A national review of vertical HIV transmission

John C. Forbes[a], Ariane M. Alimenti[a], Joel Singer[b,f], Jason C. Brophy[c], Ari Bitnun[d], Lindy M. Samson[c], Deborah M. Money[e], Terry C.K. Lee[f], Normand D. Lapointe[g], Stanley E. Read[d], the Canadian Pediatric AIDS Research Group (CPARG)

Objectives: Prevention of vertical HIV transmission has evolved significantly in Canada over the last two decades. The aim of this analysis is to describe the surveillance programme used, rate of vertical HIV transmission and changing epidemiology of HIV-affected pregnancies in Canada.

Design: National perinatal HIV surveillance programme.

Methods: From 1990, annual retrospective data was collected on demographic and clinical characteristics of HIV-infected mothers and their infants referred to 22 participating sites across Canada either before/during pregnancy or within 3 months after delivery. Factors impacting HIV transmission and demographic features were explored.

Results: Two thousand, six hundred and ninety-two mother–infant pairs were identified. The overall rate of vertical HIV transmission was 5.2%, declining to 2.9% since 1997. The rate of transmission for mothers who received HAART was 1%, and 0.4% if more than 4 weeks of HAART was given. Forty percent of women delivered by caesarean section, with no difference in transmission rate compared with vaginal delivery for women treated with HAART (1.4 vs. 0.6%, $P = 0.129$) but significant risk reduction for those who did not receive HAART (3.8 vs. 10.3%, $P = 0.016$). Black women were the largest group; proportions of black and aboriginal women increased significantly over time ($P < 0.001$ for both). Heterosexual contact was the most common risk category for maternal infection (65%), followed by injection drug use (IDU) (25%).

Conclusion: Vertical HIV transmission in Canada has decreased dramatically for women treated with HAART therapy. All pregnant women should be evaluated for HIV infection and programmes expanded to reach vulnerable populations including aboriginal, immigrant and IDU women.

AIDS 2012, **26**:757–763

Keywords: Canada, epidemiology, HIV, mother-to-child transmission, pregnancy, surveillance, vertical HIV transmission

Introduction

HIV infection in children remains a significant health issue, both globally for the estimated 2.5 million children living with HIV worldwide [1] and for the approximately 300 children presently known to be infected who are being cared for in Canada [2]. As almost all paediatric HIV infections are the result of vertical transmission from

[a]Department of Pediatrics, [b]School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, [c]Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, [d]Department of Pediatrics, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, [e]Department of Obstetrics and Gynecology, Women's Health Research Institute, British Columbia Women's Hospital and Health Centre, University of British Columbia, [f]CIHR Canadian HIV Trials Network, Vancouver, British Columbia, and [g]Department of Pediatrics, Centre Hospitalier Universitaire Sainte-Justine, Université de Montréal, Montréal, Québec, Canada.

Correspondence to Dr Ariane M. Alimenti, Oak Tree Clinic, 4500 Oak Street – B4 West, Children's and Women's Health Centre of British Columbia, Vancouver, BC V6H 3N1, Canada.

Tel: +1 604 875 2212; fax: +1 604 875 3063; e-mail: aalimenti@cw.bc.ca
Received: 2 September 2011; revised: 7 December 2011; accepted: 20 December 2011.

DOI:10.1097/QAD.0b013e328350995c

mother to child, understanding the contributing issues is vital. The overall risk of vertical HIV transmission in the absence of any intervention ranges from approximately 15 to 40% [3–7]. One of the most significant achievements in HIV has been the development of effective strategies for the prevention of mother-to-child transmission. With the current regimen of providing appropriate combination antiretroviral therapy (ART) to pregnant women beginning in the second trimester or earlier, intrapartum intravenous zidovudine, 6 weeks of oral ART to the infant and exclusive formula feeding, the risk of vertical transmission can be reduced to less than 2% [8,9]. The failures in prevention of vertical transmission have been reported to be due to failure of timely diagnosis of HIV in pregnant women, failure to control HIV replication because of inadequate implementation of standard of care interventions or because of nonadherence to therapy [10–15].

In order to understand the extent and nature of the epidemic as it affects vertically exposed children, the Canadian Perinatal HIV Surveillance Program (CPHSP) was initiated in 1990 under the auspices of the Canadian Pediatric AIDS Research Group (CPARG). Since then, it has remained an active surveillance programme generating national data annually pertaining to the status of infants and children born to women identified with HIV infection living in Canada. The overall objectives of the programme are to determine, first, the annual burden of perinatal exposure to HIV infection; second, the number of HIV-infected children living in Canada; and, third, an estimate of vertical transmission rates and associated cofactors. The purpose of this article is to describe the vertical HIV transmission in Canada between 1990 and 2010 and the changing epidemiology of HIV-affected pregnancies.

Methods

Canadian Perinatal HIV Surveillance Program

Twenty-two HIV referral health centres and health departments from all Canadian provinces and territories participate in CPHSP. In the 10 provinces, there are 19 sites which provide tertiary obstetric and/or paediatric care to the province or regional area. In the three northern territories, the participating sites are the public health units for each territory. Management of the programme is coordinated in British Columbia. Data management and analysis is provided by the Canadian Institutes of Health Research – Canadian HIV Trials Network (CTN). Support for the programme is provided by the Public Health Agency of Canada (PHAC). Ethical approval for this surveillance programme was obtained from the research ethics boards of the participating centres. Summary data is submitted annually to the HIV/AIDS Surveillance Section, Surveillance and Risk Assessment Division at PHAC and reported in its publication '*HIV and AIDS in Canada*' [16].

Data collection

Mother–infant pairs are enrolled through the participating sites upon obstetric or paediatric referral. Irrespective of the location of delivery or subsequent care received, the identified mother–infant pairs are registered by the participating sites. Retrospective chart reviews of identified mothers and infants are collated annually and clinical, demographic and HIV outcome data are submitted. Data collected include maternal country of birth, self-reported race/ethnicity according to national surveillance definitions, maternal risk category for acquiring HIV, antiretroviral regimen and duration of therapy in pregnancy, mode of delivery, gestational age and birth weight. The subsequent HIV status of the infant is reported with confirmation by virologic testing for HIV by PCR or peripheral blood mononuclear cell viral culture (confirmed on two separate samples) and/or by HIV serology beyond 18 months of life. Indeterminate HIV status refers to infants whose HIV status has not been finalized by these criteria.

Until 2007, data were reported manually by each centre to the CTN, but this is now done using a secure web-based Oracle database. Security controls of the database are installed according to CTN protocols for data confidentiality, integrity and availability. The database has standardized screens and built-in checks to allow for more complete and accurate data collection. Mother–infant pairs are entered using a pseudonymous site-specific code. Only de-identified data are available to the CTN and the study investigator group.

Study population

This analysis on vertical transmission was restricted to infants born in Canada to women with documented HIV infection who were referred to one of the participating sites, either before or during pregnancy or within 3 months after delivery. Maternal treatment was differentiated into ART regimens, defined as one or two nucleoside reverse transcriptase inhibitors (RTIs), or HAART regimens, defined as three drugs, typically including two nucleoside RTIs with either a protease inhibitor or a nonnucleoside RTI.

Statistical analysis

Summary statistics were used to describe the demographic characteristics of the population. Least-square regression statistical analysis was used to test the significance of time trend. Changes in time trends were formally tested using piecewise linear regression analysis. The rate of vertical HIV transmission across different populations was compared using Fisher's exact test. Analyses were conducted using the R statistical package.

Results

Vertical transmission and maternal antiretroviral therapy received

Two thousand, six hundred and ninety-two mother–infant pairs identified between January 1990 and December 2010 met the inclusion criteria. Ninety-five percent of the mother–infant pairs were identified before birth. Comparisons between the January 1990 to December 1996 (period 1) and January 1997 to December 2010 (period 2) cohorts were made as the approach to therapy during pregnancy changed significantly in 1997. The number of mother–infant pairs reported increased from 372 (53.1 per year) in period 1 to 2320 (165.7 per year) in period 2. Final HIV status was available for 99% of infants. A total of 33 infants lost to follow-up prior to 18 months of age and before completion of virologic testing were classified as having indeterminate HIV status, including 10 (2.7%) in period 1 and 23 (1.0%) in period 2. Infants with indeterminate status were excluded from the vertical transmission analysis.

The percentage of mothers who received ART during pregnancy and the percentage of infected infants are depicted in Figure 1. A decline in vertical transmission was observed following the rapid uptake of maternal antenatal ART regimens after 1994, and an even greater decline with the uptake of maternal HAART regimens after 1996.

The rates of vertical HIV transmission by period and maternal ART received are shown in Table 1. The overall rate of transmission in the entire cohort (excluding cases with indeterminate status) was 5.2%, declining from 20.2% in period 1 to 2.9% in period 2. The latter period included 86% of the mother–infant pairs and all the pregnancies treated with HAART. In this period, the rate of vertical transmission was 1% (17 of 1707) for mothers who received HAART, 1.6% (five of 322) for women prescribed mono-therapy or dual-therapy with nucleoside RTI (ART) and 16.4% (44 of 268) for women who received no ART. For mothers who initiated HAART more than 4 weeks before delivery, the transmission rate was 0.4% (six of 1585). The transmission rate increased to 9.0% for 122 women who received less than 4 weeks of HAART. For 305 women receiving more than 4 weeks of ART (but not HAART) in the same period, the transmission rate was 1.6%.

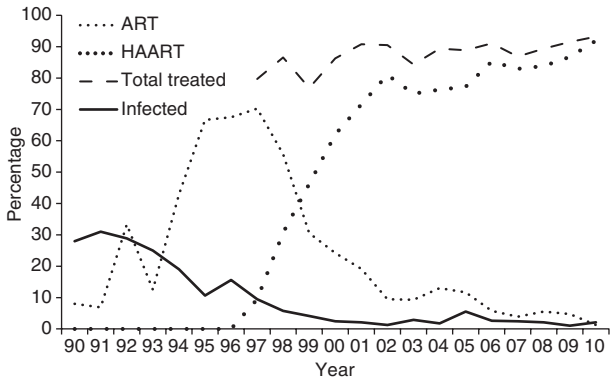

Fig. 1. Changes in maternal antiretroviral therapy and vertical transmission rate over time. HAART refers to antiretroviral regimens with three drugs including two nucleoside reverse transcriptase inhibitors (RTIs) with either a protease inhibitor or nonnucleoside RTI; antiretroviral therapy (ART) refers to antiretroviral regimens that have one or two nucleoside RTIs.

Table 1. Vertical transmission according to prescribed maternal antiretroviral therapy.

Period	HAART	ART	No therapy	Total
1990–1996				
Mother–infant pairs (*n*)	0	154	208	362
Infected infants (*n*)	0	10	63	73
Transmission rate (%)	0	6.5	30.3	20.2
1997–2010				
Mother–infant pairs (*n*)	1707	322	268	2297
Infected infants (*n*)	17	5	44	66
Transmission rate (%)	1.0	1.6	16.4	2.9

HAART refers to antiretroviral regimens with three drugs including two nucleoside reverse transcriptase inhibitors (RTIs) with either a protease inhibitor or nonnucleoside RTI; ART refers to antiretroviral regimens that have one or two nucleoside RTIs. The data excludes mother–infant pairs for whom final infant HIV status was unknown ($n = 33$).

Mode of delivery

Mode of delivery was consistently collected from 1999; however, no additional data regarding the indications for the mode of delivery or the duration of ruptured membranes were collected. For the period of 1999–2010, there were 1217 vaginal and 855 caesarean section deliveries, giving an overall caesarean section rate of 40.3% (annual rates ranged from 35 to 55%). The rates of vertical transmission for vaginal and caesarean section deliveries were 2.8 and 1.9%, respectively ($P = 0.193$). For women who received HAART, vertical transmission rates were 0.6% (six of 946) for vaginal deliveries and 1.4% (10 of 699) for caesarean deliveries ($P = 0.129$). For women who received ART or no therapy, the rate of transmission was 10.3% (28 of 271) for vaginal deliveries and 3.8% (six of 156) for caesarean deliveries ($P = 0.016$). Data distinguishing emergency and elective caesarean sections were consistently reported after 2007: there were 864 deliveries of which 519 (60.0%) were vaginal deliveries, 111 (12.8%) emergency caesarean deliveries and 215 (24.9%) elective caesarean deliveries. The numbers of infected infants in each group were 13 (2.5%), one (0.9%) and three (1.4%), respectively ($P = 0.514$).

Regional distribution

Ninety percent of mother–infant pairs were from Ontario (33%), Québec (28%), British Columbia

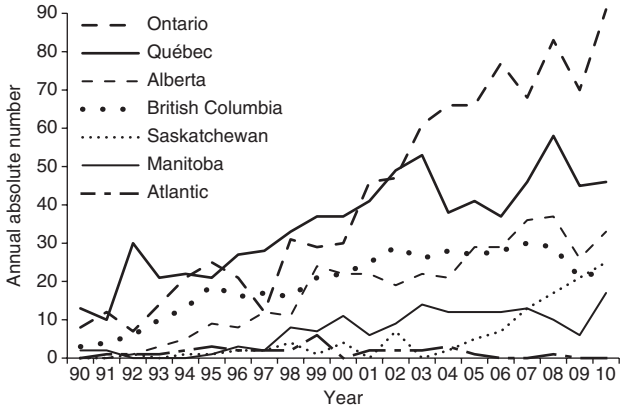

Fig. 2. Trend in regional distribution of mother–infant pairs over time. Northwest territories/Yukon data are not plotted (one reported case from 1990–2009).

(15%) or Alberta (14%). Saskatchewan and Manitoba together accounted for 9% and the Atlantic Provinces (New Brunswick, Nova Scotia, Prince Edward Island and Newfoundland and Labrador) for 1% of cases. There was only one reported case in total for Northwest Territories, Nunavut and Yukon. Regional trends over time are shown in Figure 2. In period 2, a gradual increase in mother–infant pairs in Ontario, Québec, British Columbia, Alberta, Saskatchewan and Manitoba was observed ($P < 0.001$). In British Columbia, numbers increased steadily prior to 2002, but at a slower rate thereafter compared with Ontario, Alberta and Saskatchewan ($P < 0.005$). In Saskatchewan, there was a steady increase in mother–infant pairs after 2003 ($P < 0.001$). In the Atlantic Provinces, numbers have remained extremely low.

Maternal race/ethnicity

Self-reported maternal race/ethnicity was classified as black (46%), white (28%), aboriginal (19%), Asian or South Asian (3%), Latin American (1%) and other or unknown (3%). The trend of the absolute numbers of women in each group over time is shown in Figure 3.

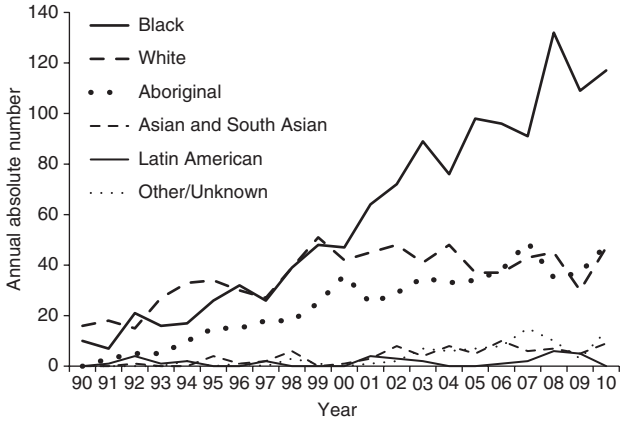

Fig. 3. Trend in maternal race/ethnicity over time.

The overall proportion of white women declined from 47% in period 1 to 25% in period 2, whereas the proportion of black and aboriginal women increased from 35 to 48% and 14 to 20%, respectively. The number of black mother–infant pairs increased steadily ($P < 0.001$) and at a faster rate since 2000 ($P = 0.046$). The increase in births to HIV-infected aboriginal women also increased ($P < 0.001$), although in a less pronounced manner ($P < 0.001$). Black race predominated in Québec (65%) and Ontario (59%); aboriginal ethnicity was most common in Alberta (46%), Saskatchewan (86%) and Manitoba (59%). A steady increase in the number of HIV-infected women born outside Canada was evident over the study period, whereas Canadian-born women remained fairly constant since 2000. The largest increase was in women of African origin, from 14% in 1990 to 1996 to 35% in 1997–2010 (data not shown).

Maternal risk category for HIV infection

Heterosexual contact was the most common reported risk category for HIV acquisition among women in the cohort (65%). IDU accounted for 25% and receipt of blood/blood products for 1%. IDU was preferentially selected over heterosexual contact if both were reported. Fifteen women who became pregnant after 2005 were themselves infected through vertical transmission (0.6%). Risk category was unknown for 8% of cases. The number of women whose risk factor was heterosexual acquisition rose over the course of the study ($P < 0.001$), whereas the number of women whose primary risk factor was IDU remained stable between 1995 and 2010 ($P = 0.812$ for the null hypothesis of no trend).

Discussion

The CPHSP is an important national tool that allows for the determination of HIV vertical transmission rates, identification of demographic trends in the national epidemic among HIV-infected women of child-bearing age and detection of gaps or failures in the prevention of vertical transmission programmes. The CPHSP surveillance shows that the rate of vertical transmission from women whose HIV status was known during pregnancy or within 3 months after delivery has declined substantially, from 20.2 to 2.9% after 1997 when HAART became the standard of care in Canada. For women who received antenatal HAART vertical transmission was 1%, a rate similar to that observed during the HAART era in other developed countries such as the UK and Ireland, France, Australia, Sweden and the USA [8,9,17–19]. The extraordinary impact of current preventive strategies is further exemplified by the fact that since 1997, the rate of transmission was only 0.4% when maternal HAART was initiated at least 4 weeks prior to delivery. This is similar to the findings reported by Townsend *et al.* of a 0.8% transmission rate in women

receiving at least 2 weeks of HAART before delivery in the UK and Ireland [8]. Likewise, Townsend *et al.* [8] and Warzawski *et al.* [9] in France found very low rates of transmission of 0.1–0.4% when mothers had undetectable viral loads at delivery. In the CPHSP since 1997, those mothers who received ART other than HAART for more than 4 weeks had a higher transmission rate of 1.6%, whereas those who received no therapy had the highest transmission rate of 16.4%.

The study population for this analysis included all mother–infant pairs identified prior to or during pregnancy and within 3 months after delivery. These defined inclusion criteria were chosen to include those mother–infant pairs who potentially could have benefited from appropriate antenatal care and ART. The number of mother–infant pairs in the CPHSP dataset who were identified 3–9 months after delivery decreased from an average of 5.4 per year in period 1 (1990–1996) to 1.7 per year for period 2 (1997–2010). The decline in late identifications is suggestive of an improvement in the early identification of HIV-affected pregnancies. Of the infants born in period 2, 50% were infected (CPHSP data, not shown). The high rate of transmission suggests risk factors associated with high HIV viral load seen with more advanced disease or recent HIV infection.

Although there has been substantial improvement in the implementation of measures to reduce vertical transmission in Canada, significant gaps remain both with respect to timely diagnosis and to provision of and access to antenatal HAART. There is limited published data describing the uptake of antenatal HIV testing in women across Canada. Updated information available in Ontario suggests 95% of women are tested in their current pregnancy [20], whereas older publications from Nova Scotia, British Columbia and Alberta document testing rates between 72 and 96% [21–23]. Rates of antenatal testing greater than 95% occur in provinces with the highest HIV prevalence which include Ontario, Québec, British Columbia and Alberta. On the basis of these rates of testing, we estimate that over 90% of HIV-infected pregnant women and/or their infants are referred to or registered with the participating sites. Furthermore, as paediatric HIV care and therapy is coordinated through the participating sites, we are confident that all known HIV-infected children who acquired their infection in Canada are accounted for in the database.

Although the current actual percentages of women not tested in pregnancy across Canada are not completely clear, it is likely that some of these women are from marginalized populations who do not access antenatal care and are potentially at greater risk of HIV infection [21]. Among women tested early in pregnancy, repeat testing later in gestation for those at risk of late pregnancy HIV acquisition is not systematically undertaken, despite expert guidelines recommending this approach [24]. A third concern is the incomplete provision of ART to women who are diagnosed with HIV infection during pregnancy. This latter point is exemplified by the fact that 268 HIV-infected women identified after January 1997 in our cohort received no ART during pregnancy. Furthermore, the proportion of women who received either no antenatal ART (range 7–13% per year) or were prescribed less than three antiretroviral medications (range 2–6% per year) has not declined significantly since 2006. The complete lack of therapy in some cases may be due to maternal diagnosis at delivery or within 3 months after the infant's birth. Exploring the reasons for these missed opportunities, however, will be important in the future if further reduction in vertical HIV transmission rate is to be achieved in Canada.

The overall rate of vertical transmission was lower but not statistically different for women who delivered by caesarean section compared with those women who delivered vaginally. In cases in which women received HAART, the rate of transmission was lower for vaginal deliveries, but did not reach statistical significance ($P = 0.129$). However, for women who received suboptimal therapy or no therapy, there was a significantly lower transmission rate for those delivered by caesarean section ($P = 0.016$). The high overall rate of caesarean sections (40%) may have been influenced by previous guideline recommendations [25]. There was no significant decrease in the caesarean section rate after 1999, despite a change in practice in Canadian centres to offer women the option of vaginal delivery if they have an undetectable HIV viral load with appropriate ART. The reporting on whether caesarean sections were elective or emergency procedures was inconsistent prior to 2007. Since then, however, two-thirds of caesarean sections were noted to be elective procedures. The number of infected infants in each caesarean section group is small and further study of this issue will be important.

The demographic profile of HIV-infected women varies widely across Canada and may reflect the distribution of different racial groups and immigrant populations. Aboriginal and black women make up 19 and 46%, respectively, of the HIV-infected pregnant women in this study and are disproportionately represented, as these groups constitute only 3.8 and 2.5%, respectively, of the Canadian population [26]. Aboriginal women predominated in western provinces (British Columbia, Alberta, Saskatchewan and Manitoba) where they accounted for 30–86% of mothers. In Ontario and Québec, approximately 60% of mothers were black women from Africa and the Caribbean, a reflection of immigration patterns to these provinces. Since 2002, more of the identified women were not born in Canada, likely reflecting both immigration patterns and differences of child-bearing choices among different

cultures. As might be expected, these observed trends in pregnant HIV-infected women closely mirror the overall trends amongst HIV-infected women in Canada [16,27].

The majority of women in our cohort were infected by heterosexual contact, a finding consistent with other countries [28,29]. Heterosexual transmission was particularly prevalent among immigrant women, being reported as the key risk category in 86% of cases. IDU, identified as the main risk category for 25% of women across the country, was more prevalent in British Columbia (47%), Alberta (36%), Saskatchewan (78%) and Manitoba (41%). Among aboriginal women, IDU was reported as the key risk category in 63% of cases. These observations reinforce the need to direct further study and resources toward more vulnerable populations, including immigrant and aboriginal women as well as women who use injection drugs, if ongoing vertical HIV transmission is to be curtailed further.

There are several limitations to this study. First, this analysis is primarily based on retrospective data collection. The database was designed so that data from previously entered mother–infant pairs can be updated at any time and new cases can be entered as they occur. Since the web-based data collection was introduced, the data collection is more efficient and complete. Second, loss to follow-up prior to finalizing the infant's HIV status may be a limitation; however this was noted in only 1.0% of cases since 1997 and there have been no cases lost to follow-up since 2008. Third, women who were not diagnosed during pregnancy or the immediate post-partum period and whose infants remained unidentified beyond 3 months of age are not included. However, the numbers of missed cases is decreasing in period 2, as the uptake of HIV testing during pregnancy in Canada has improved [20]. Fourth, although all the main referral centres from each geographic area are used for data collection, possible referral bias remains. Although missed cases outside these major referral centres are likely to be relatively few, the CPHSP is recruiting additional regional centres that have begun to provide service to HIV-infected pregnant women to minimize this further.

In conclusion, the CPHSP database is a valuable tool that provides robust annual surveillance data on vertical HIV transmission in Canada. We believe this model could be emulated by other countries or jurisdictions seeking to improve their surveillance data at relatively low cost. The consistent and relatively complete data collected by a web-based, secure system can be used to report on different population groups and regions to inform programmes and allocation of resources. The findings indicate that although rates of vertical transmission of HIV in Canada are very low for women who receive HAART, transmissions unfortunately continue to occur. All pregnant women should be evaluated for HIV infection as early in pregnancy as possible and again later in pregnancy, and programmes should be modified to ensure that they are accessible to the more vulnerable and marginalized populations which may include aboriginal, immigrant women and IDU women. These demographic observations as they relate to vertical transmission risk should be used to inform further policy development and resource allocation for prevention of vertical transmission programming in Canada.

Acknowledgements

The review was produced by the steering committee of the Canadian Perinatal HIV Surveillance Program (CPHSP) under the auspices of the Canadian Pediatric AIDS Research Group (CPARG). The programme was managed by J.C.F., A.M.A. and L.M.S. and the steering committee participants are J.C.F., A.M.A., L.M.S., J.S., J.C.B., A.B., D.M.M. and N.D.L.

J.C.F. took responsibility for writing the article and all co-authors contributed to critical revision. Data was analysed by J.S. and T.C.K.L. and interpreted by the co-authors.

The CIHR Canadian Trials Network has provided the data management for CPHSP and the data analysis, tables and figures for the manuscript.

The authors thank all the site investigators at the participating centres for contributing data annually: A.M.A., A.B., Bob Bortolussi, François Boucher, J.C.B., Jared Bullard, Jeff Cohen, Rick Cooper, Michelle Ellis, Joanne Embree, Jack Forbes, Brendan Hanley, Taj Jadavji, Chris Karatzios, Valérie Lamarre, N.D.L., Dorothy Moore, Heather Onyett, S.E.R., L.M.S., Roger Sandre, Sandi Siegel, Fiona Smaill, Isaac Sobol, Lamont Sweet, Ben Tan, Wendy Vaudry and Michael Young.

The authors wish to thank Elaine Fernandes and Evelyn Maan for managing and coordinating the study and the late Dr Susan King who was a founding member of CPHSP for her dedication and mentorship.

The CPHSP is funded by the HIV/AIDS Surveillance Section, Surveillance and Risk Assessment Division, Public Health Agency of Canada, Ottawa, Canada.

The Public Health Agency of Canada provides the funding for this study. The Canadian Institutes of Health Research – Canadian HIV Trials Network, Vancouver, British Columbia, Canada provided support for the programme.

Conflicts of interest

None of the authors have any conflict of interests to declare.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). Global report: UNAIDS report on the global AIDS epidemic 2010. http://www.unaids.org/globalreport/global_report.htm. [Accessed 20 May 2011].
2. Alimenti A, Forbes J, Samson L, Ayers D, Singer J, Money D, *et al.* **Demographics of HIV-infected children in Canada, 1990 to 2006: data from the Canadian Perinatal HIV Surveillance Programme (CPHSP).** In: *16th Annual Canadian Conference on HIV/AIDS Research*; 26–29 April 2007; Toronto, Ontario, Canada.
3. Newell M, Dunn D, Peckham C, Semprini A, Pardi G. **Vertical transmission of HIV-1: maternal immune status and obstetric factors. The European Collaborative Study.** *AIDS* 1996; **10**:1675–1681.
4. Kumar R, Uduman S, Khurranna A. **A prospective study of mother-to-infant HIV transmission in tribal women from India.** *J Acquir Immune Defic Syndr Hum Retrovirol* 1995; **9**:238–242.
5. Lallemant M, Le Coeur S, Samba L, Cheynier D, M'Pele P, Nzingoula S, *et al*. **Mother-to-child transmission of HIV-1 in Congo, central Africa.** *AIDS* 1994; **8**:1451–1456.
6. Working Group on Mother-To-Child Transmission of HIV. **Rates of mother-to-child transmission of HIV-1 in Africa, America, and Europe: results from 13 perinatal studies.** *J Acquir Immune Defic Syndr Hum Retrovirol* 1995; **8**:506–510.
7. De Cock K, Fowler M, Mercier E, de Vincenzi I, Saba J, Hoff E, *et al*. **Prevention of mother-to-child HIV transmission in resource-poor countries.** *JAMA* 2000; **283**:1175–1182.
8. Townsend C, Cortina-Borja M, Peckham C, de Ruiter A, Lyall H, Tookey P. **Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006.** *AIDS* 2008; **22**:973–981.
9. Warzawski J, Tubiana R, Le Chenadec J, Blanche S, Teglas J, Dollfus C, *et al*. **Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort.** *AIDS* 2008; **22**:289–299.
10. Centers for Disease Control (CDC). **Acquired immunodeficiency syndrome (AIDS): Canada.** *MMWR Morb Mortal Wkly Rep* 1983; **32**:635–636.
11. Bitnun A, King SM, Arneson C, Read SE. **Failure to prevent perinatal HIV infection.** *CMAJ* 2002; **166**:904–905.
12. Peters V, Liu K, Dominguez K, Frederick T, Melville S, Hsu H, *et al*. **Missed opportunities for perinatal HIV prevention among HIV-exposed infants born 1996-2000, Pediatric Spectrum of HIV Disease Cohort.** *Pediatrics* 2003; **111**:1186–1191.
13. Peters V, Liu K, Robinson L, Dominguez K, Abrams E, Gill B, *et al*. **Trends in perinatal HIV prevention in New York City, 1994-2003.** *Am J Public Health* 2008; **98**:1857–1864.
14. Whitmore S, Patel-Larson A, Espinoza L, Ruffo N, Rao S. **Missed opportunities to prevent perinatal human immunodeficiency virus transmission in 15 jurisdictions in the United States during 2005-2008.** *Women Health* 2010; **50**:414–425.
15. Siemieniuk R, Jadavji T, Gill M. **Limitations of opt-out HIV screening and mother-child HIV transmission.** *Am J Public Health* 2010; **100**:388–389.
16. Public Health Agency of Canada. *HIV and AIDS in Canada. Surveillance Report to December 31, 2009*. Surveillance and Risk Assessment Division, Centre for Communicable Diseases and Infection Control, Public Health Agency of Canada. 2010. Can be accessed at: www.phac-aspc.gc.ca/aids-sida/publication/index-eng.php#surveillance.
17. Naver L, Lindgren S, Belfrage E, Gyllensten K, Lidman K, Gisslen M, *et al*. **Children born to HIV-1-infected women in Sweden in 1982-2003: trends in epidemiology and vertical transmission.** *J Acquir Immune Defic Syndr* 2006; **42**:484–489.
18. McDonald A, Zurynski Y, Wand H, Giles M, Elliott E, Ziegler J, *et al*. **Perinatal exposure to HIV among children born in Australia, 1982–2006.** *Med J Aust* 2009; **190**:416–420.
19. Birkhead G, Pulver W, Warren B, Hackel S, Rodriguez D, Smith L. **Acquiring human immunodeficiency virus during pregnancy and mother-to-child transmission in New York: 2002–2006.** *Obstet Gynecol* 2010; **115**:1247–1255.
20. Remis R, Swantee C, Liu J. Report on HIV/AIDS in Ontario 2008. Ontario, Canada: Ontario Ministry of Health and Long-Term Care; 2010. http://www.phs.utoronto.ca/ohemu/tech%20reports.html. [Accessed 18 May 2011]
21. Plitt S, Singh A, Lee B, Preiksaitis J. **HIV seroprevalence among women opting out of prenatal HIV screening in Alberta, Canada: 2002–2004.** *Clin Infect Dis* 2007; **45**:1640–1643.
22. Downing M, Youden L, Halperin B, Scott H, Smith B, Halperin S. **Prenatal screening for HIV in Nova Scotia: survey of postpartum women and audit of current prenatal screening practices.** *Can J Infect Dis Med Microbiol* 2006; **17**:224–228.
23. British Columbia Centre for Disease Control (BCCDC). HIV and sexually transmitted infections annual surveillance report 2008. Vancouver, British Columbia, Canada: BCCDC; 2008.
24. Branson B, Handsfield H, Lampe M, Janssen R, Taylor A, Lyss S, *et al*. **Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings.** *MMWR Recomm Rep* 2006; **55**:1–17.
25. Perinatal HIV Guidelines Working Group. Public Health Service Task Force recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV transmission in the United States. 2000. pp. 1–46. http://aidsinfo.nih.gov/ContentFiles/PerinatalG02252000039.pdf. [Accessed 17 May 2011]
26. 2006 Census, from Statistics Canada website – http://www12.statcan.ca/census-recensement/2006/rt-td/index-eng.cfm. [Accessed 1 May 2010]
27. Yang Q, Boulos D, Yan P, Zhang F, Remis R, Schanzer D, *et al*. **Estimates of the number of prevalent and incident human immunodeficiency virus (HIV) infections in Canada, 2008.** *Can J Public Health* 2010; **101**:486–490.
28. Hall H, Geduld J, Boulos D, Rhodes P, An Q, Mastro T, *et al*. **Epidemiology of HIV in the United States and Canada: current status and ongoing challenges.** *J Acquir Immune Defic Syndr* 2010; **51 (Suppl 1)**:S13–S20.
29. European Centre for Disease Prevention and Control/WHO Regional Office for Europe. *HIV/AIDS surveillance in Europe 2009*. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2010.