

TITLE

HPV prevalence, vaccination coverage and intention to get vaccinated among gay, bisexual, and other men who have sex with men: Evaluation of Quebec's (Canada) HPV vaccination program

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ABSTRACT

Objectives

In Quebec, Canada, vaccination against human papillomavirus (HPV) has been publicly-funded since January 2016 for gay, bisexual, and other men who have sex with men (GBM) aged ≤ 26 years. The study aimed to analyze data collected in Greater Montreal (Engage study) to evaluate the HPV vaccination program for GBM in Quebec.

Study Design

Engage is a cohort of sexually active GBM aged ≥ 16 recruited via respondent-driven-sampling (RDS) in Canada. Participants completed a questionnaire and tested for sexually transmitted infections.

Methods

RDS-II weights were applied to adjust for recruitment. Subgroups were compared using standardized mean differences. Odds ratios of HPV vaccination and prevalence ratios of anal HPV infection adjusted for potential confounders were estimated using robust regression models.

Results

Of 1179 participants, 309 were eligible for free HPV vaccination. Vaccine coverage among eligible GBM was 42%. Among those who disclosed same-sex sexual activity and discussed HPV vaccination with their healthcare provider, coverage reached 82%. Anal HPV prevalence among eligible GBM was 26.5% for ≥ 1 HPV-6/11/16/18 genotypes without significant difference between vaccinated and unvaccinated individuals. Among unvaccinated GBM aged ≤ 26 who were aware of the vaccine, 60% intended to get vaccinated within the next year.

Conclusions

One to two years after GBM aged ≤ 26 were included in the Quebec HPV vaccination program, 42% of eligible GBM in Greater Montreal had been vaccinated. Anal HPV prevalence was high among GBM. Vaccinees were more likely to self-report a prior STI diagnosis. Offering vaccination to all preadolescents in schools appears essential to maximize vaccination benefits.

1. INTRODUCTION

In Quebec, Canada, free human papillomavirus (HPV) vaccination has been available since January 2016 for gay, bisexual, and other men who have sex with men (GBM) aged ≤ 26 [1], and since September 2016 for Grade 4 boys (9-10-years-old). Free HPV vaccination became available to immunocompromised individuals or people living with Human immunodeficiency virus (HIV) aged ≤ 26 in 2014 (≤ 45 since 2022)[1]. The quadrivalent vaccine (targeting HPV-6/11/16/18 genotypes) has been available for men through the private market since 2010[2]. The nonavalent vaccine replaced the quadrivalent in September 2016. Several reasons justified the inclusion of GBM in the program, including the high burden of HPV-related infections and lesions among GBM[3,4].

The prevalence of ano-genital HPV infections has been shown to be at least threefold higher among GBM than among heterosexual men[3–5]. HPV infections cause anogenital and oropharyngeal cancers[6,7]. Rates of anal cancers among GBM have been estimated to be 30-100 higher than those of the general male population[8]. In Quebec, approximately 66 new anal cancer cases are diagnosed annually, with approximately 90% caused by HPV, mostly HPV-16[3,6], making most anal cancers vaccine-preventable.

HPV vaccine clinical trials have shown high efficacy in males, preventing 84% of incident anal vaccine-type infections in GBM aged ≤ 26 who were HPV-naïve and had ≤ 5 lifetime sexual partners[9]. Additionally, effectiveness against anal HPV in GBM is highest with early HPV vaccination before sexual activity debut[10]. Limited data are available on HPV vaccination acceptability and effectiveness in real-world settings among sexually active GBM who may have been HPV-exposed before vaccination[11,12].

The Engage study (<https://www.engage-men.ca/>) is a Canadian cohort initiated in 2017 in the greater regions of Montreal, Toronto and Vancouver among sexually active GBM aged ≥ 16 . The study examined GBM's sexual health, presenting an opportunity to evaluate Quebec's vaccination program among GBM. Some HPV-related findings from the Engage study have been previously published[13–16]. In 2017-2019, HPV vaccination coverage (≥ 1 dose) was 26–35% for GBM aged ≤ 26 [13]. Pooled anal HPV prevalence among GBM aged ≤ 30 was 66.7% (95%CI: 59.7–73.6) for all genotypes and 25.4% (95%CI: 19.5–31.3) for HPV-6/11/16/18 genotypes[14]. These papers did not report on the acceptability of discussing sexual practices with a healthcare provider to obtain free HPV vaccination and the age at which GBM would be comfortable doing so.

Using data from the Engage Study (Greater Montreal area), we aimed to evaluate the HPV vaccination program for GBM. Specifically, we: (1) assessed HPV vaccination coverage, characteristics of vaccinated and unvaccinated GBM, as well as factors associated with vaccination; (2) examined disclosure of same-sex sexual activity to healthcare professionals to obtain the HPV vaccine; (3) measured and compared anal HPV prevalence between vaccinated and unvaccinated GBM; and (4) evaluated intention to get vaccinated among unvaccinated GBM still eligible for free HPV vaccination.

2. MATERIALS AND METHODS

2.1. Participants, Recruitment and Data Collection

We used data from the Engage study that enrolled GBM in Greater Montreal, including the Island of Montreal, Laval, and Longueuil from February 2017 to June 2018. Participants were recruited via respondent-driven sampling (RDS), a chain-referral recruitment method designed for sampling hard-to-reach populations[17].

At enrollment, to be eligible, participants had to: 1) be aged ≥ 16 , 2) identify as a cis- or transgender man and 3) have had recent sexual intercourse with another man (past 6 months).

Participants completed a questionnaire (Appendix A for the questions pertaining to key variables) and underwent sexually transmitted infections (STI) screening. Only participants aged ≤ 30 were tested for HPV infections to focus on GBM mainly targeted by free HPV vaccination program. Men self-collected anal specimens using a moistened Dacron swab. Research staff explained self-collection procedures and provided illustrated and validated instructions to participants[18].

2.2. Variables of interest

2.2.1. Eligibility for Free HPV Vaccination

In Quebec, HPV vaccination has been offered free of charge to GBM aged ≤ 26 years since January 2016. For this analysis, we distinguished between participants who were eligible for free vaccination at program launch (age ≤ 26 years in 2016) and those who remained eligible at the time of enrollment (age ≤ 26 years at enrollment).

2.2.2. HPV Vaccination Status

Participants self-reported their vaccination status and age at vaccination. Considering the study period, we assume that most participants received the quadrivalent vaccine[1]. HPV vaccination (receiving ≥ 1 dose) was treated as a binary variable. Participants were classified as unvaccinated if they answered “no” or “unsure” regarding their vaccination status, or if they were unaware of the HPV vaccine.

2.2.3. Disclosure of same-sex sexual activity

Disclosure of same-sex sexual activity to healthcare professionals was examined among participants eligible for free HPV vaccination and who had a regular healthcare professional. When applicable, participants were asked their age at first disclosure. Responses < 9 years were considered invalid and excluded.

2.2.4. HPV Genotyping

HPV DNA was extracted from self-collected swab samples using the MasterPure DNA Purification Kit (Epicentre Biotechnologies) as described previously[15]. HPV identification was performed in two stages. First, all samples underwent a generic test to detect HPV DNA presence[19]. Second, HPV DNA-positive samples were genotyped

using the Roche Linear Array HPV that identifies 36 HPV genotypes[20]. Samples reactive for HPV52 in the Linear Array were then analyzed using a validated HPV52-specific real-time PCR assay[21]. To verify sample validity, a β -globin DNA sequence was amplified, and samples were considered valid if β -globin and/or HPV DNA was detected.

High-risk oncogenic HPV genotypes were defined according to the International Agency for Research on Cancer classification[22].

2.2.5. HPV Vaccination Intention

Intention to receive the HPV vaccine free of charge was assessed among unvaccinated participants aged ≤ 26 , as they were still eligible for free vaccination at the time of enrollment. Intentions were dichotomized as “likely/very likely” versus “undecided/unlikely/very unlikely”.

2.3. Statistical Analysis

RDS recruitment is known to oversample individuals who are more visible in the community due to its chain-referral approach[17]. Weighting[23] is commonly used to adjust RDS data. For each participant, the propensity for inclusion in the sample, known as visibility score[24], was imputed and inverted to derive RDS-II weights, which were applied to produce population-level inferences about GBM.

Unadjusted proportions were calculated to characterize the full sample. Standardized mean differences (SMD) were used to compare participants, e.g. vaccinated vs unvaccinated, with thresholds for negligible (<0.2), small ($0.2-0.5$), moderate ($0.6-0.8$), and large (>0.8) differences[25].

Odds ratios (ORs) of vaccination (≥ 1 dose) were estimated by robust logistic regression with RDS-II weights. Collinearity among factors was assessed using variance inflation factor. Model selection used the Akaike information criterion to avoid overfitting. Prevalence ratios (PRs) of HPV (6/11/16/18 types) between vaccinated (≥ 1 dose) and unvaccinated GBM were estimated using robust Poisson models with RDS-II weights. Potential confounders of the association between vaccination and HPV infection were identified through literature review and the authors' expertise. Effective confounders showing imbalance ($SMD > 0.2$) were included in the model regardless of statistical significance. Lifetime self-reported diagnosis of STI was additionally evaluated as an effect modifier by including an interaction term in the model, with stratified estimates presented to aid interpretation. Regression analyses were restricted to participants with complete data. Appendix B shows the participant flowchart outlining the number of participants included in each of the analyses.

All analyses were performed using R v4.1.2 (R Core Team, 2021).

2.4. Ethical approval

The Engage Montreal Study was approved by the research ethics board of the Research Institute of the McGill University Health Centre (#MP-CUSM-15-632).

3. RESULTS

3.1. Participants' characteristics

Overall, 1179 participants were recruited in greater Montreal. Half (52.8%) identified as French Canadian, 20.9% were ≤ 26 years-old, 14.0% immigrated to Canada (last 4 years), 44.4% had university-level education, 41.9% earned $< 20\,000$ CAD annually, 81.8% identified as gay, 27.0% smoked daily, and 67.5% had a regular healthcare provider. Self-reported lifetime prevalence of STIs and condylomas was 55.0% and 23.8%, respectively. Laboratory-confirmed HIV infection was detected among 18.3% of participants.

3.2. HPV vaccine coverage

Of 1179 participants, 309 were eligible for free HPV vaccination at program launch (January 2016). Among these, 125 (40.4%) reported ≥ 1 dose of vaccine before enrollment. The RDS-adjusted estimate of vaccine coverage among GBM eligible for free HPV vaccination was 41.5% (95%CI 35.3-47.9). The median age at first dose was 23 years (IQR: 21-27 years), and 98% were vaccinated after first sexual intercourse (Figure 1).

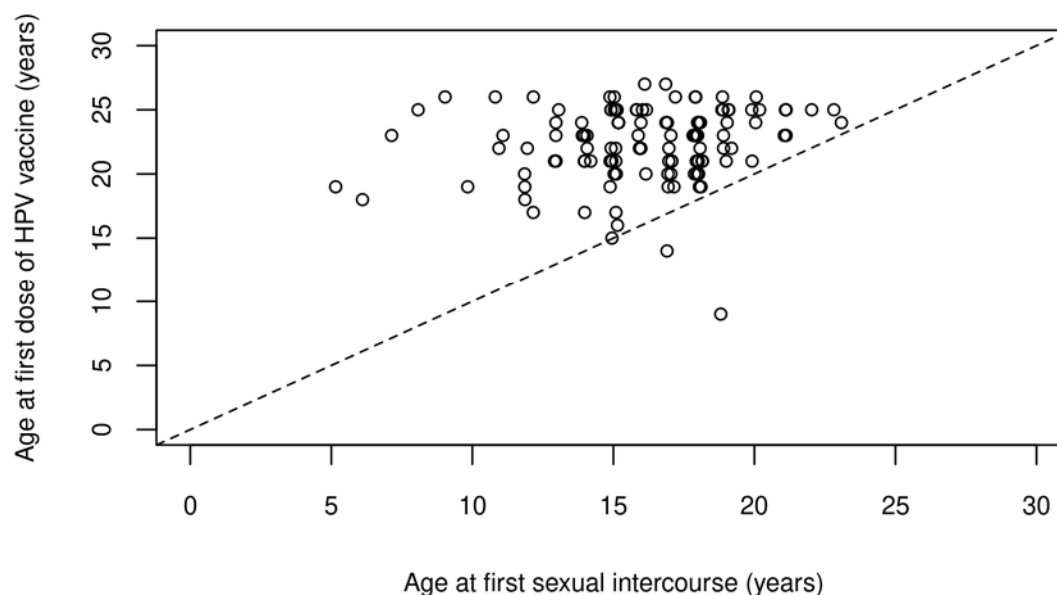


Figure 1 Age at first dose of HPV vaccine and age at first sexual intercourse among participants eligible for free HPV vaccination who reported having received ≥ 1 dose (n=125)

3.3. Differences between vaccinated and unvaccinated participants

The proportion of participants who reported having discussed HPV vaccination with a healthcare provider was 96.5% among vaccinated versus 18.3% among unvaccinated (SMD=2.4). The proportion of participants who knew that the HPV vaccine was recommended for GBM was 95.5% among vaccinated versus 45.5% among unvaccinated (SMD=1.4). Other differences with SMD>0.2 are shown in Table 1.

Table 1 Largest differences between unvaccinated and vaccinated (≥ 1 dose) GBM eligible for free HPV vaccination (n=309)

	Unvaccinated (n = 184) (%)	Vaccinated (n = 125) (%)	Standardize d mean difference
Having discussed the HPV vaccine with a healthcare provider	18.3	96.5	2.4
Knowing that the HPV vaccine is recommended for GBM	45.5	95.1	1.4
Having heard of the HPV vaccine	74.2	100.0	0.8
Self-reported past hepatitis A or B vaccination	55.4	89.7	0.8
Tested for STI or HIV (past 6 months)	42.8	80.3	0.8
Self-reported diagnosis of STI other than HPV-related (lifetime)	25.5	59.0	0.7
Self-reported diagnosis of condylomas (lifetime)	3.3	22.6	0.6
Having used HIV PrEP (past 6 months)	4.5	22.0	0.6
Having had ≥ 6 sex partners (past 6 months)	37.7	62.3	0.5
Having had ≥ 1 sex partners living with HIV (past 6 months)	7.3	26.6	0.5
Having a regular healthcare provider (at study visit)	42.4	66.1	0.5
≥ 1 annual visit to a primary healthcare provider	33.1	59.3	0.5
Born in Canada	62.2	80.1	0.4
Highest education completed: Cégep or more	66.5	84.0	0.4
Self-identified as French Canadian	39.6	60.2	0.4
Age at enrollment ≤ 26 yrs	75.2	87.6	0.3
Self-identified as gay	68.6	82.7	0.3
Having had ≥ 2 anal sex partners (past 6 months)	62.8	76.3	0.3
Attendance of group sex events (past 6 months)	13.4	26.7	0.3
Daily smokers (past 6 months)	35.6	20.3	0.3
Having private health insurance coverage (at study visit)	65.3	80.5	0.3

Notes: Standardized mean difference (SMD) represents the difference between group proportions, expressed in units of the pooled standard deviation. The following thresholds are used to interpret SMD: negligible (<0.2), small (0.2–0.5), moderate (0.6–0.8), and large (>0.8). Only variables with an SMD greater than 0.2 are presented in this table. Abbreviations: STI, sexually transmitted infection (including chlamydia, gonorrhea, syphilis, hepatitis A, B and C); HIV PrEP, Human Immunodeficiency Virus Pre-Exposure Prophylaxis.

3.4. Factors associated with HPV vaccination

Variables most strongly associated with HPV vaccination were a self-reported past hepatitis A or B vaccination (OR=7.5; 95%CI: 2.8–19.8) and a previous self-reported diagnosis of condylomas (OR=6.1; 95%CI: 1.9–19.4) (Table 2).

Table 2 Odds-ratios (OR) of vaccination (≥ 1 dose) among GBM eligible for free HPV vaccination (n=296)

	Vaccinated (≥ 1 dose) / total participants	Univariable regression	Multivariable regression
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	Count	%	OR	95%CI	OR	95%CI
Self-reported past hepatitis A or B vaccination						
Never or don't remember	15 / 88	17.0	Ref		Ref	
≥ 1 dose	108 / 208	51.9	6.9	3.5 - 13.7	7.5	2.8 - 19.8
Self-reported diagnosis of condylomas (lifetime)						
Never	98 / 262	37.4	Ref		Ref	
≥ once	25 / 34	73.5	8.3	3.5 - 20.0	6.1	1.9 - 19.4
Using HIV-PrEP (past 6 months)						
No	97 / 259	37.5	Ref		Ref	
Yes	22 / 29	75.9	9.3	3.6 - 23.8	4.3	1.4 - 13.8
Living with HIV	4 / 8	50.0	2.4	0.6 - 10.5	0.9	0.1 - 6.4
Tested for STI or HIV (past 6 months)						
No	27 / 126	21.4	Ref		Ref	
Yes	96 / 170	56.5	5.9	3.3 - 10.6	3.3	1.5 - 7.1
Age at enrollment						
≥ 27 yrs	17 / 59	28.8	Ref		Ref	
≤ 26 yrs	106 / 237	44.7	2.3	1.1 - 4.7	3.3	1.5 - 7.4
Education (highest level completed)						
High school or less	21 / 70	30.0	Ref		Ref	
Cégep (College) or more	102 / 226	45.1	2.6	1.3 - 5.0	2.8	1.2 - 6.5
Frequency of visits to primary health care provider						
No care provider or < once a year	51 / 165	30.9	Ref		Ref	
≥ once per year	72 / 131	55	2.9	1.7 - 5.1	2.4	1.2 - 4.7
Self-reported diagnosis of STI other than HPV related (lifetime)						
Never	54 / 181	29.8	Ref		Ref	
≥ once	69 / 115	60.0	4.7	2.7 - 8.1	2.1	1.0 - 4.2
Born in Canada						
No	24 / 92	26.1	Ref		Ref	
Yes	99 / 204	48.5	2.3	1.2 - 4.2	2.1	1.0 - 4.5
Number of sex partners (past 6 months)						
≤ 5	48 / 151	31.8	Ref		Ref	
> 5	75 / 145	51.7	2.9	1.7 - 4.9	1.6	0.8 - 3.2

Notes: Regression analysis performed on 296 (96%) participants with complete data. Abbreviations: STI, sexually transmitted infection (including chlamydia, gonorrhea, syphilis, hepatitis A, B and C); HIV PrEP, Human Immunodeficiency Virus Pre-Exposure Prophylaxis

3.5. Disclosure of same-sex sexual activity to obtain the HPV vaccine

Of 309 participants eligible for free HPV vaccination, 163 (52.7%) had a regular healthcare provider. Among these, 134 (82.2%) felt comfortable discussing sexual health issues with their healthcare provider, 124 (76.1%) had disclosed same-sex sexual activity, and 87 (53.4%) had discussed HPV vaccination. The median age at which participants first disclosed same-sex sexual activity to a healthcare provider was 19 years (IQR: 17-25 years) (Appendix C). Vaccine coverage among GBM eligible for free HPV vaccination who both disclosed same-sex sexual activity and discussed HPV vaccination with their healthcare provider was 81.9% (95%CI: 72.0-88.8)

3.6. Anal HPV Prevalence

Of 309 participants eligible for free HPV vaccination, 287 enrolled after HPV specimen collection began (delays occurred in starting this procedure) and provided a sample; 191 had valid HPV results. Anal HPV prevalence among GBM eligible for free vaccination

was 71.2% (95%CI: 63.4-77.9) for ≥ 1 HPV genotypes and 26.5% (95%CI: 19.8–34.5) for ≥ 1 quadrivalent genotypes (HPV-6/11/16/18) (Table 3).

Unadjusted PR of anal HPV (6/11/16/18 genotypes) comparing unvaccinated and vaccinated GBM was 1.4 (95%CI: 0.8-2.4). After adjustment for potential confounders and stratification by lifetime self-reported STI diagnosis (Appendix D), PR were 4.3 (95%CI: 1.2-13.8) and 0.6 (95%CI: 0.2-1.4) among GBM with and without a self-reported history of STIs, respectively. In the model, the interaction term between HPV vaccination and lifetime self-reported STI diagnosis was 7.5 (95%CI: 1.8-31.0).

Table 3 Anal HPV prevalence among GBM eligible for free HPV vaccination (n=191)

HPV Infections	Number of positive samples	Prevalence (%)	95%CI
≥ 1 genotypes	136	71.2	63.4 - 77.9
Simple infection (only one HPV genotype)	54	26.7	20.4 - 34.2
Multiple infections (several HPV genotypes)	82	44.5	36.7 - 52.5
≥ 1 high-risk oncogenic genotypes	87	46.1	38.3 - 54.1
Other than high-risk oncogenic genotypes	49	25.1	19.0 - 32.5
≥ 1 quadrivalent genotypes (HPV-6/11/16/18)	46	26.5	19.8 - 34.5
Other than quadrivalent genotypes	90	44.7	37.0 - 52.6
≥ 1 nonavalent genotypes (HPV-6/11/16/18/31/33/45/52/58)	67	36.4	29.0 - 44.4
Other than nonavalent genotypes	69	34.9	27.8 - 42.7

3.7. Vaccination intention among unvaccinated GBM aged ≤ 26

Of 139 unvaccinated participants aged ≤ 26 , 91 (65.4%) had heard of HPV vaccination. The RDS-adjusted proportion was 76.0% (95%CI: 66.6-83.4). Vaccination intention (within the next year) among unvaccinated GBM aged ≤ 26 aware of HPV vaccination was 60.0% (95%CI: 47.3-71.6). Table 4 presents the largest differences between GBM who intended to get vaccinated and those who did not or were undecided.

Table 4 Largest differences between GBM who intended to get vaccinated and those who did not intend or were undecided, among unvaccinated GBM aged ≤ 26 years who had heard of HPV vaccination (n=86)

	Did not intend to get vaccinated or undecided (n = 32)	Intended to get vaccinated (n = 54)	Standardized mean difference
Did not complete high school	18.6	4.8	0.5
Bathhouse attendance (past 6 months)	14.0	35.2	0.5
Feeling comfortable talking to a healthcare provider about sexual health (among those who had a regular healthcare provider)	75.2	88.7	0.4
Daily smoker (past 6 months)	36.9	52.0	0.3
Self-reported diagnosis of STI other than HPV-related (lifetime)	34.6	22.8	0.3

Notes: Standardized mean difference (SMD) represents the difference between group proportions, expressed in units of the pooled standard deviation. The following thresholds are used to interpret SMD: negligible (<0.2), small (0.2–0.5), moderate (0.6–0.8), and large (>0.8). Only variables with an SMD greater

than 0.2 are presented in this table. Analysis performed on the 86 (94.5%) participants who reported their intention to get the vaccine. Abbreviation: STI, Sexually transmitted infection (including chlamydia, gonorrhea, syphilis, hepatitis A, B and C).

4. DISCUSSION

4.1. Vaccination coverage

Over a year after Quebec extended its publicly-funded HPV vaccination to GBM aged ≤ 26 , vaccination coverage (≥ 1 dose) reached 42% among eligible GBM in Greater Montreal, the province's most populated region.

As reported in a previous Engage publication, vaccination coverage among GBM aged ≤ 26 (free vaccination age across Canada) was slightly higher in Montreal (35%) than in Toronto (33%) and Vancouver (26%)[13].

In our analysis, HPV vaccination was associated with previous hepatitis A or B vaccination, self-reported STI history, particularly genital warts, and in the past 6 months, HIV- Pre-Exposure Prophylaxis (PrEP) use and STI/HIV testing. Findings suggest that participants' sexual activity possibly led to increased contact with the healthcare system, for example, through STI testing, during which participants could be offered HPV vaccination. This hypothesis aligns with vaccinated participants' data showing 98% had already become sexually active before being vaccinated (Figure 1).

During Quebec's 2023-2024 school year, 80% of boys aged 9-10 (grade 4) received ≥ 1 dose[26]. Engage study participants were ineligible for the school-based program extended to grade 4 boys (aged 9–10) in September 2016.

4.2. Disclosure of same-sex sexual activity to a healthcare professional

Only half of Montreal GBM eligible for free HPV vaccination had a regular healthcare provider. Therefore, relying solely on them to inform GBM about free HPV vaccination eligibility is insufficient. Relying on other healthcare providers (e.g., walk-in clinics, integrated STI prevention and screening services and community organizations) appears necessary to promote HPV vaccination among GBM.

Most participants who had a regular healthcare provider disclosed same-sex sexual activity to them before age 27 and 82% felt comfortable discussing sexual health with healthcare professionals, at an age young enough for HPV vaccination to be free and most effective.

Additionally, 82% of GBM eligible for free vaccination who both disclosed same-sex sexual activity and discussed HPV vaccination with their healthcare provider were vaccinated. Although unconfirmed, this suggests that many healthcare providers were aware of the publicly-funded HPV vaccination program for GBM.

4.3. Anal HPV Prevalence

Anal HPV prevalence among Montreal GBM eligible for free vaccination was 71% for ≥ 1 genotypes and 26% for ≥ 1 HPV-6/11/16/18 (quadrivalent-vaccine-genotypes). Anal HPV

prevalence (6/11/16/18 genotypes) was not significantly lower among vaccinated GBM. Montreal Engage data and previous reports have shown that vaccinated GBM were more likely to engage in condomless receptive anal sex and to self-report a prior STI diagnosis than unvaccinated GBM, suggesting that targeted vaccination efforts are likely reaching those possibly previously HPV-exposed[13].

Clinical trials have shown 84% vaccine efficacy against incident HPV-6/11/16/18 genotypes among GBM who were HPV-naïve, aged 16-26, had <5 lifetime sexual partners and no prior HPV or HIV history, consistent with expected vaccine efficacy among preadolescents[9].

Although emerging evidence suggests some benefit of catch-up vaccination, even with previous HPV exposure[11,27], vaccine effectiveness is expected to be lower in this real-world context. HPV vaccination is unapproved for therapeutic indications[28], and most men acquire ≥ 1 HPV infection within 2–4 years of sexual debut[29].

Furthermore, almost all vaccinated participants had sexual activity before getting vaccinated and half of them self-reported an STI history, therefore it is likely that several participants were infected with HPV-6/11/16/18 before vaccination. To maximize prophylactic benefits, school-based vaccination for preadolescents appears essential.

Anal HPV-6/11/16/18 prevalence among GBM aged ≤ 30 in Montreal (27%) approximated that in Toronto (29%) and Vancouver (23%)[14]. Likewise, genital HPV-6/11/16/18 prevalence among GBM aged 18-59 in the US (2013-2016) was 19%[30].

A previous Engage analysis which pooled Montreal, Toronto and Vancouver data showed an association between HPV vaccination (≥ 1 dose) and anal HPV-6/11/16/18 prevalence[14], while the analysis of Montreal data alone based on a smaller sample did not, which does not imply the absence of association in the target population. This variation between analyses may be explained by differences between cities, smaller overall statistical power (smaller sample size) and the focus of this analysis on eligible GBM for free vaccination. Additionally, self-reported vaccination status may lead to misclassification, potentially obscuring associations between vaccination and anal HPV prevalence[31] but not likely to meaningfully change the findings[32]. An Australian study showed that many young GBM misreported their HPV vaccination status by comparing participants' self-reported vaccination status with medical records[33].

4.4. Vaccination intention among unvaccinated GBM aged ≤ 26

Among unvaccinated Montreal GBM aged ≤ 26 , three-quarters had heard of HPV vaccination. Among these, 60% intended to get vaccinated within the next year, which is encouraging. Participants who intended to get vaccinated differed from undecided or unwilling participants by having higher risk sexual behaviours (more partners, more STIs, increased bathhouse attendance, etc.) and by greater vaccine benefits awareness.

4.5. Strengths and limitations

Study strengths include the use of RDS recruitment and the RDS weights to produce population-level inference. Additionally, the Engage study, as a well characterized cohort of GBM, provided a rich dataset to evaluate the HPV vaccination program for GBM.

Limitations include self-reported HPV vaccination status and the non-negligible number of non-received or invalid HPV specimens. However, the proportion of valid specimens resembled results from other studies among GBM using self-collection methods[34]. Self-reported HPV vaccination status has good sensitivity (92%) and moderate specificity (76%)[35] but may be associated with non-differential misclassification. Without knowing the temporality between HPV vaccination and infection acquisition further complicated detection of any association. Vaccination coverage and intentions may have changed since data collection (2017-2018). The COVID-19 pandemic and social distancing measures may also have impacted HPV vaccine coverage and prevalence among GBM. Finally, this analysis focused only on HPV prevalence and not on HPV persistence, the latter having more clinical relevance, particularly for HR-HPV.

5. CONCLUSION

Over a year after Quebec extended publicly-funded HPV vaccination to GBM aged ≤ 26 , vaccination coverage among Montreal GBM eligible for free vaccination was 42%. It doubled (82%) among those who also disclosed same-sex sexual activity and discussed HPV vaccination with their healthcare provider. Although most GBM felt comfortable discussing their sexual practices with a healthcare professional before the age limit of 27, half of them did not have a regular healthcare provider. Therefore, it appears necessary to also rely on other resources to effectively promote HPV vaccination among GBM. Anal HPV prevalence, including vaccine-specific HPV-6/11/16/18 genotypes, was high among Montreal GBM eligible for free vaccination, highlighting the importance of continuing school-based vaccination efforts (before HPV exposure) to obtain maximum benefits. One quarter of unvaccinated GBM aged ≤ 26 , had not heard of HPV vaccination, but among those who had, vaccination intention was high (60%), enhancing the importance of properly informing healthcare providers and GBM about the publicly-funded HPV vaccination program.

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Data statement

Data will be made available upon reasonable request to the corresponding author.

Declaration of interests

Chantal Sauvageau is an active member of the Quebec immunization committee and the National Advisory Committee on Immunization (NACI) HPV working group. Other authors declare that they have no competing interests.

REFERENCES

- [1] Ministère de la Santé et des Services sociaux. Programmes et noms commerciaux des vaccins - Dates de début ou de modification des programmes de vaccination soutenus financièrement par le MSSS pour certaines populations n.d.
<https://www.msss.gouv.qc.ca/professionnels/vaccination/piq-programmes-et-noms-commerciaux-des-vaccins/dates-de-debut-ou-de-modification-des-programmes-de-vaccination-soutenus-financierement-par-le-msss-pour-certaines-populations/> (accessed July 23, 2025).
- [2] Merck Canada Inc. GARDASIL®- Quadrivalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine 2015.
- [3] Comité sur l'immunisation du Québec. Avis sur la vaccination contre les virus du papillome humain (VPH) des hommes ayant des relations sexuelles avec d'autres hommes (HARSAH) | INSPQ. Institut national de santé publique du Québec; 2015.
- [4] Machalek DA, Poynten M, Jin F, et al. Anal human papillomavirus infection and associated neoplastic lesions in men who have sex with men: a systematic review and meta-analysis. *The Lancet Oncology* 2012;13:487–500. [https://doi.org/10.1016/S1470-2045\(12\)70080-3](https://doi.org/10.1016/S1470-2045(12)70080-3).
- [5] Marra E, Lin C, Clifford GM. Type-Specific Anal Human Papillomavirus Prevalence Among Men, According to Sexual Preference and HIV Status: A Systematic Literature Review and Meta-Analysis. *The Journal of Infectious Diseases* 2019;219:590–8. <https://doi.org/10.1093/infdis/jiy556>.
- [6] Sauvageau C, Ouakki M, Goggin P. Portrait de l'incidence et de la mortalité des cancers associés aux virus du papillome humain (VPH). Institut national de santé publique du Québec; 2018.
- [7] De Martel C, Plummer M, Vignat J, et al. Worldwide burden of cancer attributable to HPV by site, country and HPV type. *Intl Journal of Cancer* 2017;141:664–70. <https://doi.org/10.1002/ijc.30716>.
- [8] Clifford GM, Georges D, Shiels MS, et al. A meta-analysis of anal cancer incidence by risk group: Toward a unified anal cancer risk scale. *Intl Journal of Cancer* 2021;148:38–47. <https://doi.org/10.1002/ijc.33185>.
- [9] Palefsky JM, Giuliano AR, Goldstone S, et al. HPV Vaccine against Anal HPV Infection and Anal Intraepithelial Neoplasia. *New England Journal of Medicine* 2011;365:1576–85. <https://doi.org/10.1056/NEJMoa1010971>.
- [10] Buchbinder SA, Lin J, Markowitz LE, et al. Human Papillomavirus Vaccine Effectiveness by Age, Age at Vaccination, and Timing of Vaccination Relative to Age at First Sex Among Men Who Have Sex With Men-Seattle, Washington, 2018 to 2020. *Sex Transm Dis* 2025;52:631–40. <https://doi.org/10.1097/OLQ.0000000000002192>.
- [11] Meites E, Winer RL, Newcomb ME, et al. Vaccine Effectiveness Against Prevalent Anal and Oral Human Papillomavirus Infection Among Men Who Have Sex With Men—United States, 2016–2018. *The Journal of Infectious Diseases* 2020;222:2052–60. <https://doi.org/10.1093/infdis/jiaa306>.
- [12] Grace D, Gaspar M, Paquette R, et al. HIV-positive gay men's knowledge and perceptions of Human Papillomavirus (HPV) and HPV vaccination: A

- qualitative study. PLOS ONE 2018;13:e0207953.
<https://doi.org/10.1371/journal.pone.0207953>.
- [13] Grewal R, Deeks SL, Hart TA, et al. Human papillomavirus (HPV) vaccine uptake among a community-recruited sample of gay, bisexual, and other men who have sex with men in the three largest cities in Canada from 2017 to 2019. *Vaccine* 2021;39:3756–66.
<https://doi.org/10.1016/j.vaccine.2021.05.031>.
- [14] Chambers C, Deeks SL, Sutradhar R, et al. Anal Human Papillomavirus Prevalence Among Vaccinated and Unvaccinated Gay, Bisexual, and Other Men Who Have Sex With Men in Canada. *Sexual Trans Dis* 2022;49:123–32. <https://doi.org/10.1097/olq.0000000000001560>.
- [15] Chambers C, Deeks SL, Sutradhar R, et al. Vaccine Effectiveness Against 12-Month Incident and Persistent Anal Human Papillomavirus Infection Among Gay, Bisexual, and Other Men Who Have Sex With Men. *The Journal of Infectious Diseases* 2023;228:89–100.
<https://doi.org/10.1093/infdis/jiad005>.
- [16] Alessandrini J, Cox J, de Pokomandy A, et al. Prevalence of Oral Human Papillomavirus Infection Among Urban Gay, Bisexual, and Other Men Who Have Sex With Men in Canada, 2017–2019. *The Journal of Infectious Diseases* 2024;230:e1039–48. <https://doi.org/10.1093/infdis/jiae345>.
- [17] Volz E, Heckathorn DD. Probability Based Estimation Theory for Respondent Driven Sampling. *Journal of Official Statistics* 2008;24:79–97.
- [18] Lampinen TM, Miller ML, Chan K, et al. Randomized clinical evaluation of self-screening for anal cancer precursors in men who have sex with men. *Cytojournal* 2006;3:4. <https://doi.org/10.1186/1742-6413-3-4>.
- [19] Legault V, Burchell A, Goggin P, et al. Generic Microtiter Plate Assay for Triaging Clinical Specimens Prior to Genotyping of Human Papillomavirus DNA via Consensus PCR. *J Clin Microbiol* 2011;49:3977–9.
<https://doi.org/10.1128/JCM.05646-11>.
- [20] Coutlée F, Rouleau D, Petignat P, et al. Enhanced Detection and Typing of Human Papillomavirus (HPV) DNA in Anogenital Samples with PGMY Primers and the Linear Array HPV Genotyping Test. *J Clin Microbiol* 2006;44:1998–2006. <https://doi.org/10.1128/JCM.00104-06>.
- [21] Coutlée F, Rouleau D, Ghattas G, et al. Confirmatory Real-Time PCR Assay for Human Papillomavirus (HPV) Type 52 Infection in Anogenital Specimens Screened for HPV Infection with the Linear Array HPV Genotyping Test. *J Clin Microbiol* 2007;45:3821–3. <https://doi.org/10.1128/JCM.01145-07>.
- [22] International Agency for Research on Cancer. *Cervical Cancer Screening*. vol. 18. Lyon, France: 2022.
- [23] Gile KJ, Beaudry IS, Handcock MS, et al. Methods for Inference from Respondent-Driven Sampling Data. *Annu Rev Stat Appl* 2018;5:65–93.
<https://doi.org/10.1146/annurev-statistics-031017-100704>.
- [24] McLaughlin KR, Handcock MS, Johnston LG. *Inference for the Visibility Distribution for Respondent-Driven Sampling*. ResearchGate, 2015.
- [25] Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. New York: Routledge; 1988. <https://doi.org/10.4324/9780203771587>.

- [26] Ministère de la Santé et des Services sociaux. Vaccination en milieu scolaire. FlashVigie 2025;19:7.
- [27] Goldstone SE, Giuliano AR, Palefsky JM, et al. Efficacy, immunogenicity, and safety of a quadrivalent HPV vaccine in men: results of an open-label, long-term extension of a randomised, placebo-controlled, phase 3 trial. *The Lancet Infectious Diseases* 2022;22:413–25. [https://doi.org/10.1016/S1473-3099\(21\)00327-3](https://doi.org/10.1016/S1473-3099(21)00327-3).
- [28] Meites E, Gee J, Unger E, et al. Chapter 11: Human Papillomavirus. *Epidemiology and Prevention of Vaccine-Preventable Diseases* 2024. <https://www.cdc.gov/pinkbook/hcp/table-of-contents/chapter-11-human-papillomavirus.html> (accessed July 23, 2025).
- [29] Liu Z, Nyitray AG, Hwang L-Y, et al. Acquisition, Persistence, and Clearance of Human Papillomavirus Infection Among Male Virgins Residing in Brazil, Mexico, and the United States. *The Journal of Infectious Diseases* 2018;217:767–76. <https://doi.org/10.1093/infdis/jix588>.
- [30] Sonawane K, Shyu SS, Damgacioglu H, et al. Prevalence and concordance of oral and genital HPV by sexual orientation among US men. *JNCI Cancer Spectr* 2023;7:pkac088. <https://doi.org/10.1093/jncics/pkac088>.
- [31] Greenland S, Lash TL. Chapter 19 Bias analysis. Rothman, K.J., Greenland, S., Lash, T.L. (eds.) *Modern Epidemiology*. 3rd ed., Philadelphia: Lippincott Williams & Wilkins; 2008, p. 345–80.
- [32] Chambers C, Deeks SL, Sutradhar R, et al. Self-reported Human Papillomavirus Vaccination and Vaccine Effectiveness Among Men Who Have Sex with Men: A Quantitative Bias Analysis. *Epidemiology* 2023;34:225–9. <https://doi.org/10.1097/EDE.0000000000001580>.
- [33] Chow EPF, Fairley CK, Atkinson S, et al. Validation of self-reported human papillomavirus vaccination in young adult men who have sex with men. *Human Vaccines & Immunotherapeutics* 2024;20:2371179. <https://doi.org/10.1080/21645515.2024.2371179>.
- [34] Gilbert M, Kwag M, Mei W, et al. Feasibility of Incorporating Self-Collected Rectal Swabs Into a Community Venue-Based Survey to Measure the Prevalence of HPV Infection in Men Who Have Sex With Men. *Sexually Transmitted Diseases* 2011;38:964. <https://doi.org/10.1097/OLQ.0b013e318222899d>.
- [35] Rolnick SJ, Parker ED, Nordin JD, et al. Self-report compared to electronic medical record across eight adult vaccines: Do results vary by demographic factors? *Vaccine* 2013;31:3928–35. <https://doi.org/10.1016/j.vaccine.2013.06.041>.