and *Gardasil*®9 (authorized in 2015 for protection against nine types for males and females) (11). HPV vaccine delivery through publicly funded school-based programs in Canada has been the primary method of vaccine administration in Canada since 2007 (12). Initiating the vaccine between 9–13 years of age was recommended by the National Advisory Committee on Immunization (NACI) due to higher immune response levels at this age and to increase the chance of protection from immunization before exposure to HPV at the onset of sexual activity (13). Provinces and territories (PTs) initiated school-based programs for girls between 2007-2010 and for boys between 2013-2018 (14), which have reduced HPV-related infection in the "post-vaccine era" (15).

HPV immunization is also publicly funded outside of school-based programs; however, each PT is responsible for managing their own vaccination programs and there is considerable variation regarding who in the population is eligible for publicly funded vaccines (13). Cost effectiveness is a main factor considered by decision-makers across PTs when determining eligibility for publicly fund HPV immunization (16). As of 2016, the NACI recommends the vaccine for males and females aged 9-26, and "may be used in females [and males] over 26 years of age who have not been vaccinated previously or who have not completed the series" (11). The NACI provides guidance for immunization programs across Canada, and as of 2019 their mandate has included the systematic consideration of programmatic factors into their recommendations (i.e., ethics, equity, feasibility, acceptability, and economics outlined by Erickson et al.'s *Analytic Framework* and Ismail et al.'s *EEFA framework* (17,18)). Moreover, the *Canadian Immunization Guide for Health Professionals* (which summarizes NACI guidance into a single source) states that HPV vaccination after onset of sexual activity is "beneficial because the vaccine recipient is very unlikely to be infected with all HPV types in the vaccine"(19).



HPV vaccines offer an opportunity to reduce persistent disparities in HPV-related cancers amongst underserved populations that are disproportionately impacted (4,20,21). Since 2016, many PTs targeted specific sub-populations considered at greater risk for contracting high risk types of HPV, which can receive the publicly funded vaccine up until a certain age (4). These targeted subpopulations include, but are not limited to: gay, bisexual, and other men who have sex with men (GBMSM), those living with human immunodeficiency virus (HIV), and those who are immunocompromised (4). Individuals who want the HPV vaccine but do not fall into certain eligibility categories based on jurisdiction can pay outof-pocket (OOP) and/or with private insurance. An abundance of literature has cited the OOP cost of the HPV vaccine to be a challenge to "catch-up" immunization uptake by both individuals and providers (22– 24), including the Urban Public Health Network's 2021 summary report on solutions to increase youth HPV immunization in Canada (25).

The purpose of this rapid review is to compare population eligibility criteria for publicly funded HPV immunization programs across Canada and identify OOP costs of the HPV vaccine in each PT. We provide a snapshot of eligibility gaps across HPV vaccination policies and related OOP costs, and draw attention to the impacts of these gaps to inform efforts aimed at improving access and uptake of the HPV vaccine across populations.



Methods

Academic Literature Review

A rapid review of the academic literature was conducted in May 2022 in six databases (Medline, Embase, PubMed, CINAHL, EconLit, and Scopus) using predefined search criteria, and a combination of Medical Subject Heading (MeSH) terms and text words for HPV, the HPV vaccine, OOP expenditures, and Canada. See Appendix A for further details.

Articles were included if they were in English, with a publication date of 2016 or later, available publicly or through the University of Toronto Library, published in Canada, and mentioned HPV vaccination cost (e.g., OOP, perceived financial barriers to vaccination, and/or administrative costs to deliver vaccine). Papers were excluded if they focused *only* on cost effectiveness, parental decision-making processes involving HPV vaccination, and school-based HPV vaccination programming. Additionally, we excluded studies that were considered commentaries and dissertations. The results of the search were imported into *Covidence*, an online software tool for systematic reviews, for screening and data extraction. Articles that met inclusion after title/abstract and full-text screening underwent data extraction to detail: study design, jurisdiction, target population, detailed description of costs (i.e., actual cost, perceived cost), recommendations or policy implications, and references to inequities.

Grey Literature Review

The same inclusion criteria were followed for the grey literature review, with the addition of including some sources in French that were easily translatable (e.g., using Google and DeepL Translate). We further included literature that identified populations that were eligible for publicly funded HPV vaccines across PTs. The search was conducted using Google's search engine on the websites of key government public health and immunization authorities, including the Public Health Agency of Canada, Health Canada, NACI, as well as PT public health and immunization authorities, and advisory boards/committees. Non-governmental organizations and community-based organizations focusing on HPV-related cancers, immunization, and education were also searched, including the Canadian Partnership Against Cancer and the Canadian Cancer Society. Consultations were conducted with contacts at the Canadian Partnership Against Cancer and public health experts in various PTs for validation of population eligibility criteria and OOP cost data extracted from the grey literature.

Limitations

This review has several limitations. The literature searches were limited by publication date (2016–2022) and language (English, limited French). No critical appraisal was conducted to discern the quality of studies fully extracted from the academic literature, which could affect the strength of some of the review's key findings. However, validation for the grey literature was conducted amongst contacts at the Canadian Partnership Against Cancer and public health experts in some PTs, which aided in the strength of the findings regarding PT HPV immunization eligibility criteria and OOP cost data. Furthermore, many gaps were apparent in the grey literature when identifying population eligibility criteria and OOP cost data for the HPV vaccine, as we only extracted data from publicly available websites. Finally, not all populations that may be impacted by current policies relating to the OOP cost of the HPV vaccine were identified in our search of the academic literature, prompting the need for future research to understand further population-based impacts.



Analytic Overview

As shown in Figure 1 and Table 1, PTs vary on eligibility for publicly funded HPV vaccines¹. Due to the non-uniformity of these policies, access to the vaccine in each jurisdiction varies based on an individual's age, gender, sexual orientation and sexual behaviour, and other categories considered at higher risk for contracting HPV. Although school-based programs for HPV immunization were excluded in the academic literature search criteria, identifying the variability in grades of vaccine administration and type of vaccine (like in Québec) is beneficial to illustrate.

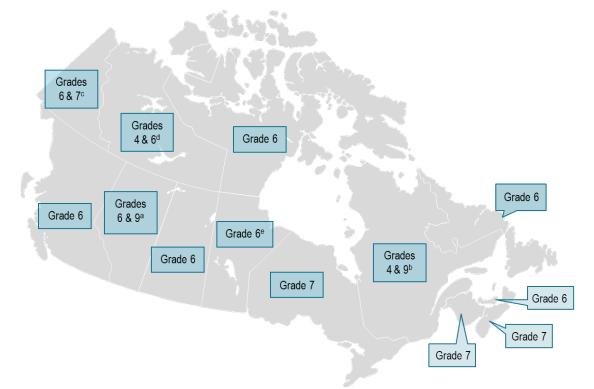


FIGURE 1. Eligibility for school-based publicly funded HPV vaccine programs in Canada

Sources: BC (4,26); AB (27); SK (28–30); MB (31,32); ON (4,29,33–35); QC (36,37); NB (38); NS (39); PE (40,41); NL (42,43); YU (44); NT (45,46); NU (4,47)

Notes.

- a Grade 9 catch-up program
- b Since September 2020, the program provides one dose of Gardasil®9 in grade 4 and one dose of Cervarix® 60 months later (grade 9 [Secondary 3])
- c Catch-up program on all immunizations for grade 7 students due to COVID-19
- d School-based program starts in grade 4 or 6 depending on community
- e Catch-up vaccinations offered due to COVID-19 pandemic (based on individual school to offer catch-up programs)

¹ Working in parallel, the Canadian Partnership Against Cancer published a resource to visually display eligibility for publicly funded HPV vaccines: <u>HPV vaccine access in Canada (2022)</u>



TABLE 1. Age-based eligibility for publicly funded HPV vaccines in Canada

Jurisdiction	ons considered higher	ered higher risk (upper age limit)			
(Sources)	Eligibility (upper age limit)	HIV+	MSM	Specific medical conditions	Other higher risk populations
BC (26,48)	26ª	26	26 ^b		B: 18º 26ª
AB (27,29)	≤26				
SK (28–30)	≤27 ^e			Unspecified ^f	
MB (31)	No age limit ^g	B/M: 26 G/W: 45	26	B/M: 26 ^h G/W: 45 ^h	26 ^d B/M: ≤18 ⁱ & 26 ^j G/W: 45 ^j
ON (4,29,33–35,49)	≤18 ^k		≤26		≤26 ⁱ
QC (36,37,50)	<18 ^m	≤45	≤26	≤45 ⁿ	
NB (38)	≤27°				
NS (39,51,52)	≤18 ^p	≤45	≤45		
PE (40,41)	No limit ^q	No limit	No limit	B/M: 26 ^r G/W: 45 ^r	B/M: 26 ^s G/W: 45 ^s
NL (42)	No limit*t				
YU (29,44,53–55)	26 ^u	45	26 ^v		26 ^w
NT (45,46)	26				
NU (4,47,56)	18 ^x				

Abbreviations: MSM (Men who have sex with men); M (Men); W (Women); B (Boys); G (Girls)

Notes.

- * Data provided by the Canadian Partnership Against Cancer
- a Catch-up program for anyone who missed vaccine in grade 6 but still initiated vaccination series before 19th birthday (for boys, only applies if born in 2006 or later)
- b Includes individuals who are not yet sexually active but questioning their sexual orientation

c Boys who are in the care of the Ministry of Children and Family Development or youth custody service centres, or who are street involved

- d Transgender, Two-spirit, and non-binary individuals
- e Females born since January 1, 1996; Males born since January 1, 2006
- f Unspecified age range and medical conditions
- g Females born on or after January 1, 1997; Males born on or after January 1, 2002; Any individual who missed one or more doses of the vaccine in school (commonly referred to as "once eligible, always eligible")

h Includes those with immunodeficiencies, current or recurrent respiratory papillomatosis, and who are under the care of a hematologist or oncologist from Cancer Care Manitoba with certain conditions; or newly diagnosed high-grade cervical histopathology (W only)

- i Males ≤18 who have been/are incarcerated
- j Victims of sexual assault

k Catch up program for all students who missed the vaccine series in grade 7; Students eligible until end of grade 12 (≤18)

I Some individuals who identify as transgender if they have not started their vaccine series before September 5, 2017

M All students ≤18 who missed vaccine as part of school-based program; Individuals can complete the vaccine series after age 18 if first dose is administered before age 18

n People who are immunocompromised

- o Females born in or after 1995; Males born in or after 2005
- p All students ≤18 who missed vaccine as part of school-based program
- q Catch up program for anyone who missed vaccine in grade 6 (since 2007 for females and 2012 for males)
- r With a history of anal-genital warts (M &W); and/or abnormal pap-smear (W)
- s If having unprotected sex with multiple partners
- t Catch-up program for anyone who missed the vaccine in grade 6 (since 2007 for females and 2017 for males)
- u Catch-up program for all Yukoners if missed vaccine in grade 6
- v If age 9–26 at time of first dose
- w Transgender individuals if age 9–26 at time of first dose
- x Catch-up program for all individuals ≤18 or until end of grade 12 if they would have been in grade 6 in 2017–18 or later and missed vaccine in school



Our search found that the price per dose of HPV vaccines vary from \$110-230 per dose, depending on the vaccine and jurisdiction (34,48,51,57,58). Sources from the Canadian Partnership Against Cancer report that Merck Canada (developer of the Gardasil® and Gardasil®9 vaccines) lists the price per dose of the Gardasil®9 vaccine across all PTs as \$170.87. The total OOP costs for consumers ineligible for publicly funded programs may be higher, as pharmacies and other healthcare clinics can mark-up the price and charge injection fees for administration – e.g., \$20 or more in British Columbia (48), and \$40 in AB for a one-time injection fee (57).

The sections below elucidate findings from the academic literature related to the experiences of eligibility and cost for HPV immunization in Canada.

Cost as a Barrier to HPV Immunization

Direct costs (out-of-pocket)

OOP cost for HPV vaccination is seen as an important factor for vaccine uptake in the literature. Specifically, a study analyzing Alberta's digital HPV Vaccine Decision Aid Tool reported that over 50% of its users inquired about the cost of the vaccine (59). Numerous studies reported the OOP cost of the HPV vaccine as a substantial barrier to immunization for various populations in Canada (60–70). Notably, the cost of the HPV vaccine was reported by over 42% of participants as a reason not to get vaccinated in a randomized control trial of women aged 18–45 years in Quebec (60). Similarly, in a cross-sectional survey among university students in Ottawa, over 45% of participants reported cost as an influential barrier to HPV vaccination (61). The authors stated that the cost of the vaccine could partly explain why some respondents wanted to defer their vaccination to the future (61).

The majority of the studies focused on understanding HPV vaccine uptake from the public's perspective, while several studies also targeted the views of healthcare providers (63,67,68). Notable findings included a 2019 cross-sectional survey of over 400 healthcare providers, in which 92–95% of respondents reported cost of the HPV vaccine as the biggest barrier for their patients (68). Additionally, certain physicians interviewed as part of the HPV Screening and Vaccine Evaluation (HPV-SAVE) study that investigated vaccine decision-making amongst older GBMSM living with HIV in Toronto, reported that OOP cost of the vaccine greatly limited their recommendation of the vaccine for their GBMSM patients older than 26 (63). The authors described this as an "economic-evidentiary conundrum" where it was unclear by national immunization guidelines whether vaccinating at an older age justified the OOP costs to patients; However, some physicians insisted that all their patients should be vaccinated regardless of age (63).

Empirical evidence has also shown varying levels of HPV vaccine uptake in Canada when the source of funding was considered. A subgroup analysis within a systematic review found that participants of publicly funded HPV vaccine programs were 4.92 times more likely to be vaccinated compared to those who had to pay OOP (66.95% vs. 13.58%, respectively) (71). Similarly, a longitudinal study using surveys found that Canadian jurisdictions with funded HPV vaccine programs for boys during both survey collection time periods (2016 and 2017), had higher odds of vaccination for boys than jurisdictions without funding for boys during both time periods (14).



Indirect cost

Other barriers mentioned in the literature include indirect costs such as time spent locating and traveling to vaccine clinics, as well as vaccine administrative costs. Specifically, Bernard-Genest et al. (2021) found that within their study evaluating telephone call reminders for HPV immunization among women in Québec, 16% of participants reported lack of time to go to vaccination clinics as a barrier. Additionally, 5% of respondents within a study exploring factors related to HPV and immunization among university students in Québec reported lack of time and a "lengthy process" for vaccination (66).

A policy analysis by Shapiro et al. (2016) reported that when vaccine programs are not publicly funded and not provided in schools, parents of school-age children incur additional time pressures to schedule appointments and submit private insurance claims. Lastly, some physicians in a qualitative study exploring healthcare providers' views on HPV vaccine uptake amongst immigrant and refugee populations in Ottawa described the challenges associated with navigating a new healthcare system (67). Some of the challenges included time and logistical constraints to find vaccination clinics/ healthcare providers, especially for newcomers who do not qualify for provincial health insurance (67).



Populations Impacted by Current Policies

Although most PTs in Canada have made changes to their HPV immunization programs to include more population groups based on risk for HPV, many studies have reported disparities in access that disproportionately impact certain populations. In the literature, cost is again seen as one of the factors for reduced HPV vaccine uptake for these populations.

Age was reported by Bird et al. (2017) in their systematic review to affect HPV vaccine uptake, as participants 18 or younger were 4.92 times more likely to be vaccinated for HPV than participants older than 18. Additionally, the majority of the targeted populations in the studies that reported cost as a barrier for HPV vaccination were adults who had to pay OOP and/or who did not have substantial private health insurance coverage for the vaccine (60–62,64–66).

Alongside and intersecting with increasing age, the consideration of gender, sexual orientation, and sexual behaviour were also emphasized in the studies that reported cost as a barrier to HPV vaccine uptake. In particular, older GBMSM living with HIV were reported to experience barriers to accessing the vaccine. Many PTs (such as Ontario) have an age cap of 26 among GBMSM for free vaccine eligibility, and do not take HIV status into consideration (62,65). Considering that GBMSM living with HIV have the highest risk for anal cancer, GBMSM living with HIV are disproportionally impacted by HPV (65). Additionally, men who do not identify as GBMSM or are older than 27 years in many PTs have to pay OOP for the HPV vaccine, even though they can still acquire high-risk HPV (65).

Women aged 20–26 years old was also mentioned as a "catch-up" population in the literature, stating that increased HPV prevalence and infection with high-risk HPV types can be persistent in this age group (66). Additionally, in a systematic review, women aged 18-30 were reported to be "most at risk of [HPV] infection", with disparities in HPV vaccine uptake persisting by "age group and setting" (3). The systematic review cited the 2014 Adult National Immunization Coverage Survey² that reported older women to have lower HPV vaccine uptake than younger women (44.7% and 8.3% uptake rates for 18–26 and 27–45 years, respectively) (3).

Immigrant and refugee populations also experience access barriers as reported in the literature. In addition to possible issues with provider/clinic accessibility, direct cost barriers were cited by a sample of Ottawa physicians as the biggest limitation of HPV immunization for adult newcomers (67). Many providers did not recommend the vaccine to many of their patients with low socio-economic status. Similarly, within a sample of adult and young adult newcomers interviewed in Ottawa regarding their knowledge and beliefs about the HPV vaccine, one-third reported that they would accept the vaccine regardless of cost, while two-thirds were undecided or would only accept the vaccine if it were free (70).

² The most recent Adult National Immunization Coverage Survey is from 2016 and reports HPV vaccine coverage for females aged 26 and under as 75.0%, and from 27-45 years as 10.6% (73).



Conclusions

This rapid review uncovered wide variation in population eligibility criteria for publicly funded HPV immunization programs across Canada and in the OOP costs for excluded populations, gaining insights from the published literature on the impacts of the direct and indirect costs. Overall prohibitive costs (both direct and indirect) for HPV immunization are experienced by many populations living in Canada. Key considerations identified in the reviewed literature to aid in improving access to HPV vaccines are outlined below.

1. Continue to expand eligibility criteria for publicly funded HPV vaccine programs

The *Canadian Immunization Guide (CIG) for Health Professionals* recommends the HPV vaccine for all populations from age 9 to 27 (19). Currently, three jurisdictions—Alberta, Yukon, and the Northwest Territories—follow this guidance. Other jurisdictions, such as British Columbia, Saskatchewan, Manitoba, New Brunswick, and Prince Edward Island, also covers individuals under 27 years old, but with some gender and age restrictions. It is important to note that most PTs classify their eligibility criteria only within the gender binary of male/boy/men and female/girl/women, which can exclude gender-diverse populations. Expanding eligibility criteria of publicly funded HPV vaccine programs to all genders until age 27 across PTs would increase vaccine access. Moreover, the CIG does "strongly consider" the HPV vaccine for GBMSM older than 27, and recommends the vaccine "may be administered to women 27 years of age and older at ongoing risk of HPV"(19). Some PTs have expanded their eligibility for certain populations until age 45 including: Manitoba, Nova Scotia, Prince Edward Island, Yukon, and Québec. Although vaccine efficacy and cost effectiveness to vaccinate populations older than age 27 is debated in the scientific community (74,63,75), existing and further research concerning the efficacy and cost-effectiveness of the HPV vaccine in populations older than 27 could inform future immunization policy.

2. Improve public awareness regarding eligibility and OOP costs of the HPV vaccine

Clear communication about eligibility criteria for the HPV vaccine and any associated OOP costs may further improve access to the vaccine. Alberta's online HPV Decision Aid Tool, for example, is a promising approach that helps an individual determine eligibility under that province's public program (59). Prior health promotion strategies for the HPV vaccine have primarily targeted cisgender girls and women, but future health promotion campaigns should be diverse in their target populations based on age, gender, sexual orientation, and sexual behaviour (62). Doing so could encourage vaccination, especially in sexual minority and gender-diverse populations. Additionally, health promotion campaigns could be widely advertised in various locations such as community health centres, colleges and university campuses, on transit systems, and in other public spaces to improve awareness of eligibility, costs and benefits of the vaccine.

3. Ensure convenient access to HPV vaccinations

Several studies suggested ways in which obtaining HPV vaccination could be more convenient for various populations, in addition to providing public funding. Examples include, but are not limited to: government-subsidized HPV vaccination programs in post-partum settings (60), administering the HPV vaccine at the same time as other needed vaccines (16) as well as together with other sexual healthcare services (64), and holding medical student-and-resident run HPV vaccination clinics at universities and colleges (66). Another way of increasing convenience would be to remove the requirement for HPV



vaccine prescription, or to allow pharmacists in all PTs to prescribe HPV vaccines. As of October 2022, pharmacists with additional prescribing authority in Alberta, Saskatchewan, Québec, New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador can prescribe HPV vaccines (76). Pharmacists in Manitoba can prescribe the HPV vaccine, but only for populations eligible for the publicly funded program (76). Additionally, vaccines that are part of a routine immunization program in British Columbia and vaccines included in the Québec Immunization Protocol (PIQ) do not require a prescription (76,77).

4. Support healthcare provider recommendation and education of the HPV vaccine, especially for populations considered higher risk for HPV

Many authors have stated the importance for healthcare provider recommendation and education regarding the vaccine, especially for populations considered at higher risk and/or impacted by current policies due to cost (14,62–67,69,70). The literature reported primary care and gynecology clinics, sexual health and HIV clinics, and student health clinics to be important locations where discussions regarding HPV risk, vaccine recommendation, and eligibility for publicly funded vaccines can occur from provider to patient (65,66). Furthermore, recommendations from healthcare providers serving newcomers in Canada reported the need for having the HPV vaccine at hand in primary care clinics, and having culturally and language-appropriate resources available (67).

5. Strengthen HPV immunization record systems

Finally, some studies called for the improvement of HPV vaccine record systems in Canada. Specifically, two studies recommended a national immunization records database that includes HPV vaccine records (3,67). A national immunization records database could aid in provider recommendation of the HPV vaccine for individuals moving from other PTs (67). Furthermore, having vaccine records that collect socio-demographic information could help during program evaluations to identify sub-populations that would benefit from targeted interventions to reduce disparities in HPV vaccine uptake (3). Additionally, having a centralized digital vaccine record system available to the public would allow individuals to keep track of their immunizations, including HPV (67). Currently, British Columbia and Alberta have electronic immunization record systems that can be accessed via web portal and/or mobile app without having to contact public health units and/or healthcare providers (78,79).



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Appendix A. Detailed Methodology

Academic Literature Review

A rapid review of the academic literature was conducted in May 2022 in six databases (Medline, Embase, PubMed, CINAHL, EconLit, and Scopus) using predefined search criteria, and a combination of Medical Subject Heading (MeSH) terms and text words for HPV, the HPV vaccine, OOP expenditures, and Canada (see Table A1).

TABLE A1. Search terms and text words

Condition	Coverage	Setting
"HPV vaccine"	"Health expenditures"	Canada
"Human papillomavirus vaccine"	"Out-of-pocket"	Canadian
"Human papilloma virus"	"Financial"	(province/territory)
"Papillomavirus vaccines"	"Utilization"	
"HPV vaccin*"	"Health care cost"	
"HPV immuniz*"	"Drug cost"	
	"Cost*"	

TABLE A2. Electronic database search strategy (May 27, 2022)

MEDLINE	SYNTAX	RESULT
1	"HPV vaccine".mp. or exp Papillomavirus Vaccines/	10896
2	"Human papillomavirus vaccine".mp.	1793
3	(("human papilloma virus" or "HPV") adj2 vaccin*).mp. [mp=title, abstract, original title, name of substance word, subject heading word,floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, raredisease supplementary concept word, unique identifier, synonyms]	10497
4	"HPV vaccin*".mp.	9472
5	"HPV immuniz*".mp	283
6	"papillomavirus vaccine".mp. or exp Papillomavirus Vaccines/	9933
7	"health expenditures".mp. or exp Health Expenditures/	26357
8	exp Insurance, Health/ or "out-of-pocket".mp.	162057
9	"financial".mp.	126870
10	"utilization".mp. or exp Drug Utilization/	259360
11	"health care cost".mp. or exp Health Care Costs/	72581
12	"drug cost".mp. or exp Drug Costs/	18075
13	"cost*".mp.	827012
14	canada.mp. or exp Canada/	218738
15	Alberta.mp. or exp Alberta/	14722
16	"British Columbia".mp. or exp British Columbia/	15900
17	Manitoba.mp. or exp Manitoba/	5589
18	"New Brunswick".mp. or exp New Brunswick/	1663
19	"Newfoundland and Labrador".mp. or exp "Newfoundland and Labrador"/	1796
20	Nova Scotia.mp. or exp Nova Scotia/	4002
21	Ontario.mp. or exp Ontario/	47893
22	Prince Edward Island.mp. or exp Prince Edward Island/	690
23	Quebec.mp. or exp Quebec/	22037



24	Saskatchewan.mp. or exp Saskatchewan/	4342
25	Northwest Territories.mp. or exp Northwest Territories/	786
26	Nunavut.mp. or exp Nunavut/	708
27	Yukon.mp. or exp Yukon Territory/	792
28	1 or 2 or 3 or 4 or 5 or 6	13393
29	7 or 8 or 9 or 10 or 11 or 12 or 13	1248746
30	14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27	239287
31	28 and 29 and 30	63
32	limit 31 to yr="2016-Current"	25

Articles were included if they were in English, with a publication date of 2016 or later, available publicly or through the University of Toronto Library, published in Canada, and mentioned HPV vaccination cost (e.g., OOP, perceived financial barriers to vaccination, and/or administrative costs to deliver vaccine). Papers were excluded if they focused *only* on cost effectiveness, parental decision-making processes involving HPV vaccination, and school-based HPV vaccination programming. Additionally, we excluded studies that were considered commentaries and dissertations. See Table A3 for a list of inclusion and exclusion criteria.

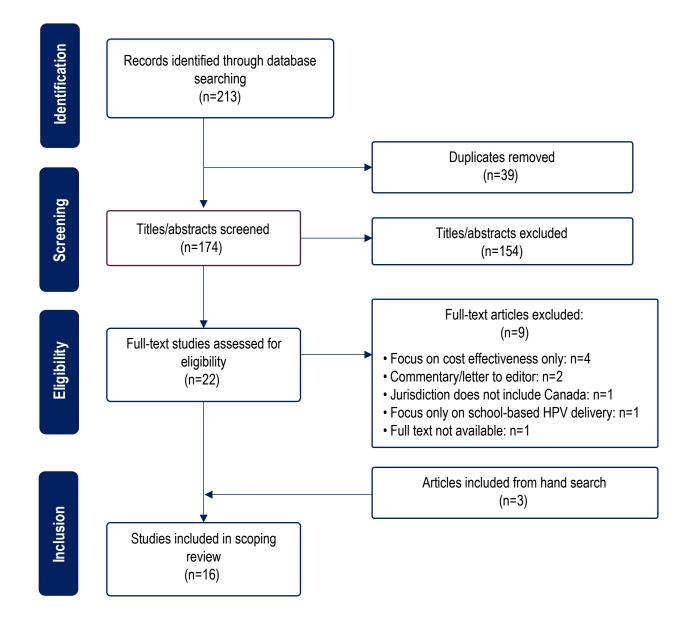
TABLE A3. Inclusion/exclusion criteria

Inc	lusion criteria	Exc	lusion criteria
-	Published in 2016 to present	-	Published <2016
-	Published in Canada	-	Setting outside of Canada
-	English	-	Any article with no mention of cost
-	Reports cost (e.g., out of pocket, perceived	-	Only focuses on cost effectiveness
	financial barrier, administrative) associated with	-	Study type (e.g., commentary, dissertations)
	HPV vaccine		
-	General reviews of HPV vaccine in Canada, for		
	example: uptake, HPV vaccine administration		
	programs, drug coverage if COST is mentioned		
-	Examines funding/access of HPV vaccine amongst		
	varying population groups (including school-based		
	programs if certain population are excluded)		

Three steps were involved in the screening process and data extraction stage. The results of the search were imported into *Covidence*, an online software tool for systematic reviews. First, duplicates were removed using Covidence, and the remaining articles were screened by their titles and abstracts for applicability. Second, full-text articles were reviewed by two authors (IU, MS) to assess their relevance to the study inclusion criteria. Articles whose inclusion was unclear were noted and discussed with the other reviewers until consensus was reached. Third, data extraction from the studies was performed by two authors (MS, MA) using a spreadsheet. Variables that were extracted included: study design, jurisdiction, target population, detailed description of costs (i.e., actual cost, perceived cost), recommendations or policy implications, and references to inequities.



FIGURE A1. PRISMA Flowchart



Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta analyses: the PRISMA statement. PLoS Med. 2009 Jul 1;6(7):e1000097. doi:10.1371/journal.pmed1000097



Appendix B. Summary of the Academic Review Literature

TABLE B1. Summary of academic literature findings regarding effects off OOP costs for HPV vaccines in Canada

Author (year)	Type of Paper	Jurisdiction	Population Targeted	Summary of Results	Recommendations and Policy Implications
Bernard- Genest et al. (2021)	Randomized controlled trial (single-blind)	QC	Females aged 18–45 without prior HPV immunization	 Barriers reported by participants: Cost of vaccination (42.3%) Lack of time to go to vaccination clinics (16.5%) 43% of patients currently living in Quebec do not have private health insurance coverage 	 Public insurance should offer coverage for HPV immunization to more people, e.g., government financial aid for vaccination program in post-partum setting.
Bird et al. (2017)	Literature search	CA	Males and females • 2 studies with participants >18 who had to pay OOP for vaccine • 10 studies with participants ≤18 whose vaccine was publicly funded	 Participants in publicly funded programs were 4.92 times more likely to be vaccinated for HPV compared to those who had to pay OOP. Mentions of equity: As of 2015, only 4 provinces (AB, NS, BC, PEI) offered free vaccination to males. 	 Expand HPV vaccination programs to include young males and older females. Subsidize the costs of vaccination and develop a national immunization surveillance program.
Fernandes et al. (2018)	Observational study; Cross- sectional online survey	ON	Females aged 18–25	 Cost was one of biggest obstacles to vaccination for the unvaccinated women: 3.9% of the group was willing to pay the actual cost of the vaccine series (\$100-\$175/dose). 55.1% of the unvaccinated women were willing to pay up to \$100 for the entire vaccine series. 10.7% of this group was unwilling to pay regardless of cost. Vaccinated women had significantly more positive 	Offer HPV vaccination for women aged 18– 25.
Grace et al. (2018)	Qualitative study; Semi- structured interviews	ON	Males aged 31–68	 views towards accepting the vaccine than non-vaccinated women. Most vaccinated participants relied on private insurance to cover the cost of the vaccine; some stated that cost was the main barrier to vaccination. 	 Physicians should recommend that their patients get the HPV vaccine while clearly communicating the benefits.



Author (year)	Type of Paper	Jurisdiction	Population Targeted	Summary of Results	Recommendations and Policy Implications
				 Few participants were aware that the HPV vaccine is freely available to men ≤26 in Ontario. Most believed that it is important to offer such coverage even if they were not able to benefit personally. A clear and strong recommendation by a physician was a primary facilitator to be vaccinated. 	 Important for physicians to avoid suggesting that the vaccine is less essential because of cost barriers.
Grace et al. (2019)	Qualitative study; Semi- structured interviews	ON & BC	Physicians (focusing on their GBMSM patients)	 Physicians said that they would dearly recommend the HPV vaccine to GBM aged ≤ 26 or those with health insurance. Some physicians explained that the only potential negative "side effect" of the vaccine was the financial burden. The current "patchwork" system of drug coverage in Canada means that only a subgroup of older GBM who can afford the vaccines are benefitting from them. 	 Need to examine the role of socioeconomic status (SES) in vaccine decision-making and recommendation practices. Improve patient health literacy through public health messages and provider communication. Consider the upstream determinants of vaccination access in Canada.
Grewal et al. (2021)	Observational study; Cross sectional cohort study	ON	Men aged ≥16 years (mean age was 51years)	 None of the vaccinated men reported getting the vaccine through public coverage (even if eligible) 39% used full private insurance coverage 33% paid entirely OOP (\$420-\$560 for three doses) 17% used partial private insurance coverage 	 Primary care and HIV clinics could be the best places to begin implementing interventions to increase uptake of HPV vaccinations. Need to improve physician and patient awareness regarding coverage for the vaccine.
				 Mentions of equity: Clear differences in demographics (i.e., SES, age, etc.) between those vaccinated and unvaccinated. The substantial cost of the HPV vaccine may prevent physicians from bringing up the topic. 	



Author (year)	Type of Paper	Jurisdiction	Population Targeted	Summary of Results	Recommendations and Policy Implications
				 40% of unvaccinated men had some form of extended health coverage outside government benefits. 	
Grewal et al. (2021)	Analysis of the ENGAGE study (cohort study)	BC, ON, QC	Men aged 16-80 who had sex with another man in the past six months	 Men ≥27 with private insurance were nearly twice as likely to be vaccinated compared to men with no insurance coverage. Men who had a STI/HIV test or visited their HIV specialist within the last 6–12 months were also more likely to get vaccinated if they had private insurance. Mentions of equity: Men identifying as Latin American were less likely to initiate vaccination compared to white men. May be attributed to several factors (i.e., SES, less comfort disclosing sexual preferences, etc.) to health care providers, and lack of knowledge around HPV. 	 Vaccine uptake would likely be increased by implementing a universal vaccination program. Bundling HPV vaccination with other sexual healthcare services may be a solution to help increased uptake Need to incorporate conversations with healthcare professionals around HPV risk, cost, and potential insurance coverage options for older men ineligible for publicly funded programs.
Highet et al. (2021)	Observational study; Cross- sectional analysis	AB	Unspecified	 Individuals who were considering the vaccine for themselves were more likely to be concerned about the cost of the vaccine. The most frequently asked question was "How much does it cost?" (50.5%) 	 Reducing structural barriers should be prioritized as a means for increasing HPV immunization rates among individuals aged 18–26. Important to continue monitoring the evolution of questions and concerns about the HPV vaccine in Alberta—now that eligibility to receive the vaccine at no direct cost has been extended up to ≤26.
Piedmonte et al. (2018)	Phase 1: Observational study; Self- administered questionnaire Phase 2: Experimental study	QC	University students with mean age 24.8 ± 7.5	 25% of participants had not received HPV vaccine due to financial barriers—cost ranged from \$90–\$160/dose. Many students were not aware of their insurance policy. 5% reported the lengthy process/lack of time was barriers to vaccination. 	 Continue to employ educational campaigns on university campuses since they increase vaccine uptake. Should also focus on identifying barriers to vaccination to guide future initiatives and maximize impact.



Author (year)	Type of Paper	Jurisdiction	Population Targeted	Summary of Results	Recommendations and Policy Implications
Rubens- Auguston et al.Qualitative study; Semi- structured interviews	dy; Semi- on their newcomer ctured patients)	 Cost was described by many physicians as the biggest barrier to vaccine uptake. One physician argued that assuming newcomers cannot afford the HPV vaccine was a barrier in itself. 	 Addressing cost at the institutional level is critically important because it influences provider's decision to recommend—or not — the vaccine, which in turn impacts vaccine uptake 		
				 Mentions of equity: Cost severely limited vaccine uptake, and greatly impacted providers' recommendation of the vaccine given some of their patients' low SES. Some clinics would serve refugees without 	
				health insurance, but these are difficult to find.	
Shapiro et al. (2016)	Policy analysis	CA	Men/boys	 Routine HPV vaccination for boys appears to be cost effective. The vaccine is about \$150/dose and multiple doses are recommended. When the government does not fund a vaccine, it appears as though Canadians may perceive vaccination as unnecessary. Additional barriers to vaccination when not part of publicly funded program include logistical challenges such as scheduling appointments and making private insurance claims. 	 Need to reduce the cost of the vaccine by negotiating price with pharmaceutical companies and implementing a two—rather than three—dose schedule. Important to include all men in vaccination programs because: HPV infection also causes cancer in males Current rates of female vaccination are too low to protect heterosexual males MSM are not protected by female-only programs
Shapiro et al. (2017)	Qualitative study; Multiple streams analysis	CA	Males	 Expanding the HPV program to males can save lives, reduce disease and be cost effective; the health care system could save over \$13.4 million. Mentions of equity: Funding HPV vaccination for males will increase equity. Herd immunity from vaccinating only females does not protect MSM; some even argue that it doesn't adequately protect heterosexual men. 	 Priority should be to focus on lowering vaccine costs through price negotiations and reducing delivery costs (by administering more than one vaccine at the same time). Need to analyze what led to policy development in Canada, since Canada is an international leader in funding HPV vaccination for boys.



Author (year)	Type of Paper	Jurisdiction	Population Targeted	Summary of Results	Recommendations and Policy Implications
Shapiro et al. (2022)	Observational study; Survey and logistic regression	CA	Parents of children aged 9–16	 Boys in areas where vaccine funding was available were more likely to be vaccinated than boys in areas without funding Vaccination was associated with consistent determinants in boys and girls including health care provider recommendation and perceived affordability. 	 Publicly funded school-based programs are very important for vaccine uptake and therefore should be a priority.
				Mentions of equity:	
				 Various socio-demographic, psychosocial and policy decisions continue to pose challenges for immunization programs. 	
Steben et al. (2019)	Observational study; Cross- sectional survey	CA	Physicians	 Cost was reported as the number one barrier to vaccination by over 92-95% of physicians. 	 Professional development activities for physicians and health care providers should be directed to: Increase knowledge of HPV Increase the capacity of providers to offer preventive counselling and vaccination to adults.
Steben et al. (2019)	Observational study; Cross- sectional survey	CA	Women aged 18-45; Men aged 18-26	 Not having a recommendation from a physician was the most commonly reported barrier to vaccination—reported by 38% of respondents. 	 Critical for physicians to communicate the benefits of vaccination to unvaccinated patients and prescribe the vaccine whenever possible.
				 Cost was only reported as a barrier to vaccination by 18–20% of respondents. 	 Public health messages regarding HPV vaccination must be inclusive of all adults and should convey the significance of HPV vaccination beyond adolescence.
Wilson et al. (2021)	Qualitative study; Survey and semi- structured interviews	ON	Newcomers to Canada (i.e., immigrants, refugees, students, undocumented migrants)	 One-third of respondents indicated that they would get vaccinated even if they had to pay OOP. The remaining two-thirds were either unsure or stated that they would only accept the vaccine if it was free. 	 Newcomers should be informed regarding HPV vaccines and their availability. This can be achieved by: Providing culturally and language- appropriate information in doctors' offices or in the community; and Educating them during the immigration process.



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