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COMMENTARY

Prevalence of human T cell lymphotropic virus 1 infection in Canada

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Human T cell lymphotropic virus 1 (HTLV-1) is a bloodborne retrovirus that infects at least 5–20 million people around the world[1]. The virus is known to be endemic in Central and West Africa, the Caribbean, East Asia, and Central and South America, and in intravenous drug users in the United States[2]. Active surveillance and targeted programs to decrease the vertical transmission of HTLV-1 are in place in Japan[3], but in the United States and Canada, the virus remains mostly neglected by medical regulatory authorities and does not appear on the list of notifiable bloodborne pathogens. However, in 1990, Canada began screening the blood supply for HTLV-1 serology to minimize the risk of transmission from blood donors. That initiative resulted in a decline in the HTLV-1 rate from 9.35 per 100,000 donations in 1990 to 1.1 per 100,000 donations in 2010[4]. The HTLV-1 and -2 retroviruses are transmitted mainly during prolonged breastfeeding, through sexual contact, or parenterally, including through blood transfusions and intravenous drug use.

Although the HTLV-1 virus confers a lifelong chronic infection, most people with it typically remain asymptomatic. However, the virus can also be associated with potentially devastating diseases.

It was shown that up to 5% of people infected with the virus develop adult T cell leukemia/lymphoma (ATLL)[5], a subtype of cutaneous T cell lymphoma recognized by the World Health Organization[6]. On average, it takes approximately 20–30 years for symptoms of ATLL to appear[5]. Importantly, based on current knowledge, ATLL does not occur in uninfected individuals.

Also, HTLV-1–associated myelopathy/tropical spastic paraparesis, a devastating demyelinating neurologic condition, can occur in affected patients[7]. Infective dermatitis, HTLV-1–associated uveitis, arthropathy, and opportunistic infections, including *Strongyloides stercoralis* hyperinfection have also been reported in people with HTLV-1 infection [1]. Notably, even in healthy HTLV-1 carriers, an impaired immune response against the Epstein–Barr virus has been observed[8]. One way in which HTLV-1 leads to immunodeficiency is by impairing thymic function, as demonstrated by the low percentage of naïve T cells in HTLV-1 carriers[9].

In Canada, HTLV-1 is known to be prevalent in native populations (that is, First Nations) and in immigrants from the endemic regions mentioned earlier. Importantly, a number of molecular studies in the First Nations communities of British Columbia and Nunavut documented the appearance of the virus in Canada during the pre-Columbian era (more than 1500 years ago) and the fact that the virus in Canada shares an ancestral source with the HTLV-1 that is endemic in Japan and Eastern Asia[4,10–15]. Phylogenetic findings show that the virus was not introduced into native communities from a single source at some point after the Columbian expeditions[14,15].

Unfortunately, there are no reliable estimates of the overall burden of this infection in Canada. Furthermore, the Canadian government, the media, and previous studies that tried to estimate rates of infection have sent conflicting messages about the commonality of the virus in Canada and in First Nations communities specifically[4,10–13].

We recently used the Canadian Cancer Registry, the Registre québécois du cancer, and the Canadian Vital Statistics (mortality) database to analyze the incidence and mortality rates for cutaneous T cell lymphoma and its variants in Canada[16,17]. That work established that, in Canada from 1992 to 2010, approximately 200 cases of ATLL were diagnosed (40% in women, 60% in men), resulting in 75 reported deaths[16,17].

Given that up to 5% of patients infected with HTLV-1 will progress to ATLL (lifetime cumulative risk of 4.0% in men and 4.2% in women, if infected during childhood[5]), the number of HTLV-1–infected individuals can be extrapolated to be approximately 4000–5000 [200 cases of ATLL during the 19 years of the study (1992–2010) divided by the approximately 4%–5% lifetime risk for ATLL after HTLV-1 infection]. Considering that the average lifespan in Canada is approximately 80.8 years, which is 4.25 times the surveillance period (19 years) of the study, the foregoing result would have to be multiplied by 4.25, which equates to approximately 17,000–21,250 HTLV-1–infected people in total (or 54.71–67.55 per 100,000 population). We also used the same methodology described in our earlier report[16] to estimate the age-specific incidence of ATLL across Canada (Table I).

Using the same calculation and methodology, we also extrapolated data for the Canadian provinces and territories (Table II). It is notable that, based on a conservative estimate of a 5% lifetime risk of ATLL in HTLV-1–positive individuals, Quebec has the highest estimated number of infected people (approximately 8100 or 108.78 per 100,000 population) and the highest prevalence of HTLV-1 infection of all Canadian provinces. Quebec is home to many francophone immigrants from Africa and the Caribbean, including Haiti.

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Based on our earlier studies[16,17], confirmed by public reports in the media[10,11,13], 3 cases of ATLL have been reported in Nunavut, which would suggest that at least about 60 individuals in that territory are affected by HTLV-1, within an estimated population of 30,000 (that is, a rate of approximately 200 per 100,000). As described in the original study[16], we were also able to obtain ATLL mortality results from the Canadian Vital Statistics database, which are presented here for completeness (Table III).

We also highlight the report in a previous study that, based on the 1990–2010 records of blood donation, the prevalence of HTLV-1 positivity is approximately 1 per 10,000 first-time blood donors[3]. Hence, our finding of 54.71 HTLV-1–positive people per 100,000 population (or approximately 5 per 10,000) appears to be a reasonable estimate, considering that people likely to volunteer to donate blood constitute a select group, and that group might include fewer newly settled immigrants, intravenous drug users, or individuals residing in northern communities.

TABLE I Estimated incidence of adult T cell leukemia/lymphoma (ATLL), by age group

Age group	Diagnosed ATLL cases[a] *(n)*	Population at risk[b]	Incidence per year (per 100,000)[a]
0–29 Years	25	12,247,000	0.011
30–59 Years	80	13,470,000	0.031
≥60 Years	95	5,320,000	0.094

[a] Randomly rounded (up or down) to the nearest 5 per the rules of the Canadian Cancer Registry or the Registre québécois du cancer. Cases of ATLL were defined based on the *International Classification of Diseases for Oncology,* 3rd edition (code 9827).
[b] Estimates rounded to nearest thousand.

The analysis presented here has a number of important limitations. Considering that ATLL is a rare disease that can mimic certain variants of cutaneous T cell lymphoma, accurately diagnosing and surveying its incidence causes difficulties. Because of the requirements set out by the Canadian Cancer Registry and the Registre québécois du cancer to round the number of cases or deaths to a multiple of 5 and to group jurisdictions so that the combined number of cases reaches a minimum of 5 for presentation, we were not able to describe in detail the mortality incidence in each province or territory. Also, because we could not reliably determine the occurrence of HTLV-1 infection in the studied individuals in early childhood, we were not able to make use of some of the available calculation models that link HTLV-1 infection rates with the ATLL incidence[5]. Finally, because the databases we used do not collect data about race or ethnicity (as described in our earlier work[16,17]), we are not able to comment on the race or ethnicity of HTLV-1–infected individuals in Canada.

In summary, based on our findings, HTLV-1 remains a rare infection in Canada, even considering that the virus is endemic in First Nations communities. This report for the first time estimates the rate of HTLV-1 infection across the country and highlights Quebec as the province with the largest number of ATLL cases. Hence, a significant number of HTLV-1–positive people likely reside in Quebec (that is, more than 8000). Combining those results suggests that it might be important to raise awareness of HTLV-1–associated health risks in select provinces and territories and to consider implementing programs to decrease HTLV-1 transmission, as are currently in place in Japan[3].

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TABLE II Incidence of adult T cell leukemia/lymphoma (ATLL) and corresponding extrapolated prevalence of HTLV-1 infection in Canada based on 2007 life expectancy at birth

Geographic area	Incidence[a]	Estimates of ...				
		Population[b]	Average life expectancy (years)[c]	HTLV-1–infected individuals[d]	Annualized HTLV-1 prevalence per 100,000 individuals	
					Value	95% CI
Atlantic Canada[e]	10	2,356,000	79.72	840	35.65	33.24 to 38.06
Quebec	95	7,446,000	81.0	8100	108.78	106.41 to 111.15
Ontario	70	11,868,000	81.2	5980	50.39	49.11 to 51.66
Manitoba, Saskatchewan, Nunavut	10	2,196,000	79.24	835	38.02	35.44 to 40.60
Alberta	10	3,109,000	80.5	845	27.18	25.35 to 29.01
British Columbia	10	4,040,000	81.4	855	21.16	19.74 to 22.58
Canada	200	31,087,000	80.8	17,010	54.71	53.90 to 55.54

[a] Randomly rounded (up or down) to the nearest 5 per the rules of the Canadian Cancer Registry or the Registre québécois du cancer. Cases of ATLL were defined based on the *International Classification of Diseases for Oncology,* 3rd edition (code 9827).
[b] Rounded to nearest thousand.
[c] Based on data obtained from the 2007–2009 Statistics Canada report. Rate estimates are extrapolated. The confidence interval calculations are approximate and do not account for the full variation of the extrapolated estimate.
[d] Using the conservative assumption that 5% of individuals infected with HTLV-1 are at risk of developing ATLL.
[e] Newfoundland and Labrador, New Brunswick, Nova Scotia, and Prince Edward Island.
CI = confidence interval.

TABLE III Mortality in adult T cell leukemia/lymphoma (ATLL) based on 2007 life expectancy at birth

Geographic area	ATLL-related deaths[a] *(n)*	Estimates of ...		
		Population[b]	Annualized ATLL mortality rate per million individuals	
			Value	95% CI
Atlantic Canada[c]	5	2,356,000	0.11	0.013 to 0.21
Quebec	20	7,446,000	0.14	0.080 to 0.20
Ontario	25	11,868,000	0.11	0.067 to 0.15
Alberta, Manitoba, Saskatchewan, Nunavut	15	5,305,000	0.15	0.073 to 0.22
British Columbia	10	4,040,000	0.13	0.050 to 0.21
Canada	75	31,087,000	0.13	0.98 to 0.16

[a] Randomly rounded (up or down) to the nearest 5 per the rules of the Canadian Cancer Registry or the Registre québécois du cancer. Cases of ATLL were defined based on the *International Classification of Diseases for Oncology,* 3rd edition (code 9827).
[b] Rounded to nearest thousand.
[c] Newfoundland and Labrador, New Brunswick, Nova Scotia, and Prince Edward Island.
CI = confidence interval.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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