
Trends in Vaccine-induced Immunity to Hepatitis B among Canadian Street-involved Youth

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ABSTRACT *In Canada, universal and publicly funded hepatitis B immunization programs have been available since 1998 in all provinces and territories. This present study estimates the proportion of having vaccine-induced immunity to hepatitis B virus (HBV) infection and its associated determinants among street-involved youth aged at 15–24 years old in Canada using the data collected by the Enhanced Surveillance of Canadian Street Youth. Vaccine-induced immunity was identified by blood test results of anti-HBc negative and anti-HBs positive. Of the 4,035 participants included in this study, the overall proportion of those with vaccine-induced immunity to HBV was 51.7% during the study period compared to over 90% among the general adolescent population. The proportion of street-involved youth immunized with HBV vaccine increased from 34.7% in 1999 to 64.4% in 2005. Immunity was higher among females (aOR=1.43, 1.17–1.75) and among those with a reported history of sexually transmitted infection (aOR=1.30, 1.03–1.63). The proportion of youth with the immunity decreased as age increased (aOR=0.78, 0.76–0.81, per year increase). Despite an overall increase in the proportion of Canadian street-involved youth with vaccine-induced immunity to HBV, the proportion was still significantly lower than that observed in the general adolescent population. This highlights the need to improve the access to basic health care and the immunization programs to HBV for street-involved youth through creative outreach programs and other multi-faceted approaches.*

KEYWORDS *Hepatitis B, Infectious diseases, Sexually transmitted infections, Immunity, Vaccination, Survey*

INTRODUCTION

Infection caused by hepatitis B virus (HBV) may result in lifelong infection, cirrhosis of the liver, liver cancer, liver failure, and death. The World Health Organisation estimates that more than one third of the world's population has been infected with HBV, and it is associated with more than one million deaths each year.¹ In Canada,

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HBV surface antigen (HBsAg) seroprevalence is estimated to be between 0.5% and 1.0%, and the distribution of cases varies by ethnic origin and risk group.² The highest incidence of the disease is seen in teenagers and young adults.^{1,3} HBV is transmitted through percutaneous or mucosal contact with infected biological fluids. In countries where the prevalence of chronic HBV infection is low (<2%), the major routes of HBV infection include sexual contact with an infected person and percutaneous exposure to needles and other “sharps” that have been contaminated with HBV (this includes injecting drug use and tattoos with absence of a precautionary perception). Vertical transmission from infected pregnant women to their newborns can occur but is rare.^{1,2} In Canada, the major risk factors associated with acute HBV infection include injecting drug use (19%), non-injecting drug use (9%), and high-risk sexual activities such as having multiple sex partners (13%) and sex with HBV-infected individuals (13%). About 8% of the infection cases are related to health care including blood or blood transfusion, hemodialysis, surgery, and dental surgery.⁴

HBV infection is also vaccine-preventable. A safe and effective vaccine against HBV infection was introduced in the early 1980s. As of March 2002, over 150 countries have introduced routine HBV vaccine within their national immunization programs.¹ To prevent HBV infection, universal publicly funded immunization programs are available in all provinces and territories in Canada for infants or adolescents, as is universal screening of all pregnant women for HBsAg, pre-exposure immunization, or individuals at increased risk and post-exposure intervention for those exposed to HBV, particularly infants born to HBV-infected mothers. High-risk groups include men who have sex with men (MSM), persons with a recent history of sexually transmitted infections (STIs) or multiple sexual partners, injecting drug users (IDU), inmates of correctional facilities, household and sexual contacts of HBV-infected persons, and health care and emergency service workers and pregnant women.^{5,6} In 1992, British Columbia became the first province in Canada to introduce a universal school-based immunization program against hepatitis B. As of 1998, all Canadian provinces and territories provided free vaccine against HBV to targeted students. However, HBV immunization is not mandatory in Canada, and legislation or regulations under provincial/territorial Health Protection Acts do not require proof of immunization to HBV for school entrance. The grade at which HBV immunization is provided varies between provinces and territories ranging from grade three to seven.⁵ The implementation of publicly funded immunization programs has greatly contributed to the decrease in incidence of HBV infection in the general population in Canada. Vaccine efficacy studies have demonstrated that adherence to licensed HBV immunization schedules results in a protective level of antibody to hepatitis B surface antigen (≥ 10 mIU/ml) in 90–100% of healthy recipients.⁷ However, the risk of HBV infection remains high for certain populations including immigrants from countries where HBV is endemic,^{8,9} street-involved youth,^{10,11} IDU,¹² and MSM.¹³

Street-involved youth are particularly vulnerable to HBV infection because of transient school attendance, unstable living conditions, substance abuse, and other factors that may prevent them from accessing the publicly funded immunization programs (for example, the school-based immunization program against HBV and other publicly funded immunization programs available through shelters, drop-in clinics, or mobile vans). These social and contextual factors may also place them at higher risk for practices that are associated with the transmission of sexually transmitted blood-borne infections (STBBIs), including HBV.^{10,11} Furthermore, since

effective immunization against HBV requires at least two consecutive vaccinations over the course of 6 months, it is often difficult to complete the full vaccination schedule for this hard-to-reach population at high risk for HBV infection. While several studies suggest that the prevalence of HBV infection is more than ten times higher among street-involved youth than that observed in general youth population,^{10,11,14} few studies have focused on the proportion of having vaccine-induced immunity to HBV in this population. This present analysis was performed to examine trends in the proportion of street-involved youth who have vaccine-induced immunity to HBV and associated determinants in Canada.

METHODS

For this study, we used the data collected through Enhanced Surveillance of Canadian Street Youth (E-SYS). The E-SYS is an ongoing, multi-center enhanced surveillance system that captures changing patterns of STBBIs and associated determinants and contextual factors among street-involved youth in seven Canadian cities (Vancouver, Edmonton, Saskatoon, Winnipeg, Toronto, Ottawa, and Halifax). Data collection relied on repeated cross-sectional behavioral surveys accompanied by biological sampling (blood and/or urine testing), starting in 1999 and repeated in 2001, 2003, and 2005.¹⁵

Participants were recruited through drop-in centers, outreach work, and mobile vans. The recruitment of youth involved snowball-sampling methods, using word-of-mouth to advertisement to potential participants. This technique has been shown to be effective in hard-to-reach populations such as street-involved youth.¹⁶ In order to minimize sampling bias within sentinel sites, at least two of the larger drop-in centers in each city were selected to capture a cross-section of street-involved youth. This also allowed each site to meet the sample size required. Furthermore, nurses experienced in working with street-involved youth were trained to ensure that recruitment was conducted using the same approach at all sites. Youth were invited to participate if they were (a) between 15 and 24 years old; (b) able to understand spoken English or French; (c) able to provide informed consent; and (d) in the previous 6 months, had either run away from home or other place of residence for three consecutive days or more, or been thrown out of home or other place of residence for three consecutive days or more, or been without a fixed address for three consecutive days or more. Youth could participate in the survey only once during each data collection year. All participating youth provided informed consent prior to their participation in the study.

An interviewer-administered questionnaire was used to collect information on demographics, social factors, sexual practices, substance use, attitudes, and knowledge of risk behaviors and family history. Interviews were conducted in places where privacy and confidentiality could be maintained. Interviewers with experiences in working with street-involved youth were selected and trained to ensure the accuracy of answers to the questions, especially to those sensitive questions including high-risk sexual behaviors, drug use, and history of abuse. In addition to the questionnaire, consenting youth were asked to provide a urine sample and a blood sample for laboratory testing for chlamydia, gonorrhea, syphilis, HBV, hepatitis C virus, human immunodeficiency virus (HIV), herpes simplex virus, and human t-cell lymphotropic virus.

In this analysis, we included all participants who had definitive testing results for antibodies to hepatitis B core antigens (anti-HBc) and antibodies to hepatitis B surface antigens (anti-HBs). Vancouver did not participate in the survey in 2001. Data from Winnipeg and Ottawa (in 2005) were excluded due to a high percentage of missing

values for anti-HBc or anti-HBs, giving a total of 4,035 participants in the final analysis. Vaccine-induced immunity was identified by blood test results of anti-HBc negative and anti-HBs positive. Blood tests for anti-HBc and anti-HBs were conducted at local laboratories by using a commercially available enzyme-immunoassay kit. Major exposures examined in the analysis included demographic characteristics (age, gender, education, birth place, and ethnicity), social factors (social workers, foster care, and group home), correctional services (jail and probation), and length of time not living with parents. Also examined were substance use (smoking, drinking, and drug use), tattooing, piercing, sexual behaviors (sexual activity, sexual partnering, condom use, sex trade, and sex with STI positive partners), and previous STI diagnosis. Since the target age and year of implementation of school-based immunization program varied between jurisdictions, to assess the age eligibility of the immunization program for each participating youth from different sites and survey years, age of youth at the interview collected was converted to age at the year of implementation of the school-based immunization program in the province where he/she was living. A youth was considered to be eligible for a school immunization program if the converted age was younger than the target age of the immunization in the province.

Temporal trends in proportion of street-involved youth who had vaccine-induced immunity to HBV were assessed by chi-square linear trend test. Chi-square test was used to examine the differences in distributions of the proportions of youth with vaccine-induced immunity across demographical, social, and behavioral factors, with a two-tailed p value of <0.05 defined as statistically significant. Factors with p value of <0.1 were candidates for multivariate logistic regression models. In logistic regression, age was modeled as a continuous variable in terms of the linear relationship with the outcome. Potential interactions between age, gender and educational level, and gender with correctional services were tested. The adjusted odds ratios (aORs) of vaccine-induced immunity along with their 95% confidence intervals (CIs) for the factors in final regression model were used to assess their association with the outcome. All analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC, USA).

This study was approved by the Health Canada Research Ethics Board and the Research Ethics Board in participating Cities.

RESULTS

Demographics

Of the 4,035 participants included in this study, the mean age was 19.1 years with 19.6 years for males and 18.0 years for females. Males accounted for almost two thirds of the total participants. About 90% of youth completed some secondary education (up to grade 12). The vast majority (91%) were born in Canada. Ethnic background varied with 62.1% reporting Caucasian ethnicity and 31.4% reporting Aboriginal ethnicity. Other reported ethnicities included African (5.4%), Caribbean (3.4%), Hispanic (2.8%), Asian (1.7%), and Middle Eastern (1.4%). Of note, participating youth could report multiple ethnicities.

HBV Markers

Of the 4,035 study subjects, 2,152 street-involved youth (53.3%) tested positive for anti-HBs, 83 (2.1%) were positive for anti-HBc, and 64 (1.6%) were positive for both anti-HBs and anti-HBc. Among those 1,883 street-involved youth who were

negative for anti-HBs testing, 19 were anti-HBc positive, giving a prior HBV exposure rate of 1.0%.

Vaccine-induced Immunity

The overall proportion of youth with vaccine-induced immunity to HBV was 51.7% (2,088/4,035) during the study period. The proportion has significantly increased from 34.7% in 1999 to 64.4% in 2005 ($p < 0.001$ for linear trend test). Compared to their older counterparts aged 20–24 years, younger youth aged 15–19 years had a higher proportion of vaccine-induced immunity (58.6% vs. 42.3%, $p < 0.001$) and presented a greater increase in the proportion of vaccine-induced immunity during the study period (by 95.6% vs. 83.3%, Figure 1).

Despite the overall increased trend in the proportion of having vaccine-induced immunity, geographical variations were observed among street-involved youth during the study period. The overall proportion of vaccine-induced immunity ranged from 23.8% to 58.6% (Figure 2).

Overall, 65.2% of the participating youth were age-eligible for the school-based HBV immunization program, and among these youth, 63.8% had the vaccine-induced immunity. In contrast, among those not age-eligible for school-based immunization, only 29.2% had vaccine-induced immunity ($p < 0.0001$). Table 1 shows the percentages of youth who were eligible for school immunization programs and the proportion having vaccine-induced immunity stratified by year, city, and age at interview. We found that although an increasing temporal trend in vaccine-induced immunity level was still observed, the rate of the increase was much lower than that observed among overall study participants (by 29.1% vs. 85.6%). Geographic discrepancies in the proportion of having vaccine-induced immunity observed in overall participants (Figure 2), however, no longer existed among youth who were age-eligible for school immunization (Table 1). In addition, among participating youth who were eligible for school-based immunization, the proportion of having vaccine-induced immunity is still lower in older youth compared to their younger counterparts.

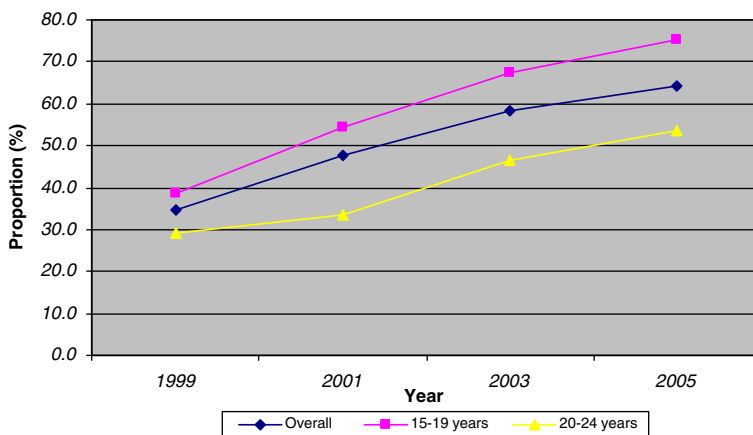


FIGURE 1. Temporal trend in proportion of vaccine-induced immunity to hepatitis B virus among street-involved youth in 1999, 2001, 2003, and 2005.

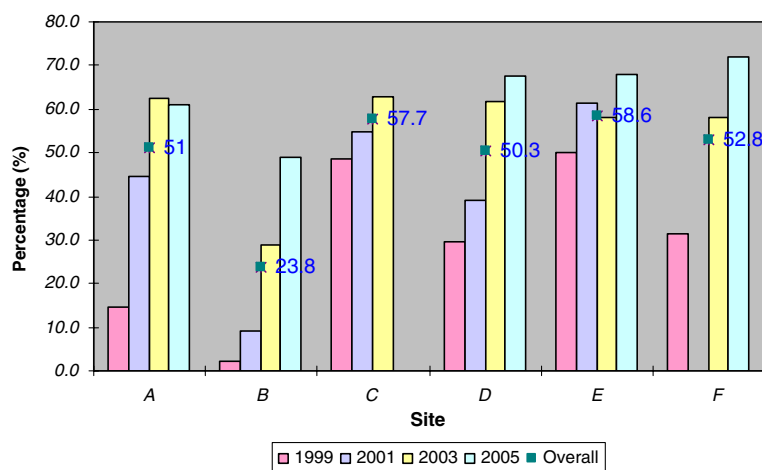


FIGURE 2. Temporal trend in proportion of vaccine-induced immunity to hepatitis B virus among street-involved youth by site in 1999, 2001, 2003, and 2005.

Determinants of Vaccine-induced Immunity

Table 2 presents the crude and aORs of vaccine-induced immunity for statistically significant factors in univariate or multivariate logistic regression. Results from multivariate logistic regression show that age, gender, and self-reported history of STIs are independently associated with the proportion of vaccine-induced immunity. Males and older street-involved youth were less likely to have vaccine-induced immunity to HBV. Compared to youth who did not report prior STI diagnosis, youth who reported a history of STI were more likely to receive the vaccine. Statistical significance of the association for educational level was marginal in

TABLE 1 Percentages of youth who had eligible age^a for school hepatitis B virus (HBV) immunization and the vaccine-induced immunity levels, 1999, 2001, 2003, and 2005

Stratified by	Total number of youth	Youth with eligible age (number (%))	Immunity for youth with eligible age (number (%))	<i>p</i> value
Overall	4,035	2,630 (65.2)	1,678 (63.8)	
Year				<0.0001
1999	977	302 (30.9)	163 (54.0)	
2001	880	532 (60.5)	314 (59.0)	
2003	1,222	965 (79.0)	622 (64.5)	
2005	956	831 (86.9)	579 (69.7)	
City				0.3832
A	922	564 (61.2)	369 (65.4)	
B	349	89 (25.5)	55 (61.8)	
C	357	304 (85.2)	181 (59.5)	
D	587	400 (68.1)	253 (63.3)	
E	1,257	865 (68.8)	568 (65.7)	
F	563	408 (72.5)	252 (61.8)	
Age at interview				0.0003
15–19	2,337	1,952 (83.5)	1,284 (65.8)	
20–24	1,698	678 (39.9)	394 (58.1)	

^aAge at implementation year of school HBV immunization that is younger than targeted age of the immunization program

TABLE 2 Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of vaccine-induced immunity to hepatitis B virus (HBV) for selected factors^a among street-involved youth in 1999, 2001, 2003, and 2005 (N=2,114)^a

Factor	Immunity		Univariate model				Multivariate model			
	%	(n/N)	OR	95% CI	p value	OR	95% CI	p value		
Age ^b (year)	–	–	0.79	0.77	0.81	<0.0001	0.78	0.76	0.81	<0.0001
Gender						<0.0001				<0.01
Male	48.1	(1,226/2,551)	1				1			
Female	58.1	(861/1,483)	1.50	1.32	1.70		1.43	1.17	1.75	
Highest level of education						0.06				0.059
Primary (up to grade 6)	43.1	(47/109)	1				1			
Secondary (up to grade 12) +	52.3	(2,029/3,882)	1.44	0.98	2.12		1.77	0.97	3.21	
Live with parents						<0.0001	Not in final model			
No, ≥1 year	53.7	(1,037/1,932)	1							
No, <1 year	64.6	(475/735)	1.58	1.32	1.88					
Yes	55.0	(236/429)	1.06	0.86	1.30					
Correctional services						<0.001	Not in final model			
No	56.2	(789/1,404)	1							
Yes	49.4	(1,296/2,623)	0.76	0.67	0.87					
Binge drinking						0.05	Not in final model			
No	54.3	(881/1,623)	1							
Yes	50.7	(714/1,408)	0.87	0.75	1.00					
Self-reported prior STI						<0.05				<0.05
No	50.8	(1,584/3,116)	1				1			
Yes	55.0	(502/912)	1.18	1.02	1.37		1.30	1.03	1.63	
Body tattooing						<0.01	Not in final model			
No	59.4	(1,075/1,809)	1							
Yes	54.0	(674/1,249)	0.80	0.69	0.93					
Body piercing						0.08	Not in final model			
No	54.6	(361/661)	1							
Yes	58.5	(1,318/2,255)	1.17	0.98	1.39					

^a*p*<0.1 in univariate regression model

^aSample size for multivariate regression

^bAge at implementation year of school HBV immunization

multivariate logistic regression. Factors associated with vaccine-induced immunity, which were statistically significant in univariate logistic regression included living with parents, receiving correctional services, having binge drinking, and having a body piercing or tattooing. No significant interactions between the selected variables were found.

INTERPRETATION

The proportion of street-involved youth with vaccine-induced immunity to HBV in this study has almost doubled from 34.7% in 1999 to 64.4% in 2005. The increased trend did not change after age eligibility for school immunization program was considered. The trend towards increased vaccine-induced immunity was present across all urban centers studied, but the rate of increase varied between sites. It is likely that the publicly funded, school-based immunization program in Canada has resulted in increased coverage of Canadian youth.

However, despite an increased trend in vaccine-induced immunity over time, the overall proportion of street-involved youth with this immunity is significantly lower than the reported vaccination completion rate among pre-adolescent population in Canada (51.7% vs. >90%, respectively).^{2,17} Of concern is our finding that more than one third of the participating street-involved youth who were of an age to have received HBV vaccination through a school-based immunization programs had not been effectively immunized against HBV. Indeed, we may have underestimated the proportion of unimmunized study-involved youth given that repeat participants in the study (~10% of study population) would have been counselled and offered the HBV vaccine if necessary in a previous study cycle. A US study¹⁸ observed an even bigger gap showing that hepatitis B immunization coverage among older homeless children and adolescents (10–18 years) was less than half of the estimated national average.

The marginalized position of street-involved persons puts them at increased risk for not receiving immunization including school-based immunization to HBV. Studies have demonstrated the association between low income and poor HBV vaccine coverage.^{18,19} In an investigation on success of implementation of grade seven HBV immunization, Linton et al.¹⁹ found that schools in the highest economic quartile had a much higher average HBV immunization coverage than those schools in the lowest quartile (89% vs. 48%).

School attendance is another important factor associated with the coverage of school HBV immunization. Our study found a marginal association between educational level and the vaccine-induced immunity to HBV. Street-involved youth who completed secondary education (up to grade 12) might have more chances to get them immunized against HBV compared to those who only completed primary education which is up to grade 6 (aOR, 1.77; 95% CI, 0.97–3.21; $p=0.059$). Many street-involved youth attend school erratically due to frequently moving from one place to another or dropping out of school for other reasons. We found that more than two thirds of the participants who provided information on school leave experienced being kicked out of school or dropping out of school (data not shown). This might greatly limit their access to school-based HBV immunization program.

In our study, youth who reported having prior diagnosis with STIs were more likely to have been immunized to HBV, suggesting that access to health care is an important consideration for vaccine coverage. However, immunization of street-involved youth through the traditional medical service model presents a challenge since most street-involved youth may not trust traditional medical programs and thus they access the health system infrequently.^{3,19} In addition, due to their mobile tendencies, it is difficult to establish follow-up care. Therefore, outreach services and other models for health care provision are critical to enhance access and provide care for street-involved youth within their particular social context.

The lower proportion of having the immunity to HBV compared to the national average that was observed in this study could also result from a subset of participating youth who have completed the HBV immunization but have anti-HBs levels which have fallen below the 10-mIU/ml cutoff.^{6,20} This could lead to underestimating the proportion of youth who have received the vaccination. Lower response to anti-HBs is often observed among persons with chronic diseases (e.g., diabetes and chronic liver diseases) and those who are immunosuppressed (e.g., infected with HIV or hemodialysis patients). In addition, seniors (≥ 60 years), obese people, smokers, and those with alcoholism may also respond poorly to vaccination compared with healthy individuals. Studies found that people who are healthy and young have high seroprotection rates ($\geq 95\%$), and the best response rate to the

vaccine is observed in children aged between 5 and 15 years old (99%).⁶ Since the prevalence of HIV was low among the included street-involved youth (data not shown), it is less likely that the observed low level of immunity to HBV was associated with their low response rate to anti-HBs.

We found that female street-involved youth were more likely to receive HBV immunization than their male counterparts. This is consistent with the findings of a previous study that focused on school- or clinic-based HBV immunization programs in general adolescents.²¹ Our preliminary analysis did not find gender disparities in rates of dropping out or being kicked out of school among those youth who responded to these two survey questions (data not shown). Gender difference in frequencies of health care access might influence the immunization coverage. Besides prenatal care, studies have demonstrated that women use more health care services than men after adjusting for health care services that are specific for women, such as gynecology.^{22,23} This could lead to more opportunities for immunization among women.

Immunization is an effective and cost-saving means to prevent the transmission of HBV infection. Elimination of HBV infection in our population would require universal immunization. Given the high prevalence of HBV infection in street-involved youth^{10,11,14} and their relatively low level of immunity, efforts to improve HBV vaccine coverage in street-involved youth is important. The primary challenge in the prevention and control of HBV infection in this population is to enhance access to health care given their mobility. Although school-based immunization programs have been demonstrated to be an effective means to deliver HBV immunization,^{24,25} such programs alone are not sufficient for street-involved youth who attend school erratically. Creative outreach programs are needed to increase HBV vaccine coverage. A HBV immunization outreach project²⁶ conducted in Montreal in 1997 has demonstrated how outreach work increases the HBV immunization rate among the street-involved youth through three major components of the project involved in community outreach initiatives, accessible vaccination clinics in community organizations frequently visited by street-involved youth, and an active and innovative recall system. The first year data of the project showed that about 80% of the street-involved youth have received at least two doses of the vaccination, and over 50% completed the vaccination schedule, compared to the three dose completion rate of 12% in another street-involved youth study in Montreal in 1996.²⁷

HBV immunization among street-involved youth can also be provided through youth services and the primary health care system. It is important to include hepatitis B immunization in a set of standard youth services provided to street-involved youth. These social and medical services need to be youth-friendly and easily accessible. The immunization provision can be part of the clinical services offered. In Canada, routine pre-immunization serologic testing for HBV, including HBsAg, anti-HBs, or anti-HBc, is recommended for people at high risk of HBV infection. This testing helps identify who needs the immunization and who should have a medical follow-up in terms of the infection. Therefore, it is important for health care providers to follow the recommendation and verify HBV immunization status of youth when they visit a clinic for other medical services/consultations to help provide a catch-up immunization when it is needed. Furthermore, specifically targeted educational programs play an important role in increasing vaccine coverage. Schwarz, et al.²⁸ reported a successful shelter-based HBV immunization program for homeless children and adolescents in Baltimore. This program has

increased the coverage rate to 85% from the baseline of 68% among 328 participants by applying a culturally appropriate educational session with an HBV video in addition to other intervention efforts (e.g., reminders and incentives) among caregivers and adolescents in the shelters.

Some considerations in interpreting the findings of this study should be noted. First, the cross-sectional study design limits our ability to determine causality of the associations identified. Second, the lack of geographic sampling frame in the recruitment makes it impossible to get a random sample, which could produce a selection bias, although the informal snowball-sampling method used for the recruitment of youth in this study has been shown to be effective in hard-to-reach populations. Third, information on most of the risk factors examined relied on self-reported data, by which information bias could be introduced. For example, street-involved youth in this study might have been reluctant to report socially undesirable behaviors such as unprotected sex, abuse, and injecting drug use and, as a consequence, these behaviors may have been under-reported. Finally, findings based on samples limited to the urban centers in six cities included in this analysis across Canada may not be generalizable to other geographic areas or cities, and especially, may not be applicable to less populated areas.

CONCLUSIONS

The proportion of having vaccine-induced immunity observed in street-involved youth who participated in the E-SYS increased between 1999 and 2005. However, it was still significantly lower than the national average, especially for male street-involved youth, and those who were older. There are multiple factors which might be impacting on this level of HBV vaccine-induced immunity. Creative outreach programs and other multi-faceted approaches are needed to ensure that these youth have ready access to basic health care and various HBV immunization programs.

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