Missed Opportunities for the Prevention of Vertical HIV Transmission in Canada, 1997 – 2016

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Meetings at which parts of the data were presented:

Data from the Canadian Perinatal HIV Surveillance Program (CPHSP) are presented annually at the Canadian Conference on HIV/AIDS Research (CAHR). Presentations with a specific focus on missed opportunities for vertical HIV transmission prevention were given at the 24th Annual Canadian Conference on HIV/AIDS Research (CAHR), Toronto, Ontario, April 30 – May 3, 2015 (Oral presentation O090) and the International AIDS Society (IAS) meeting, July 19 to July 22, 2015, Vancouver, British Columbia, Canada (poster MOPEC445).

Funding Source:

The Canadian Perinatal HIV Surveillance Program is supported by the Public Health Agency of Canada. No specific funding was secured for this study.

Competing interests: None of the author have a conflict of interest in relation to this work

Running head: Vertical HIV transmission prevention, Canada

Word count: 2548

ABSTRACT

Background: Vertical HIV transmission (VT) has declined significantly in Canada, but missed opportunities for prevention continue to occur.

Methods: The Canadian Perinatal HIV Surveillance Program collects data on mothers living with HIV and their infants. Receipt of adequate antiretroviral treatment (ART) (antenatal combination ART [cART] ≥4 weeks, intrapartum zidovudine receipt, 4-6 weeks infant zidovudine receipt) and predictors of inadequate antenatal cART (none/<4 weeks) were determined.

Results: 3785 mother-infant pairs were identified (1997-2016). Uptake of ≥4 weeks of antenatal cART improved over time across all provinces/territories and regardless of maternal risk category or race/ethnicity (p<0.001). During the 2011–2016 period, 6.5% of women received no/<4 weeks of antenatal cART, 10.7% of women received no intrapartum intravenous ZDV and 3.1% of infants received <4 weeks of oral zidovudine. In multivariate analysis restricted to the 2011–2016 period, better uptake of ≥4 weeks of antenatal cART was seen in black women (versus indigenous [p=0.02], versus white [p=0.06]) and in British Columbia/Yukon compared to Alberta, Ontario and Quebec (p=0.04 for all). Of 14 VT events during the 2011-2016 period (VT rate 1.0%), maternal diagnosis was established prior to onset of labour in only 5 cases and only 2 received ≥4 weeks of antenatal cART.

Conclusions: Efforts to improve timely access to care, HIV screening and treatment for all women, combined with enhanced resources targeting populations at increased HIV risk, will be needed if VT is to be eliminated in Canada.

KEY WORDS: Human immunodeficiency virus, vertical transmission, child, missed opportunities, combination antiretroviral therapy

INTRODUCTION

With provision of combination antiretroviral therapy (cART) to women during pregnancy, intravenous zidovudine (ZDV) during labor, 4-6 weeks of oral ZDV to the newborn and exclusive formula feeding, the risk of vertical HIV transmission (VT) has declined to between 0.27% and 2.9% in developed countries.[1-6] Canadian data for the period between 1990 and 2010 demonstrated a VT rate of 16.4% when mothers received no antenatal cART, 1.6% when mothers were prescribed antenatal mono or dual nucleoside analogue therapy, and 1.0% when mothers were prescribed antenatal cART.[4]

Unfortunately, missed opportunities for the prevention of VT continue to occur in developed countries.[7,8] For example, among women enrolled in the European Collaborative Study, 9% of pregnant women between the years 2000 and 2009 (n=2148) received less than two weeks of antenatal cART or no antenatal cART, despite 50% of these women having been diagnosed with HIV infection before conception.[7] Risk factors that have been associated with ongoing VT include absent or inadequate antenatal care, late maternal diagnosis, maternal injection drug use (IDU), lack of antiretroviral treatment (ART) during pregnancy, labor and delivery, preterm delivery, and incomplete avoidance of breastfeeding.[7-11]

The objectives of the present study were to determine the adequacy, and changes over time in adequacy, of antenatal and intrapartum maternal and postpartum neonatal ART uptake for the prevention of VT, and determine the VT rate over time, and according to adequacy of antenatal ART, during the cART era (1997-2016) in Canada. We further sought to evaluate recent trends by investigating predictors of inadequate antenatal ART uptake for the 2011-2016 period.

METHODS

The Canadian Perinatal HIV Surveillance Program (CPHSP) collects data from 23 HIV referral health centers and health departments from across Canada that includes representation from all provinces and territories. Twenty of the 23 centers are obstetric and/or pediatric care centers located in the 10 provinces; the remaining three are public health units of each of the three northern territories. The program was initiated in 1990 under the auspices of the Canadian Pediatric & Perinatal HIV/AIDS Research Group (CPARG) and is supported by the Public Health Agency of Canada (PHAC). Data management and analysis is conducted at the CIHR Canadian HIV Trials Network (CTN) data center in Vancouver, British Columbia. Ethical approval for the surveillance was obtained from the Research Ethics Boards of all participating centers.

The CPHSP methodology has been previously described.[4] Data is collected by retrospective chart review on an annual basis, and since 2008, submitted electronically via a secure web-based Oracle™ database. Maternal data includes country of birth, risk category for HIV acquisition, date of HIV diagnosis, self-reported race/ethnicity (according to national surveillance definitions), viral load, antenatal ARV regimen(s) and receipt of intrapartum ZDV. Infant data includes place of birth, mode of delivery, gestational age at birth, birth weight, sex, ART prophylaxis and HIV status. Of the variables listed above, two (maternal VL, infant birth weight) began being collected systematically in 2008. Infant HIV status was reported as confirmed if HIV was detected in two separately timed virologic assays prior to 18–24 months of age or by HIV serology after that age. HIV negative status was defined by having ≥ 2 separately timed negative virologic assay results taken at one month of age or later during the first 18 months of

life or by negative HIV serology after that age. Indeterminate status was reserved for cases not finalized by these criteria.

To be eligible for inclusion in this study, children had to be born in Canada between January 1, 1997 and December 31, 2016 to a mother with confirmed HIV infection. Inadequate ART was defined by receipt of <4 weeks of antenatal cART, failure to receive intrapartum intravenous ZDV or receipt of <4 weeks of oral ZDV by the infant, the latter two in accordance with current Canadian guidelines.[12,13] The specific study objectives were to describe: (a) the proportion of mothers and infants who received inadequate ART interventions; (b) changes over time in the proportion of mothers and infants who received inadequate ART interventions; (c) VT rates over time and according to adequacy of antenatal ART; (d) predictors of inadequate antenatal ART. The analysis of predictors of inadequate antenatal cART uptake was restricted to the 2011–2016 period as this was deemed most relevant to the current situation.

Demographic characteristics were summarized using percentages, means with standard deviations or medians with ranges as appropriate. Chi square or Fisher's exact test was used to compare the maternal risk category, maternal race/ethnicity, geographic region of birth, timing of maternal diagnosis, and ART rates across time periods as appropriate. Time trend of rates were assessed using logistic regression with child birth year being modelled as a continuous variable. Logistic regression modelling was used to examine the relationship between antenatal cART uptake and potential explanatory variables including demographic and clinical characteristics and year of birth (mother-infant pairs [MIPs] with missing documentation of antenatal cART receipt were excluded). For detailed review of VT events, all cases were included regardless of data completeness. Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

3785 infants were born in Canada to mothers with documented HIV infection during the study period. Their baseline maternal characteristics and delivery related factors are shown in Table 1. In 60 MIPs (1.6%) infant HIV status was indeterminate, with explanation documented in 19 (death [n=10]; moved out of Canada [n=8]); the remaining 42 were lost to follow-up. All deaths occurred within five months of birth and none were attributed to HIV. The VT rate for the 3725 (98.4%) MIPs for whom final infant HIV status was available for the full study period was 3.4% (125/3725). During the 2011–2016 period the VT rate was 1.0% (14/1385). The VT rate for the full study period was 28.9% in the absence of antenatal cART, 4.3% with <4 weeks of antenatal cART and 0.2% with ≥4 weeks of antenatal cART.

ART uptake information was complete in 3724 of 3785 MIPs (98.4%); information was missing on antenatal cART for 21 cases, intrapartum intravenous ZDV for 50 cases and infant ZDV for 12 cases. Inadequate ART was noted in 29.9% (n=1112) of MIP including: 21.4% (n=804) of mothers who received either no antenatal cART (9.5%; n=359) or <4 weeks of antenatal cART (11.8%; n=445); 14.0% (n=523) of mothers who received no intrapartum intravenous ZDV; 6.3% (n=237) of infants who received <4 weeks of oral ZDV. The proportion of mothers receiving ≥4 weeks of antenatal cART improved significantly over time, in all regions regardless of maternal risk category or race/ethnicity (Figure 1). Receipt of intrapartum intravenous ZDV and ≥4 weeks of neonatal ZDV also improved significantly over time (OR per calendar year 1.05 [95% CI 1.03, 1.07], p<0.001 and OR per calendar year 1.13 [95% CI 1.10, 1.16], p<0.001, respectively). Nevertheless, during the 2011–2016 period, 6.5% (n=92) of women received inadequate antenatal cART (none 3.6% [n=51], <4 weeks 2.9% [n=41]; Table 2), 10.7% (n=146) of women received no intrapartum intravenous ZDV and 3.1% (n=43) of infants received <4

weeks of oral ZDV. Among women diagnosed prior to the third trimester during this period (n=1302), 2.5% received <4 weeks of antenatal cART and 1.8% received no antenatal cART.

Timing of maternal diagnosis, available for 3317 (87.6%) MIPs, was established prior to the third trimester in 92.5%, increasing from 67.4% in 1997 to 94.4% in 2016 (OR per calendar year 1.16 [95% CI 1.13, 1.19]; p<0.001). For the 2011–2016 period (n=1355), maternal diagnosis prior to the third trimester was lower for indigenous women (92.9%) compared to white women (97.2%; p=0.025) and black women (97.8%; p<0.001) and for women with IDU as their risk category compared to women with heterosexual as their risk category (92.7% vs. 97.8%; p<0.001). For both indigenous and white women, diagnosis prior to the third trimester was lower in those with IDU as risk category compared to those with heterosexual as risk category (91.3% vs. 96.7% for indigenous women, p=0.10; 95.1% vs. 98.1% for white women, p=0.21). There were no black women with IDU noted as risk category.

During the 2011–2016 period, maternal risk category and maternal race, but not province of delivery, were significantly associated with adequacy of antenatal cART (Table 2). Among women with heterosexual as risk category, adequate antenatal cART was received by 90.5% of indigenous women compared to 95.5% of black women (p=0.047) and 94.4% of white women (p=0.31). Among white women whose risk category was IDU, 85.0% received ≥4 weeks of antenatal cART, 1.7% received <4 weeks of antenatal cART and 13.3% received no antenatal cART. The corresponding proportions for indigenous women whose risk category was IDU were 91.1%, 2.6% and 6.3%, respectively. In Ontario and Quebec, where IDU accounted for <10.0% of cases, receipt of ≥4 weeks of antenatal cART among women who inject drugs was 72.7% and 75.0%, respectively. By contrast, in Saskatchewan, British Columbia, Manitoba and Alberta,

where IDU accounted for a higher proportion of cases, 90.9–95.2% of such women received ≥4 weeks of antenatal cART (p=0.006).

Univariate and multivariate analysis of potential predictors of adequate antenatal cART uptake for the 2011–2016 period are depicted in Table 3. In univariate analysis, better uptake of antenatal cART was observed among black women compared to both indigenous women and white women and among women whose risk category was heterosexual compared to IDU. In the multivariate analysis, better uptake of cART among black women compared to indigenous women remained significant, while that for black women compared to white women showed borderline significance. Having delivered in British Columbia/Yukon was associated with better antenatal cART uptake compared to Alberta, Ontario and Quebec. The impact of risk category was no longer significant in the multivariate model. Gestational age at birth and birth year were not significantly associated with antenatal cART uptake in either the univariate or multivariate analysis. In a separate multivariate analysis, that included a race-risk category interaction term, adequate antenatal cART among women with heterosexual as risk category was significantly better for black women compared to indigenous women (OR 3.94 [1.53, 10.14], p=0.004) and borderline-significant for white women compared to indigenous women (OR 2.93 [1.00, 8.65], p=0.051).

Of 125 documented VT events, 111 occurred during the 1997–2010 period and 14 occurred during the 2011–2016 period (Figure 2). Eighty-six (68.8%) VT events involved mothers who were diagnosed intrapartum (n=18) or post-partum (n=68). Of the 36 VT events involving mothers diagnosed antenatally, maternal cART was not taken during pregnancy in 12 cases, taken for <4 weeks before delivery in 18 cases and taken for ≥4 weeks before delivery in 5 cases (maternal treatment status unknown in one case). Poor maternal adherence was documented in

three of the latter five infants. Salient MIP characteristics for the 14 VT cases that occurred in the 2011–2016 period are shown in Table 4. Maternal diagnosis was established prior to the third trimester in only 5 of these 14 cases, and only 2 received ≥4 weeks of antenatal cART.

DISCUSSION

A major finding of this study was the significant reduction in VT over time, corresponding with a steady improvement in early diagnosis and ART uptake antenatally and intrapartum among pregnant women living with HIV and in their children during the neonatal period. Nevertheless, as demonstrated by the 14 children who acquired HIV vertically between 2011 and 2016 and by the observation that 6.5% of women (n=92) received <4 weeks or no antenatal cART during the same period, there remains room for improvement in prevention efforts in Canada.

Although improvement in ART uptake was observed across all regions and irrespective of maternal risk category or race, our findings suggest that certain populations in Canada continue to have lower rates of timely diagnosis and antenatal cART uptake. IDU was associated with late maternal diagnosis and, in Ontario and Quebec (where IDU was relatively uncommon as maternal risk category), with a lower rate of adequate antenatal cART uptake. The importance of substance abuse as a predictor of late diagnosis, suboptimal ART, and VT is corroborated by multiple studies from the U.S. and Europe.[3,7,9,14-16] The lower uptake of antenatal cART in the adjusted analysis for Ontario and Quebec compared to British Columbia/Yukon may reflect, in part, the low uptake of antenatal cART among women who inject drugs in the former two provinces. In this regard, it is noteworthy that the uptake of antenatal cART was relatively uniform across maternal risk categories for all provinces except Ontario and Quebec. Potential explanations for the lower uptake of antenatal cART among indigenous women compared to

black and white women cannot be determined from our data, but likely reflects differences in access to care.[17]

Experience from the French Perinatal Cohort whereby no VT events were observed from the 2651 women initiated on cART prior to conception and had an undetectable VL at delivery supports the possibility that with effective interventions, VT can be eliminated.[5] Our results suggest that this is an achievable goal in Canada, although this would require concerted commitment and effort given that over two-thirds of VT events in our cohort occurred in MIPs where the woman was diagnosed after delivery, and of those involving mothers diagnosed antenatally, only 14% (5/36) had received ≥4 weeks of cART before delivery. Enhanced efforts aimed at engaging all women in care and screening them for HIV infection preferably prior to conception or as early in pregnancy as possible followed by prompt initiation of cART will be required.[5,14] Treating each VT event as a sentinel health event, whereby system failures are identified and corrected was associated with a reduction in VT rate from 4.3% to 0% in Philadelphia, and could potentially be helpful in Canada.[18] Applying such a strategy will require adequate resources for Public Health, close collaboration between public health and frontline healthcare providers, and perhaps most importantly, strong community engagement.

A limitation of the CPHSP database is that it does not capture pregnant women living with HIV whose status is unknown either because they did not access antenatal care, declined HIV testing or had a post-testing seroconversion in pregnancy. In addition, there may be children living with HIV who are not yet identified because they and their mothers remain undiagnosed. It is also possible that a small proportion of MIPs were missed because they received their care at non-CPHSP sites. However, due to the provincial referral systems in place, we believe there to be very few MIPs who are not captured in this national surveillance system. The usual limitations of

retrospective data collection apply, although the impact of this was tempered by our ability to obtain missing data in the process of routine infant follow-up. Incomplete data on maternal ART (1.6%) or final infant HIV status (1.6%) was uncommon and therefore unlikely to have impacted key study findings.

In conclusion, while there has been a steady decline in the rate of VT of HIV in Canada, infant infections continue to occur primarily as a result of incomplete implementation of known, evidence based interventions. A major gap is the significant number of women who either do not receive antenatal cART or are not initiated on cART until late in gestation. Efforts to improve women-centered timely access to care, HIV screening and treatment for all women, combined with enhanced resources targeting populations at increased HIV risk, will be needed if VT is to be eliminated in Canada.

ACKNOWLEDGEMENTS

We wish to acknowledge Dr.'s Susan King (deceased), Stanley E. Read, Dorothy Moore, Normand Lapointe and John Forbes for their foresight in establishing the Canadian Pediatric & Perinatal Research Group (CPARG) as well as the Canadian Perinatal HIV Surveillance Program (CPHSP) in the early 1990's without which this research would not be possible.

The authors thank all the site investigators at the participating centres for contributing data annually: Francois Boucher, Natalie Bridger, Jared Bullard, Jeff Cohen, Rick Cooper, Michele Ellis, Scott Halperin, Brendan Hanley, Taj Jadavji, Chris Karatzios, Kirk Liefso, Athena McConnell, Heather Onyett, Joan Robinson, Roger Sandre, Sandi Seigel, Michael Young.

The CPHSP is funded by the HIV/AIDS Surveillance Section, Surveillance and Risk Assessment Division, Public Health Agency of Canada, Ottawa, Canada. The Canadian Institutes of Health Research – Canadian HIV Trials Network, Vancouver, British Columbia, Canada provided support for the programme.

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Figure 1:

Title: Uptake of antenatal cART ≥ 4 weeks prior to delivery by year.

Legend: Percentage receiving antenatal maternal cART ≥ 4 weeks according to risk category (a), race/ethnicity (b) and geographic region (c). By logistic regression, with year as a continuous variable, there was statistically significant time-trend improvement in antenatal cART uptake ($p<0.001$ for all categories in the three plots). For Saskatchewan and Manitoba, data from earlier years were not shown due to small numbers.

Figure 2:

Title: Perinatal infections by birth year and antenatal maternal cART.

Table 1: Maternal and delivery related characteristics, 1997–2016 (n=3785) ▪ §

Maternal risk category (n=3459) †	
Heterosexual	2555 (73.9%)
Intravenous drug use	788 (22.8%)
Perinatal	44 (1.3%)
Other	72 (2.1%)
Maternal race/ethnicity (n=3723) ‡	
Black	1868 (50.2%)
White	843 (22.6%)
Indigenous	778 (20.9%)
Other	234 (6.3%)
Timing of maternal diagnosis (n=3317) €	
Before conception	2593 (78.2%)
First trimester	197 (5.9%)
Second trimester	278 (8.4%)
Third trimester	103 (3.1%)
At delivery	53 (1.6%)
After delivery	93 (2.8%)
Antenatal cART (n=3764)	
≥ 4 weeks	2960 (78.6%)
< 4 weeks	445 (11.8%)
None	359 (9.5%)
Maternal VL nearest delivery (n=2467) ●	
< 50 copies/mL	2031 (82.3%)
50–999 copies/mL	270 (10.9%)
≥ 1000 copies/mL	166 (6.7%)
Mode of delivery (n=3680)	
Vaginal	2235 (60.7%)
Elective Caesarean section	961 (26.1%)
Emergency Caesarean section	484 (13.2%)
Gestational age at birth (n=3394)	
≥ 37 weeks	2825 (83.2%)
34–36 weeks	396 (11.7%)
< 34 weeks	173 (5.1%)
Province/territory of Birth (n=3785) ¶	
Ontario	1294 (34.2%)
Quebec	859 (22.7%)
Alberta	575 (15.2%)
British Columbia/Yukon *	493 (13.0%)
Saskatchewan	288 (7.6%)
Manitoba	247 (6.5%)
Atlantic Provinces	29 (0.8%)

Abbreviations: VL = viral load

▪ Total available data points (n) indicated for each variable

§ Mean gestational age and birth weight was 38.2 weeks (SD=2.41; n=3394) and 3.04 kg (SD=0.65, n=3072), respectively; 51.4% were male

† Intravenous drug use was most prevalent as maternal risk category in Saskatchewan (76.2%), British Columbia (41.1%) and Manitoba (34.1%)

‡ Black ethnicity/race predominated in Quebec (68.9%), Ontario (65.4%) and Alberta (45.0%); Indigenous ethnicity/race predominated in Saskatchewan (87.5%) and Manitoba (59.9%)

€ For 416 cases diagnosis was prior to onset of labor, but the precise timing was unknown

● Maternal viral load consistently collected since 2008

¶ No cases from the North West Territories or Nunavut

* < 5 cases from Yukon

Table 2: Antenatal cART uptake and duration prior to delivery, 2011–2016

Variable	Maternal cART and its duration ‡			p value
	≥ 4 weeks	< 4 weeks	None	
Maternal risk category §				0.015
Heterosexual	899 (94.8%)	23 (2.4%)	26 (2.7%)	
Injection drug use	237 (89.8%)	7 (2.7%)	20 (7.6%)	
Perinatal	29 (90.6%)	2 (6.3%)	1 (3.1%)	
Other	37 (97.4%)	0 (0.0%)	1 (2.6%)	
Maternal ethnicity/race ¶				0.003
Black	698 (95.2%)	21 (2.9%)	14 (1.9%)	
Indigenous	277 (90.2%)	10 (3.3%)	20 (6.5%)	
White	230 (91.6%)	6 (2.4%)	15 (6.0%)	
Other	91 (95.8%)	3 (3.2%)	1 (1.1%)	
Province/territory *				0.43
Ontario	474 (93.5%)	13 (2.6%)	20 (3.9%)	
Quebec	226 (93.8%)	6 (2.5%)	9 (3.7%)	
Alberta	209 (92.1%)	10 (4.4%)	8 (3.5%)	
Saskatchewan	159 (92.4%)	5 (2.9%)	8 (4.7%)	
British Columbia/Yukon	142 (96.6%)	5 (3.4%)	0 (0.0%)	
Manitoba	100 (93.5%)	2 (1.9%)	5 (4.7%)	
Atlantic	5 (83.3%)	0 (0.0%)	1 (16.7%)	

‡ Premature delivery occurred in 17.9%; the rate was 17.5% for mothers who received ≥4 weeks of antenatal cART, 22.0% for mothers who received <4 weeks of antenatal cART and 26.7% for mothers who received no antenatal cART (p=0.23)

¶ Black ethnicity predominated in Quebec (73.9%), Ontario (67.1%) and Alberta (65.1%), whereas Indigenous ethnicity predominated in Saskatchewan (86.7%) and Manitoba (57.4%)

§ Injection drug use was the predominant risk category in Saskatchewan (74.0%); it was also listed a risk category for more than 10% of cases in British Columbia (39.0%), Manitoba (19.6%) and Alberta (16.7%); In Ontario and Quebec it accounted for 6.7% and 5.0% of listed risk category, respectively

* No cases from North West territories or Nunavut; < 5 cases from Yukon

Table 3: Predictors of ≥4 weeks of antenatal cART uptake, 2011–2016

Variable	Univariate		Multivariate	
	OR (95% CI)	p value	OR (95% CI)	p value
Maternal risk category ‡				
Heterosexual vs. injection drug use	2.09 (1.28, 3.42)	0.003	1.55 (0.77, 3.11)	0.22
Perinatal vs. injection drug use	1.10 (0.31, 3.86)	0.88	0.77 (0.21, 2.82)	0.69
Other vs. injection drug use ¶	4.21 (0.56, 31.93)	0.16	1.61 (0.28, 9.17)	0.59
Maternal ethnicity/race				
Black vs. Indigenous	2.16 (1.30, 3.59)	0.003	2.99 (1.23, 7.26)	0.02
White vs. Indigenous	1.19 (0.66, 2.13)	0.57	1.60 (0.69, 3.70)	0.28
Other vs. Indigenous	2.46 (0.85, 7.18)	0.10	2.12 (0.65, 6.87)	0.21
Black vs. White	1.82 (1.04, 3.19)	0.04	1.87 (0.99, 1.27)	0.06
Province/territory †*				
British Columbia/Yukon vs. Alberta	2.45 (0.89, 6.74)	0.08	3.31 (1.06, 10.32)	0.04
British Columbia/Yukon vs. Saskatchewan	2.32 (0.81, 6.68)	0.12	1.33 (0.42, 4.24)	0.62
British Columbia/Yukon vs. Manitoba	1.99 (0.61, 6.44)	0.25	2.14 (0.63, 7.29)	0.22
British Columbia/Yukon vs. Ontario	1.98 (0.76, 5.16)	0.16	3.16 (1.08, 9.26)	0.04
British Columbia/Yukon vs. Quebec	1.88 (0.67, 5.30)	0.23	3.44 (1.09, 10.84)	0.04
British Columbia/Yukon vs. Atlantic	5.68 (0.56, 58.08)	0.14	5.48 (0.10, 314.49)	0.41
Birth year §	1.05 (0.93, 1.19)	0.44	1.10 (0.96, 1.27)	0.16
Gestational age at birth	1.07 (0.99, 1.15)	0.10	1.04 (0.95, 1.14)	0.37

‡ In a separate analysis, stratified by region (British Columbia/Yukon vs. Alberta/Saskatchewan/Manitoba vs. Ontario/Quebec), the odds ratio for ≥4 weeks of antenatal cART uptake for heterosexual vs. injection drug use (adjusted for province, birth year, race, gestational age) was 2.75 (95% CI 1.02, 7.39; p=0.045) for Ontario/Quebec, 0.73 (95%CI 0.26, 2.05; p=0.551) for Alberta/Saskatchewan/Manitoba and 3.70 (95% CI 0.45, 30.68; p=0.225) British Columbia/Yukon.

¶ "Other" refers to infection acquired via transfusion or other less common mechanisms

† All other pairwise comparisons between provinces were non-significant

* No cases from North West territories or Nunavut; < 5 cases from Yukon

§ Odds ratios shown are per year increase

Table 4: Maternal and infant characteristics for vertically infected infants, 2011–2016 †

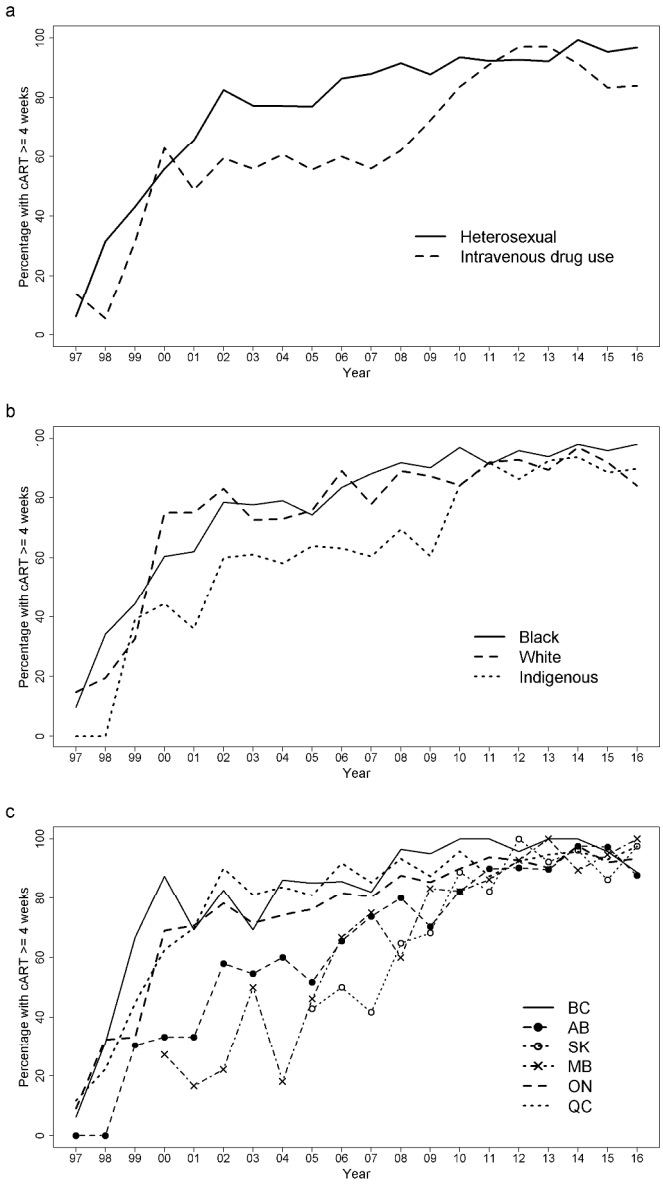
Case	Maternal HIV diagnosis timing	Antenatal cART duration	Maternal adherence	Maternal VL (copies/mL)	Mode of delivery	GA at birth (weeks)	Birth weight (kg)	Sex	Infants first positive HIV PCR (days)	Infant ART prophylaxis ‡
1	Preconception	≥4 weeks	Suboptimal	≥1000	Elective C/S	37	3.28	F	1	ZDV/3TC/NVP
2	Preconception	<4 weeks	Suboptimal	Unknown	SVD	36	1.64	M	1	ZDV/3TC/NVP
3	Preconception	<4 weeks	Suboptimal	Unknown	SVD	36	2.27	F	1	ZDV/3TC/NVP
4	Preconception	<4 weeks	Suboptimal	<50	SVD	38	2.65	F	1309	ZDV/3TC
5	2nd trimester	≥4 weeks	Suboptimal	Unknown	SVD	34	2.11	F	2	ZDV/3 dose NVP
6	Intrapartum	N/A	N/A	50-999	SVD	40	2.97	M	10	ZDV/3TC/3 dose NVP
7	Intrapartum	N/A	N/A	Unknown	SVD	39	2.76	M	2	ZDV/3TC/NVP
8	Intrapartum	N/A	N/A	Unknown	SVD	33	1.75	F	1	ZDV/1 dose NVP
9	Intrapartum	N/A	N/A	≥1000	SVD	35	1.75	F	1	ZDV/3TC/NVP
10	Intrapartum	N/A	N/A	≥1000	SVD	39	2.76	M	2	ZDV/3TC/ NFV §
11	After delivery	N/A	N/A	Unknown	SVD	39	3.00	F	129	None
12	After delivery	N/A	N/A	Unknown	Elective C/S	41	Unknown	M	122	None
13	After delivery	N/A	N/A	Unknown	Elective C/S	37	3.40	M	264	None
14	After delivery	N/A	N/A	Unknown	SVD	40	2.88	F	484	None

Abbreviations: ART = antiretroviral therapy; cART = combination antiretroviral therapy; C/S = Caesarean section; GA = gestational age; HIV = human immunodeficiency virus; N/A = not applicable; PCR = polymerase chain reaction; SVD = spontaneous vaginal delivery; VL = viral load; ZDV = zidovudine; 3TC = lamivudine; NVP = nevirapine; NFV = nelfinavir

† Maternal risk category: heterosexual (n=9), injection drug use (n=5); Maternal race: black (n=7), indigenous (n=6), white (n=1); Province of birth: Quebec (n=5), Saskatchewan (n=5), Ontario (n=3), Alberta (n=1)

‡ All medications were administered at treatment doses unless specified otherwise.

§ Also received 3 doses of nevirapine during first week of life.



Title: Uptake of antenatal cART ≥ 4 weeks prior to delivery by year.

Legend: Percentage receiving antenatal maternal cART ≥ 4 weeks according to risk category (a), race/ethnicity (b) and geographic region (c). By logistic regression, with year as a continuous variable, there was statistically significant time-trend improvement in antenatal cART uptake ($p<0.001$ for all categories in the three plots). For Saskatchewan and Manitoba, data from earlier years were not shown due to small numbers.

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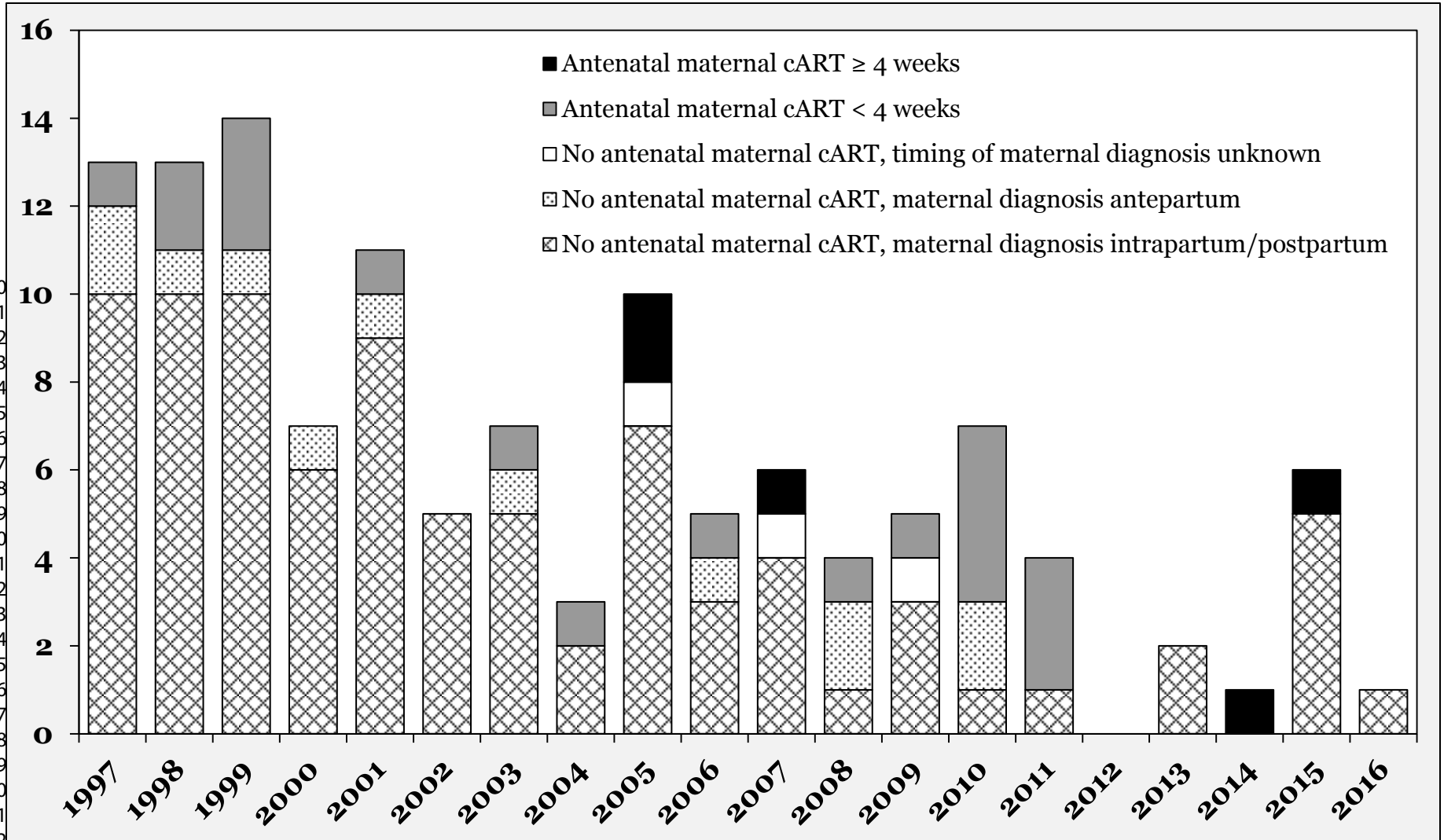

n=124;
One vertical transmission case not shown as maternal cART status was unknown