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HIV pre-exposure prophylaxis and opportunities for vaccination against hepatitis A virus, hepatitis B virus and human papillomavirus: an analysis of the Ontario PrEP cohort study

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ABSTRACT

Objectives Populations who seek HIV pre-exposure prophylaxis (PrEP) are disproportionately affected by hepatitis A virus (HAV), hepatitis B virus (HBV) and human papillomavirus (HPV). We examined immunity/vaccination against these infections among participants in the Ontario PrEP cohort study (ON-PrEP).

Methods ON-PrEP is a prospective cohort of HIV-negative PrEP users from 10 Ontario clinics. We descriptively analysed baseline immunity/vaccination against HAV (IgG reactive), HBV (hepatitis B surface antibody >10) and HPV (self-reported three-dose vaccination). We further performed multivariable logistic regression to identify characteristics associated with baseline immunity/vaccination. We used cumulative incidence functions to describe vaccine uptake among participants non-immune at baseline.

Results Of 633 eligible participants, 59.1% were white, 85.8% were male and 79.6% were gay. We found baseline evidence of immunity/vaccination against HAV, HBV and HPV in 69.2%, 81.2% and 16.8% of PrEP-experienced participants and 58.9%, 70.3% and 10.4% of PrEP-naïve participants, respectively. Characteristics associated with baseline HAV immunity were greater PrEP duration (adjusted OR (aOR) 1.41/year, 95% CI 1.09 to 1.84), frequent sexually transmitted and bloodborne infection (STBBI) testing (aOR 2.38, 95% CI 1.15 to 4.92) and HBV immunity (aOR 3.53, 95% CI 2.09 to 5.98). Characteristics associated with baseline HBV immunity were living in Toronto (aOR 3.54, 95% CI 1.87 to 6.70) or Ottawa (aOR 2.76, 95% CI 1.41 to 5.40), self-identifying as racialised (aOR 2.23, 95% CI 1.19 to 4.18), greater PrEP duration (aOR 1.39/year, 95% CI 1.02 to 1.90) and HAV immunity (aOR 3.75, 95% CI 2.19 to 6.41). Characteristics associated with baseline HPV vaccination were being aged ≤26 years (aOR 9.28, 95% CI 2.11 to 40.77), annual income between CAD$60 000 and CAD$119 000 (aOR 3.42, 95% CI 1.40 to 8.34), frequent STBBI testing (aOR 7.00, 95% CI 1.38 to 35.46) and HAV immunity (aOR 6.96, 95% CI 2.00 to 24.25). Among those non-immune at baseline, overall cumulative probability of immunity/vaccination was 0.70, 0.60 and 0.53 among PrEP-experienced participants and 0.93, 0.80 and 0.70 among PrEP-naïve participants for HAV, HBV and HPV, respectively.

Conclusions Baseline immunity to HAV/HBV was common, and a sizeable proportion of non-immune participants were vaccinated during follow-up. However, HPV vaccination was uncommon. Continued efforts should be made to remove barriers to HPV vaccination such as cost, inclusion in clinical guidelines and provider recommendation.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Populations who typically seek HIV pre-exposure prophylaxis (PrEP) often have a higher incidence of hepatitis A virus (HAV), hepatitis B virus (HBV) and human papillomavirus (HPV).
⇒ There is little evidence on the immune/vaccine status of these infections in PrEP users.

WHAT THIS STUDY ADDS

⇒ Immunity to HAV and HBV was common in Ontario PrEP users and a sizeable proportion of non-immune individuals were vaccinated during follow-up.
⇒ Both baseline vaccination and vaccine uptake was low for HPV, even among those eligible for publicly funded vaccination.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Efforts should be made to promote vaccination throughout the duration of PrEP care and remove barriers such as cost, eligibility for publicly funded vaccination, provider recommendation and access to sexual health services.

INTRODUCTION

Pre-exposure prophylaxis (PrEP) is a safe and highly effective intervention that decreases the risk of infection with HIV.[1] PrEP involves taking oral medication either daily or 'on-demand' before potential HIV exposures to prevent infection. In

September 2017, the public drug formulary in Ontario, Canada (named the Ontario Drug Benefit) started covering the cost of PrEP for those aged ≥65 years, on social assistance, receiving home care or residing in long-term care facilities.[2] In January 2018, PrEP coverage was expanded to include all Ontarians aged <25 years through a programme called OHIP+.[2] Other Ontario residents can seek partial PrEP coverage by applying for a subsidy programme called Trillium.[2] With a 6.6-fold subsequent increase in the number of individuals dispensed PrEP between 2016 and 2019, PrEP has become an essential part of Ontario's HIV prevention strategy.[3]

According to the Canadian guideline on HIV PrEP and non-occupational post-exposure prophylaxis, laboratory screening for sexually transmitted and bloodborne infections (STBBIs) is recommended at baseline and quarterly follow-up visits.[4] Based on the results of serological screening, vaccination against hepatitis A virus (HAV) and/or hepatitis B virus (HBV) is recommended for non-immune PrEP users.[4] Because gay, bisexual and other men who have sex with men (GBM) are over-represented in outbreaks of viral hepatitis, make up the greatest proportion of PrEP patients and are eligible for publicly funded vaccination in Ontario, PrEP care presents an opportunity to promote HAV and HBV vaccination among this important group.[5–8] Other sexually active PrEP-using populations may derive benefit from these vaccines as well. This is especially important for HBV, since the most common PrEP medications (ie, tenofovir disoproxil fumarate, tenofovir alafenamide and emtricitabine) have anti-HBV activity, which could predispose those with chronic infection to hepatitis flares during sudden PrEP discontinuation.[4]

Although not included in Canadian or international PrEP guidelines, experts also recommend vaccination against human papillomavirus (HPV) alongside HAV and HBV.[9 10] Since anal carriage of high-risk HPV is prevalent among GBM, integrating HPV vaccination within PrEP care may reduce the burden of HPV-related anal cancers in this over-represented population.[11 12] This may also further the reach of publicly funded vaccine programmes, since GBM aged ≤26 years are eligible for free HPV vaccination in Ontario.[8]

To date, no study has investigated immunity to or vaccination against each of HAV, HBV and HPV among PrEP users in a Canadian context. Our objectives were to: (1) quantify the proportion of Ontario PrEP users who were immune to/vaccinated against HAV, HBV and HPV at study baseline; (2) identify participant characteristics that were associated with baseline immunity/vaccination and (3) measure vaccine uptake over time among individuals who were non-immune at baseline.

METHODS

Study design

This study analysed data from the Ontario PrEP cohort study (ON-PrEP), an ongoing, prospective cohort of HIV-negative individuals using PrEP in Ontario. ON-PrEP involves follow-up visits every 6 months for 2 years. During each visit, participants completed a web-based questionnaire, which gathered data on biological, behavioural, experiential and engagement in care outcomes. Additionally, study staff entered clinical information into the study database, including results of STBBI testing performed at study sites. STBBI serological testing and vaccination was performed according to the judgement of treating clinicians and was not prescribed by the study protocol. To improve data capture for STBBI screening conducted outside of ON-PrEP, we asked participants for permission to access additional test results from the Public Health Ontario Laboratory (PHOL), whose records include the majority of STBBI testing done in the province. PHOL data covered the entire study period plus 5 years after enrolment. We deterministically linked PHOL and ON-PrEP data sources using provincial health card numbers. Participants were given CAD$30 at baseline and CAD$20 for follow-up visits as compensation.

Participants

Enrolment into ON-PrEP began in February 2018 with a target sample size of 800 individuals. Participants were recruited from 10 clinical facilities across Ontario, including 5 sites in Toronto and 1 site in each of Guelph, Hamilton, London, Ottawa and Sudbury. We also sought self-referrals through community outreach activities in collaboration with 20 community-based organisations. Eligible participants were aged ≥16 years, initiating or currently using any PrEP regimen, HIV-negative within 3 months before enrolment as documented by standard serology and had sufficient English language proficiency to complete study activities.

There were 713 participants enrolled in ON-PrEP at the time of data extraction (ie, 2 June 2023). However, laboratory data were not collected for 80 participants enrolled through the community outreach activities. Therefore, 633 participants were eligible for inclusion in our analysis. The first participant was enrolled on 28 February 2018 and the last study visit was on 18 April 2023. Participants completed a median of 3 (IQR 4) study visits and were followed for a median of 196 (IQR 462) days.

Outcome variables

Our outcomes of interest were immunity to/vaccination against each of HAV, HBV and HPV. We determined HAV and HBV immunity using both laboratory results (ie, HAV IgG reactive, hepatitis B surface antibody titre >10) and self-reported completion of vaccine series (ie, two doses for HAV, three doses for HBV) from the following data sources: (1) PHOL serology results; (2) laboratory testing conducted at ON-PrEP sites and (3) self-reported vaccination as recorded in the study database. However, participants had varying degrees of data completeness across these sources, especially since permission to access PHOL records was optional and 109 (17.2%) participants opted out.

To optimise the accuracy of our immunity measures, we created binary outcome variables that incorporated data from each of the three sources hierarchically, prioritising PHOL serological results over site-level screening and finally self-reported vaccination (figure 1). Self-reported vaccine status was collected by study staff directly into the study database, as opposed to via participant-completed questionnaires. Therefore, those with unknown vaccine status were individuals in whom neither the participant nor the study staff (on review of available medical records) could ascertain the true vaccine status.

Unlike HAV and HBV, there are no readily available laboratory tests that can determine immunity towards HPV. Consequently, we used participants' self-reported vaccine status to create a binary outcome variable for completion of HPV vaccine series (ie, two or less doses vs all three doses).

Covariates

To explore participant characteristics associated with baseline immunity/vaccination, we pre-identified potential covariates through a combination of literature review and consultation with our multidisciplinary study team of sexual health providers, HIV researchers and community members. This process yielded the following list of candidate demographic variables: city of

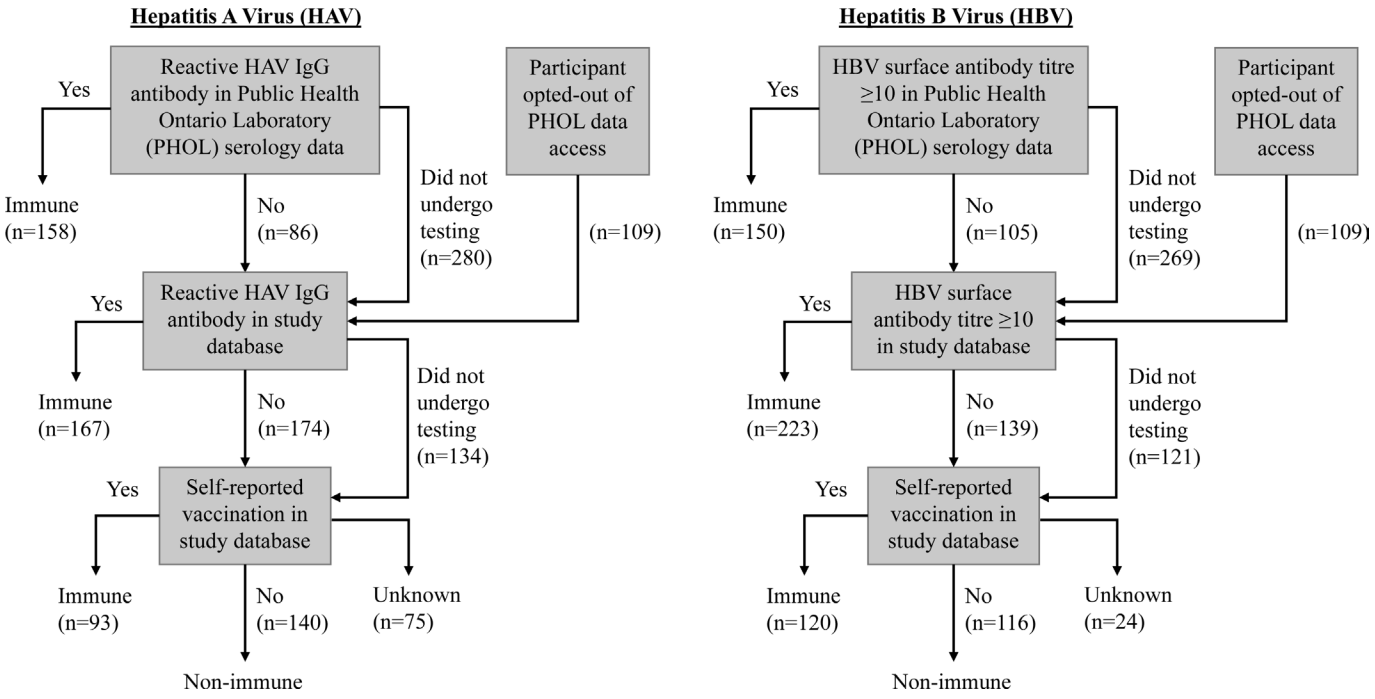

Figure 1 Flow chart used to determine hepatitis A virus (HAV) and hepatitis B virus (HBV) immune status among participants in the Ontario pre-exposure prophylaxis (ON-PrEP) cohort study (n=633). Our hierarchical classification system used both laboratory results (ie, HAV IgG reactive, hepatitis B surface antibody (HBsAb) titre >10) and self-reported completion of vaccine series (ie, two doses for HAV, three doses for HBV). Data sources included Public Health Ontario Laboratory (PHOL) serology results, laboratory testing conducted at ON-PrEP sites and self-reported vaccination as recorded in the study database. Counts (n) represent the number of participants falling under each classification.

residence, age, region of birth, race, gender identity, sexual orientation, annual income and Drug Use Disorders Identification Test (DUDIT) score.[13] Since sexual behaviour may influence uptake of STBBI prevention measures, we further included the following variables: having a primary partner, having casual partners and number of male sex partners in the last 6 months. Likewise, we considered variables regarding participants' healthcare access, including having a primary care provider, duration of PrEP use, frequency of STBBI testing in the year preceding enrolment and perceived discrimination in healthcare as represented by Discrimination in Medical Setting scores.[14] Recognising that STBBI vaccination may be performed simultaneously, we also included the HAV, HBV and HPV outcome variables as covariates in models where it was not the model outcome.

Statistical analysis

We descriptively analysed sociodemographic characteristics among eligible ON-PrEP participants, using counts and percentages for categorical variables and median and IQR for continuous variables. To achieve our first objective, we calculated the proportion of participants with baseline immunity/vaccination against each of HAV, HBV and HPV, stratified by PrEP status (ie, whether participants were PrEP-naïve or PrEP-experienced at the time of enrolment). Participants with unknown immune/vaccination status were reported for results up until this point but were excluded from all subsequent analyses henceforth.

For our second objective, we used the 'purposeful selection of covariates' model—building strategy from Hosmer-Lemeshow-Sturdivant to identify characteristics associated with baseline immunity/vaccination.[15] All models were constructed using a complete case analysis. First, we built univariable logistic regression models between each pre-identified covariate and the outcomes of interest. All univariable relationships with a p value <0.15 were included in preliminary multivariable models. Variables with >40% missing responses (eg, DUDIT score, HPV vaccination for HAV and HBV models) or limited variability (eg, gender identity, sexual orientation, having a primary provider, city of residence for the HPV model) were excluded. Within the preliminary multivariable models, covariates that produced a p value >0.05 were consecutively removed, but reintroduced if their deletion modified any beta-coefficient by >20%.[15] This iterative process was repeated until all essential variables were included in the model. We then performed diagnostic testing for multicollinearity using variance inflation factors ≥10 and non-linearity using partial residual plots; however, none of the included covariates suggested evidence of either phenomenon. Once elucidated, we used OR and 95% CI to quantify associations in the final multivariable logistic regression models.

To fulfil our third objective, we produced cumulative incidence functions (CIFs) to examine uptake of HAV, HBV and/or HPV vaccination among participants who were non-immune at baseline and in whom vaccination was indicated according to the Ontario public vaccination schedule (ie, GBM and transgender women for HAV and all adults beyond grade 7 for HBV/HPV).[16–18] One participant who was HAV non-immune at baseline was removed from the HAV CIF because vaccination was not indicated. Since the recommended vaccine schedules for HAV, HBV and HPV are typically completed in <12 months, we estimated the cumulative probability of vaccine series completion after 1 year in ON-PrEP.[16–18] We further estimated cumulative probabilities at the longest length of individual follow-up which was 730 days. Participants who were lost to follow-up were censored at their last date of observation. All analyses were conducted in R Studio V.2022.02.3.

Patient and public partnership

The ON-PrEP study team includes a multidisciplinary group of HIV researchers, sexual health providers and community members who were involved in identifying research questions, developing data collection instruments, recruiting participants and disseminating results. For this specific analysis, we consulted team members in identifying participant characteristics that may be associated with STBBI immunity/vaccination to leverage the perspectives of those with expertise or lived experience.

RESULTS

Of 633 eligible participants, 374 (59.1%) were white, 543 (85.8%) were male, 504 (79.6%) self-identified as gay and 396 (62.6%) were aged 27–49 years (table 1). The majority resided in major cities, with 332 (52.4%) living in Toronto and 198 (31.3%) in Ottawa. In terms of PrEP initiation, 441 (69.7%) were already taking PrEP before entering the cohort (median duration of PrEP use was 1 year, IQR 1), whereas 192 (30.3%) initiated PrEP within a week after enrolment.

Among PrEP-experienced participants, 305 (69.2%) were HAV immune at baseline, 76 (17.2%) were non-immune and 60 (13.6%) had unknown status. For HBV, 358 (81.2%) were immune, 67 (15.2%) were non-immune and 16 (3.6%) had unknown status. For HPV, only 74 (16.8%) had completed the vaccine series, 77 (17.5%) had received two doses or fewer (ie, 53 completely unvaccinated) and the remaining 290 (65.8%) had unknown status. Of 41 PrEP-experienced participants who were eligible for publicly funded HPV vaccination (ie, GBM aged ≤26 years) at baseline, only 10 (24.4%) were fully vaccinated.

Among PrEP-naïve participants, 113 (58.9%) were HAV immune at baseline, 64 (33.3%) were non-immune and 15 (7.8%) had unknown status. For HBV, 135 (70.3%) had baseline immunity, 49 (25.5%) were non-immune and 8 (4.2%) had unknown status. For HPV, only 20 (10.4%) had completed the vaccine series, 33 (17.2%) had received two doses or fewer (ie, 20 completely unvaccinated) and the remaining 139 (72.4%) had unknown status. Of 30 PrEP-naïve participants who were eligible for publicly funded HPV vaccination at baseline, only 6 (20.0%) were fully vaccinated.

In multivariable analysis, the following variables were associated with baseline HAV immunity (table 2): greater duration of PrEP use (aOR 1.41/year, 95% CI 1.09 to 1.84), testing for STBBIs three or more times in the year preceding enrolment (aOR 2.38, 95% CI 1.15 to 4.92) and HBV immunity (aOR 3.53, 95% CI 2.09 to 5.98). For HBV, the following variables were associated with baseline immunity: living in Toronto (aOR 3.54, 95% CI 1.87 to 6.70) or Ottawa (aOR 2.76, 95% CI 1.41 to 5.40), self-identifying as racialised (aOR 2.23, 95% CI 1.19 to 4.18), greater duration of PrEP use (aOR 1.39/year, 95% CI 1.02 to 1.90) and HAV immunity (aOR 3.75, 95% CI 2.19 to 6.41). Finally, the following variables were associated with baseline HPV vaccination: being aged ≤26 years (aOR 9.28, 95% CI 2.11 to 40.77), having an annual salary between CAD$60 000 and CAD$119 000 (aOR 3.42, 95% CI 1.40 to 8.34), testing for STBBIs three or more times in the year before enrolment (aOR 7.00, 95% CI 1.38 to 35.46) and HAV immunity (aOR 6.96, 95% CI 2.00 to 24.25).

Using CIFs, we observed that the probability of becoming immune/vaccinated against each of HAV, HBV and HPV increased steadily over time for participants who were non-immune at baseline (figure 2). However, the likelihood of vaccine series completion was lower for HPV. After 1 year, the cumulative probability of immunity/vaccination was 0.48 for HAV, 0.41 for

Table 1 Demographic characteristics of participants enrolled in the Ontario PrEP cohort study at baseline (n=633)

Characteristic	N	%
City of residence		
Ottawa	198	31.3
Toronto	332	52.4
Other	103	16.3
Age (years)		
≤26	77	12.2
27–49	396	62.6
≥50	94	14.8
Missing	66	10.4
Race		
White	374	59.1
Racialised*	195	30.8
Missing	64	10.1
Born in Canada		
Yes	400	63.2
No	168	26.5
Missing	65	10.3
Citizenship status		
Canadian citizen	504	79.6
Permanent immigrant	49	7.7
Refugee	5	0.8
Temporary worker	10	1.6
Other	1	0.2
Missing	64	10.1
Current gender identity		
Female	14	2.2
Male	543	85.8
Other gender identity†	13	2.1
Missing	63	10.0
Sexual orientation		
Bisexual	49	7.7
Gay	504	79.6
Lesbian	1	0.2
Heterosexual	6	0.9
Questioning	1	0.2
Two-spirit	2	0.3
Other	6	0.9
Do not know	1	0.2
Missing	63	10.0
Employment status		
Organisationally employed‡	436	68.9
Self-employed	44	6.9
Unemployed	90	14.2
Missing	63	10.0
Annual income (CAD$)		
≤59 999	197	31.1
60 000–119 000	204	32.2
≥120 000	140	22.1
Missing	92	14.5
DUDIT score (median, IQR)	5.0 (5.0)	
Primary partner		
Yes	266	42.0
No	302	47.7
Missing	65	10.3
Casual partners		
Yes	500	79.0
No	133	21.0

Continued

Table 1 Continued

Characteristic	N	%
Number of male sex partners in past 6 months (median, IQR)	9.5 (16.0)	
Primary care provider		
Yes	461	72.8
No	73	11.5
Missing	99	15.7
PrEP status		
Started PrEP prior to enrolment	441	69.7
Starting PrEP within a week after enrolment	192	30.3
Number of years taking PrEP (median, IQR)	1.0 (1.0)	
Frequency of STBBI testing in the past year		
Never	50	7.9
Once or twice	237	37.4
Three or more times	254	40.1
Missing	92	14.5
DMS score (median, IQR)	8.0 (6.0)	

*Racialised category includes East, South and Southeast Asian; African, Caribbean and North American black; First Nations, Inuit, Metis, Indigenous; Caribbean Indian; Latin American and Middle Eastern.
†Other gender identities category includes genderqueer and non-binary.
‡Organisationally employed category includes permanent and contract employment.
DMS, Discrimination in Medical Setting; DUDIT, drug use disorders identification test; PrEP, pre-exposure prophylaxis; STBBI, sexually transmitted and bloodborne infection.

HBV and 0.19 for HPV among non-immune PrEP-experienced participants compared with 0.37 for HAV, 0.32 for HBV and 0.36 for HPV among non-immune PrEP-naïve participants. At the longest length of individual follow-up, cumulative probabilities were 0.65 for HAV, 0.60 for HBV and 0.53 for HPV among PrEP-experienced participants compared with 0.93 for HAV, 0.80 for HBV and 0.70 for HPV among PrEP-naïve participants. Of 116 participants who were HBV non-immune at baseline, only 3 underwent HBV core antibody (HBcAb) testing during follow-up, and none were positive for HBcAb, suggesting that the vast majority of HBV immunity acquired during the study was attributable to vaccination rather than infection.

DISCUSSION

In this analysis, we found that most ON-PrEP participants were immune to HAV and HBV at baseline. However, a sizeable proportion was non-immune, especially among those who were initiating PrEP for the first time (ie, 33.3% for HAV and 25.5% for HBV). HPV vaccination was particularly low in both PrEP-experienced and PrEP-naïve groups and the high prevalence of unknown vaccine status highlights important gaps in promoting comprehensive STBBI prevention within PrEP care. The proportions of non-immune/unvaccinated PrEP users observed in this study mirror those found in other settings. In a small cohort of GBM initiating PrEP at a primary care clinic in New York City, USA, 41.7% of participants were non-immune to HAV at baseline.[6] Likewise, among individuals initiating PrEP at a sexual health clinic in Paris, France, 42.3% were HAV non-immune, 26.6% were HBV non-immune and 98.8% were HPV unvaccinated.[19] Similar to our findings, baseline HPV vaccination was only slightly higher among those eligible for free vaccine coverage.[19]

Promoting vaccination against HAV, HBV and HPV among PrEP users continues to be important. Clinically, HBV is treatable but not curable and there is currently no antiviral treatment for either HAV or HPV. At the population level, GBM (the most common PrEP-seeking group in our setting) have been over-represented in sporadic HAV outbreaks across Canada. For instance, during an outbreak of acute HAV in Toronto from January 2017 to November 2018, 80% of confirmed cases were male and 64% reported having sex with men.[20] Likewise, GBM have historically been disproportionately affected by HBV when compared with other Canadians; 9.9% of acute HBV infections in Canada between 2005 and 2010 were among GBM.[21] Given the emergence of novel PrEP medications that no longer function as HBV treatment, notably long-acting injectable cabotegravir, diligent HBV vaccination is essential to prevent increases in HBV infection in this important group.[22] Although previous studies indicate that knowledge of HPV vaccine is high among Canadian GBM eligible for publicly funded vaccination, rates of vaccine initiation and series completion are limited to 26%–35% and 43%–66%, respectively.[23]

Our findings suggest that PrEP care presents a valuable opportunity for vaccination against these common infections. For HAV and HBV, greater duration of PrEP use was associated with increased odds of baseline immunity. Among those non-immune, the overall probability of immunity was 0.65 for HAV and 0.60 for HBV among PrEP-experienced participants and 0.93 for HAV and 0.80 for HBV among the PrEP-naïve group, suggesting that providers likely recommended vaccination and uptake was high. Nevertheless, PrEP-experienced participants having higher baseline prevalence of HAV/HBV immunity and subsequently lower likelihood of vaccine uptake during follow-up suggests a greater emphasis on STBBI prevention early in PrEP care. Continued effort should be made to promote vaccination among those already taking PrEP.

More work is needed to improve HPV vaccination in PrEP care, since the estimated probability of vaccine series completion at both 1 year and longest length of individual follow-up were low when compared with HAV and HBV. Although the stringent eligibility criteria for publicly funded vaccination in Ontario likely played a role, a previous study found that PrEP stakeholders (ie, providers, clinic staff, patients) perceived the exclusion of HPV vaccine in PrEP management guidelines to be the greatest barrier to integrating HPV vaccination within PrEP care.[24] Putting this into context, pooled estimates from a recent meta-analysis found that only 24% of patients initiated HPV vaccination without provider recommendations compared with 60% whose provider recommended getting vaccinated.[25] Including HPV vaccine in both Canadian and international PrEP guidelines and encouraging providers to recommend HPV vaccination during PrEP consultations are important strategies for improving vaccine uptake among PrEP users.

Findings from our multivariable modelling can inform hypotheses about how to increase the reach of vaccination in PrEP care. Like other investigators, we found that prior immunity to another STBBI increased the odds of being immune/vaccinated against each of HAV, HBV and HPV.[23] Additionally, more frequent STBBI testing was associated with higher odds of HAV and HPV immunity/vaccination. Taken together, our results suggest that greater involvement in sexual healthcare may be a strong predictor of baseline immunity/vaccination. Continued effort should be made to promote vaccination among those with infrequent access to sexual health services, including education to primary care providers about indications for publicly funded vaccine. Despite Ontario implementing universal HBV vaccination for all grade seven students in 1994, we found that living in major cities like Toronto or Ottawa increased the likelihood of baseline HBV immunity, highlighting potential geographic disparities in access to HBV vaccination outside of school-based programmes across Ontario.[26] For HPV, participants within the eligible age range for publicly funded vaccination

Table 2 Univariable and multivariable relationships between characteristics and baseline immunity/vaccination against HAV, HBV and HPV among participants in the Ontario PrEP cohort study

	HAV (n=473)				HBV (n=419)				HPV (n=165)			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
Characteristic	OR (95% CI)	P value	aOR (95% CI)	P value	OR (95% CI)	P value	aOR (95% CI)	P value	OR (95% CI)	P value	aOR (95% CI)	P value
City of residence		<0.01		0.02		<0.01		<0.01		0.03		
Other	Ref		Ref		Ref		Ref		Ref			
Toronto	2.84 (1.69 to 4.77)		1.59 (0.87 to 2.90)		4.52 (2.69 to 7.61)		3.54 (1.87 to 6.70)		2.66 (1.29 to 5.44)			
Ottawa	0.92 (0.54 to 1.56)		0.73 (0.39 to 1.37)		2.58 (1.50 to 4.42)		2.76 (1.41 to 5.40)		0.00 (2.28e-25 to 1.72e+18)			
Age (years)		0.43				0.01				0.14		0.01
≥50	Ref				Ref				Ref		Ref	
27–49	0.85 (0.48 to 1.52)				2.29 (1.36 to 3.85)				1.12 (0.51 to 2.47)		1.37 (0.51 to 3.68)	
≤26	0.63 (0.31 to 1.30)				2.30 (1.09 to 4.86)				2.62 (0.89 to 7.69)		9.28 (2.11 to 40.77)	
Born in Canada		0.03				0.17				0.65		
No	Ref				Ref				Ref			
Yes	0.60 (0.37 to 0.95)				0.71 (0.44 to 1.16)				0.87 (0.47 to 1.59)			
Race		0.76				0.02		0.01		0.91		
White	Ref				Ref		Ref		Ref			
Racialised*	1.07 (0.70 to 1.63)				1.74 (1.08 to 2.81)		2.23 (1.19 to 4.18)		1.04 (0.57 to 1.87)			
Annual income (CAD$)		0.16				0.47				0.04		0.03
≤59 999	Ref				Ref				Ref		Ref	
60 000–119 000	0.87 (0.55 to 1.38)				0.97 (0.60 to 1.58)				2.39 (1.18 to 4.84)		3.42 (1.40 to 8.34)	
≥120 000	1.49 (0.86 to 2.59)				1.36 (0.77 to 2.42)				1.91 (0.90 to 4.07)		2.29 (0.92 to 5.71)	
Primary partner		0.45				0.74				0.76		
No	Ref				Ref				Ref			
Yes	1.17 (0.78 to 1.75)				0.93 (0.61 to 1.42)				0.91 (0.52 to 1.62)			
Casual partners		0.88				0.68				0.37		
No	Ref				Ref				Ref			
Yes	1.04 (0.65 to 1.66)				0.90 (0.54 to 1.50)				1.49 (0.62 to 3.58)			
Number of male sex partners in past 6 months	1.11 (0.91 to 1.36)	0.30			1.27 (0.99 to 1.65)	0.06			1.11 (0.92 to 1.34)	0.29		
Years on PrEP	1.72 (1.36 to 2.18)	<0.01	1.41 (1.09 to 1.84)	0.01	1.55 (1.22 to 1.96)	<0.01	1.39 (1.02 to 1.90)	0.04	1.01 (0.85 to 1.21)	0.92		

Continued

Table 2 Continued

Characteristic	HAV (n=473)				HBV (n=419)				HPV (n=165)			
	Univariable		Multivariable		Univariable		Multivariable		Univariable		Multivariable	
	OR (95% CI)	P value	aOR (95% CI)	P value	OR (95% CI)	P value	aOR (95% CI)	P value	OR (95% CI)	P value	aOR (95% CI)	P value
Frequency of STBBI testing in last year		<0.01		0.06		0.01		0.18		0.07		0.02
Never	Ref		Ref		Ref		Ref		Ref		Ref	
0–2	2.43 (1.26 to 4.68)		1.70 (0.83 to 3.48)		1.98 (1.02 to 3.87)		1.21 (0.55 to 2.65)		2.47 (0.63 to 9.60)		3.48 (0.69 to 17.65)	
≥3	3.64 (1.86 to 7.12)		2.38 (1.15 to 4.92)		3.00 (1.51 to 5.95)		1.89 (0.84 to 4.24)		4.00 (1.03 to 15.53)		7.00 (1.38 to 35.46)	
DMS score	1.00 (0.74 to 1.35)	0.99			1.12 (0.80 to 1.56)	0.51			0.76 (0.51 to 1.13)	0.18		
HAV immunity						<0.01		<0.01		<0.01		<0.01
Non-immune					Ref		Ref		Ref		Ref	
Immune					4.57 (2.91 to 7.18)		3.75 (2.19 to 6.41)		5.89 (2.16 to 16.06)		6.96 (2.00 to 24.25)	
HBV immunity		<0.01		<0.01						0.03		
Non-immune	Ref		Ref						Ref			
Immune	4.57 (2.91 to 7.18)		3.53 (2.09 to 5.98)						2.66 (1.12 to 6.29)			

*Racialised category includes East, South and Southeast Asian; African, Caribbean and North American black; First Nations, Inuit, Metis, Indigenous; Caribbean Indian; Latin American and Middle Eastern.
aOR, adjusted OR; DMS, Discrimination in Medical Setting; HAV, hepatitis A virus; HBV, hepatitis B virus; HPV, human papillomavirus; PrEP, pre-exposure prophylaxis; Ref, reference; STBBI, sexually transmitted and bloodborne infection.

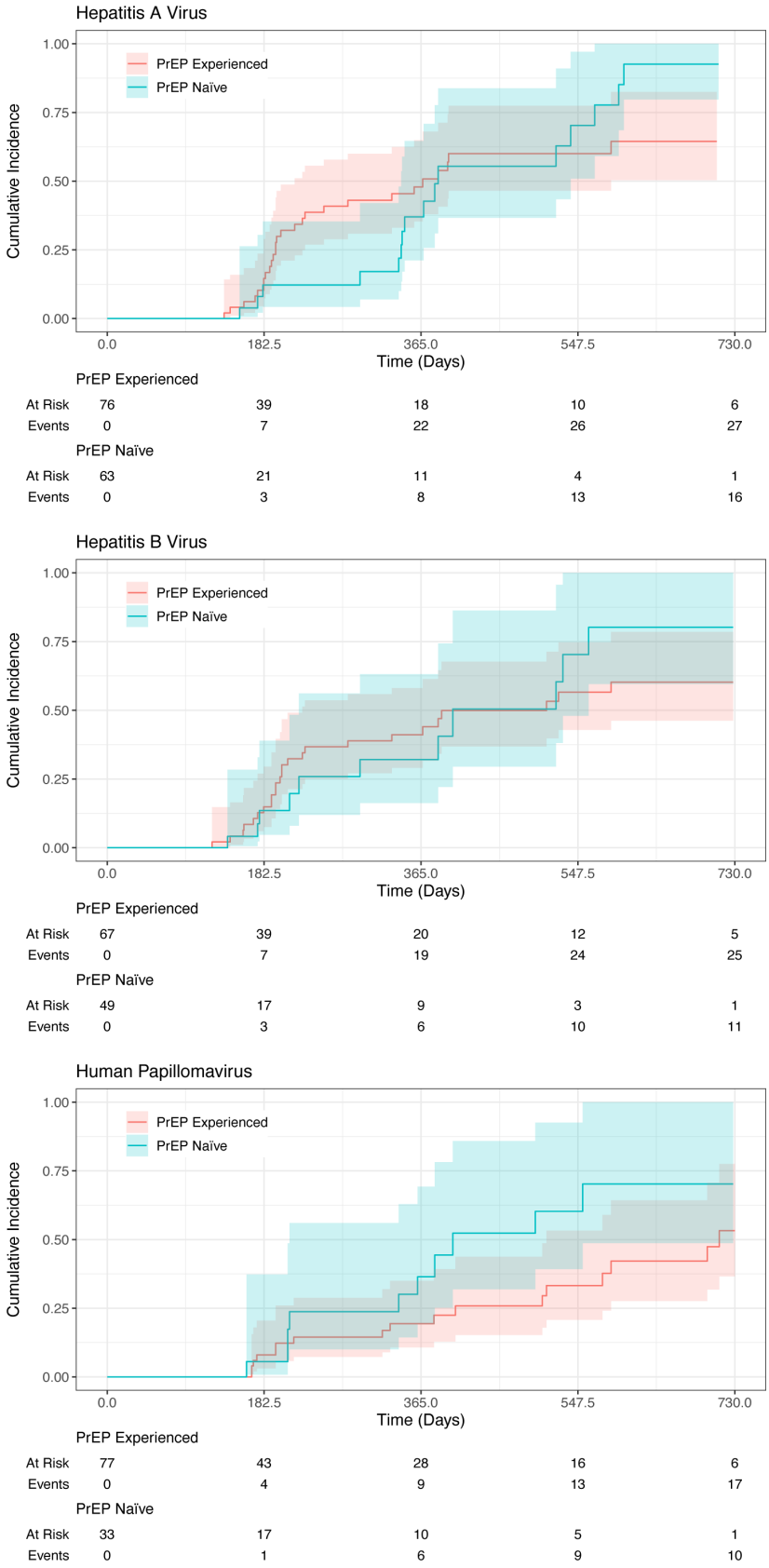

Figure 2 Cumulative incidence function (CIF) for hepatitis A virus (HAV), hepatitis B virus (HBV) and human papillomavirus (HPV) among participants non-immune/unvaccinated at baseline. CIFs included participants in the pre-exposure prophylaxis (PrEP) cohort study who had available data, who were non-immune/unvaccinated at baseline and in whom vaccination was indicated according to the Ontario public vaccination schedule (ie, gay, bisexual and other men who have sex with men and transgender women for HAV and all adults beyond grade 7 for HBV/HPV). CIFs were stratified by PrEP status. Coloured bands represent the 95% CI. Cumulative probabilities were reported from baseline to longest length of individual follow-up. Participants who were lost to follow-up were censored at their last date of observation.

had greater odds of baseline vaccination. Moreover, those with higher annual salaries had increased odds of HPV vaccination, suggesting that income may be a barrier among those not eligible for free vaccination. By combining these predictors with the observed low proportions of baseline HPV vaccination, our study highlights the need to remove financial barriers to HPV vaccination in Ontario. One strategy is to expand the eligibility criteria for publicly funded HPV vaccination to reflect that of other Canadian provinces; free HPV vaccine is offered to GBM aged ≤45 years in Nova Scotia and GBM of all ages in Prince Edward Island.[27]

Interestingly, we observed that self-identifying as racialised was predictive of HBV immunity at baseline. The reasons for this association were unclear. Notably, we found no association between region of birth and baseline immunity during multivariable modelling. One possible explanation is a high prevalence of natural immunity due to over-representation of first-generation and second-generation newcomers to Canada from HBV-endemic countries within the cohort.

Our analysis had limitations that warrant consideration. First, our multivariable models were constructed using a complete case analysis which may have produced biased estimates as data may not have been missing completely at random. Second, our analysis has limitations in terms of generalisability, since included participants were largely born in Canada and self-identified as gay, white, males. Because viral hepatitis is most prevalent in sub-Saharan Africa and East Asia, and newcomers from these regions account for most infections in North America, our results may underestimate HAV and HBV immunity among PrEP users not reached in this sample.[28] Third, ON-PrEP took place during the COVID-19 pandemic which imposed unprecedented challenges for completing study activities, laboratory screening and vaccination due to the shift to virtual care.[29] Consequently, unavoidable missing data was a limitation and our CIFs may underestimate vaccine uptake during follow-up. However, creating binary variables that included a hierarchy of data sources reduced the severity of missingness for HAV and HBV immunity measures. Fourth, our definitions considered completion of the HBV vaccine series equivalent to lab-confirmed immunity, although we recognise that HBV vaccine non-responders account for roughly 5% of immunocompetent individuals receiving vaccination.[30] Finally, we included self-reported data which may have been subject to recall and social desirability biases.

CONCLUSION

Our analysis found that HAV and HBV immunity was common among ON-PrEP participants and vaccine uptake was high among non-immune individuals, suggesting that PrEP care presents a valuable opportunity for vaccination. Because both baseline vaccination and uptake were lower for HPV, continued effort should be made to remove barriers to HPV vaccination such as cost and inclusion in PrEP guidelines. By identifying characteristics associated with baseline immunity/vaccination, we generated hypotheses on populations that would benefit most from vaccination within PrEP care, such as those with infrequent healthcare access, who live outside major cities, with lower income and not eligible for publicly funded vaccination.

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