Toxoplasmosis and Toxocariasis: An Assessment of Human Immunodeficiency Virus Comorbidity and Health-Care Costs in Canada

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Abstract. *Toxoplasma gondii* and *Toxocara* spp. are zoonotic parasites with potentially severe long-term consequences for those infected. We estimated incidence and investigated distribution, risk factors, and costs associated with these parasites by examining hospital discharge abstracts submitted to the Canadian Institute for Health Information (2002–2011). Annual incidence of serious toxoplasmosis and toxocariasis was 0.257 (95% confidence interval [CI]: 0.254–0.260) and 0.010 (95% CI: 0.007–0.014) cases per 100,000 persons, respectively. Median annual health-care costs per serious case of congenital, adult-acquired, and human immunodeficiency virus (HIV)-associated toxoplasmosis were \$1,971, \$763, and \$5,744, respectively, with an overall cost of \$1,686,860 annually (2015 Canadian dollars). However, the total economic burden of toxoplasmosis is likely much higher than these direct health-care cost estimates. HIV was reported as a comorbidity in 40% of toxoplasmosis cases and accounted for over half of direct health-care costs associated with clinical toxoplasmosis. A One Health approach, integrating physician and veterinary input, is recommended for increasing public awareness and decreasing the economic burden of these preventable zoonoses.

INTRODUCTION

Toxoplasmosis and toxocariasis are neglected infections of poverty that are underreported due to lack of surveillance, even in resource-rich countries with robust health systems.¹ They are also underdiagnosed, due predominantly to the nonspecific, mild, or asymptomatic natural history of disease following infection. Both parasites are overrepresented in specific cultural groups and those with low socioeconomic status in North America and appear to be emerging as significant food-borne infections.^{1,2}

It is estimated that one-third of the global population has been exposed to *Toxoplasma gondii*, making toxoplasmosis one of the most prevalent and important parasitic zoonoses in the world.³ The life cycle includes domestic or wild felids as definitive hosts and a variety of mammals as intermediate hosts. People are infected by ingesting tissue cysts in undercooked meat or infective oocysts in cat feces, through infected blood products/organ transplants, or by transplacental transmission.⁴ Women first exposed to *T. gondii* during the third trimester of pregnancy are at highest risk of transmitting the parasite to their fetus; however, sequelae related to congenital infection are most severe for fetuses infected during the first trimester.⁵ Congenitally infected infants might experience visual impairment, hearing loss, and/or below average intellectual development; approximately 2% of these cases are fatal.⁶ For adults, exposure to *T. gondii* commonly causes self-resolving flu-like symptoms, unless immunity is otherwise compromised. Toxoplasmosis is an opportunistic infection among people living with human immunodeficiency virus (HIV). Toxoplasmic encephalitis (TE) remains an important cause of morbidity and mortality for HIV patients in North America and elsewhere.^{7,8} In Canada, the annual incidence of

domestically acquired toxoplasmosis was previously estimated at 28.1 cases/100,000 people, with 50% of cases estimated to be caused by food-borne exposure.⁹ A 1986 study estimated that 140–1,400 infants were born with congenital health consequences annually, with 70–280 of these cases resulting in severe life-long health consequences.⁵ The national incidence rate for toxoplasmosis is unknown for Canada, although various seroprevalence estimates in indigenous communities have been reported (3–65%).^{10,11} In the United States, one case of TE has a direct treatment cost of approximately US\$10,379 (1992 U.S. dollars), and overall economic losses associated with congenital toxoplasmosis are estimated at US\$0.4–8.8 billion annually.⁶ This latter estimate takes into account medical costs (≈US\$45 million/year), income losses scaled to the level of disability (US\$2.8 billion/year), and special residential/education needs due to mental or physical impairment (US\$2.4 billion/year over a 40-year lifespan). Seropositivity for *T. gondii* has been associated with increased odds of exposure to *Toxocara* species nematodes, possibly mediated through common sources of environmental exposure (i.e., soil contaminated with cat and dog feces).¹²

Toxocariasis occurs in temperate and tropical climates and is a common endoparasite of dogs and cats (especially juveniles). It is caused by zoonotic *Toxocara* spp. nematodes, which have direct life cycles utilizing canid or felid definitive hosts and paratenic life cycles utilizing small mammals. People are infected by ingesting *Toxocara* eggs that have embryonated in the environment after being shed by dogs and cats, or by ingesting raw meat containing encysted larvae.¹³ The three recognized presentations of toxocariasis are characterized by the intensity, location, and presentation of migrating larvae: 1) ocular larval migrans (OLM); 2) visceral larval migrans (VLM); and 3) covert toxocariasis. Risk factors for exposure include young age, low socioeconomic status, low education level, pica, and possibly, dog ownership.^{14–16} Toxocariasis seroprevalence in industrialized countries is estimated to range from 2% to 14%, which mirrors the range observed in indigenous communities (less than 1–13%) in Canada.^{11,17} A comprehensive serosurvey conducted in the United States found that 13.9% ($N = 20,395$) of individuals had been

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exposed.¹⁵ Toxocariasis is believed to cause significant economic losses, especially in nonindustrialized tropical countries. Treatment costs of OLM are likely higher than other forms (VLM and covert).¹⁸

Costs associated with toxocariasis and all types of toxoplasmosis have not previously been calculated using Canadian data. The objectives of this article are to report incidence and risk factors associated with serious toxoplasmosis and toxocariasis (i.e., those severe enough to require emergency or hospital care) and to estimate the health-care costs of treating toxoplasmosis in Canada.

METHODS

Risk factor analysis. We obtained discharge abstracts from the Canadian Institute for Health Information (CIHI) for Canadians diagnosed with toxoplasmosis and/or toxocariasis between 2002 and 2011. Together, the Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS) capture information of patients who are hospitalized or require ambulatory services including outpatient clinics, emergency departments, or day surgeries. Québec patients were only included if they were treated out-of-province, but all other provinces and territories were included (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Newfoundland and Labrador, Nova Scotia, New Brunswick, Yukon Territories, Northwest Territories, and Nunavut). All data originating from the northern territories (Yukon Territories, Northwest Territories, and Nunavut) were combined to avoid identifying patients in areas of low population density. Dataset limitations included omissions for New Brunswick (2002–2003) and Manitoba (2002) due to a gradual province-by-province upgrade to International Classification of Diseases (ICD) version 10. As well, only Ontario facilities were mandated to report ambulatory cases (NACRS) throughout the study period.

Each individual in the dataset was assigned a Meaningless But Unique Number, and these numbers were compared to ensure that duplicate records were deleted. Cost and length of stay were available for two fiscal years (2009–2010 and 2010–2011), and were combined for any individual who received care on multiple occasions. Other variables included age, gender, patient health region, neighborhood income quintile, urban/rural residence, and discharge disposition (the expected status/location of a patient after leaving a hospital). Urban/rural data were classified into four categories according to Statistics Canada definitions¹⁹: 1) rural (outside or fringe of census metropolitan areas [CMAs] or census agglomerations [CAs]); 2) urban core (large urban area with $\geq 50,000$ people for CMA or $\geq 10,000$ people for CA); 3) urban fringe (small urban areas inside CMA or CA but separated from the urban core); 4) urban areas outside CMAs/CAs (small towns with a population of 1,000–10,000 people and population density of ≥ 400 persons/km²).

Datasets were analyzed using SPSS statistical software (version 20; IBM, Chicago, IL). To identify demographic risk factors (gender, age, province of residence, and urban/rural location), we stratified cases per capita using 2006 population estimates²⁰ as the denominator for each factor, and compared by z score at the 1% level of significance (two-tailed P value). Within each stratum, the group with the largest number of cases was used as the reference group. Only DAD hospitalization data were used to compare provincial cases; if the patient province of residence was unavailable, we used the submitting hospital province instead. The urban/rural comparison

included only individuals older than 14 years because of limitations in Statistic Canada reference data. Our calculation of incidence rates included only serious new cases diagnosed during the study period as reported by DAD and NACRS, but did not include mild cases (i.e., those not requiring a visit to an acute care facility). We extrapolated Ontario ambulatory data (NACRS) to the Canadian population excluding Québec to correct for dataset limitations, and reported the mean incidence rate including 95% confidence interval (CI) over the 10-year study period.

Economic analysis. Using a public payer perspective, we estimated the average direct health-care costs of serious toxoplasmosis in Canada (i.e., acute care, inpatient, emergency room, and outpatient clinics). We used ICD-10 diagnostic codes to identify and extract incidence and cost data from both national DAD and NACRS databases for each of the three different types of serious toxoplasmosis: congenital, adult acquired, and HIV associated. The cost data of DAD cases were included for all provinces (excluding Québec); however, as Ontario was the only province with mandatory NACRS reporting for the entire study period, we extrapolated its average incidence for toxoplasmosis-related emergency room visits to the rest of Canada to calculate NACRS-associated toxoplasmosis costs. Furthermore, as CIHI does not include physician costs, we consulted infectious disease clinicians and medical health officers to determine average specialist rates, and used length of stay data combined with the provincial fee schedule for general practitioner remuneration to estimate the cost of physician care in emergency and hospital settings. Using these assumptions and parameters, we estimated both the average and the median cost per serious case per year in Canada. These average cost estimates did not include mild cases of toxoplasmosis. We calculated the average cost estimates for each type of serious toxoplasmosis using the equation:

$$(\text{Average physician cost in hospital} + \text{average cost per patient in hospital}) \times \% \text{ of patients seen in hospital} + (\text{average physician cost in emergency} + \text{average cost per patient in emergency}) \times \% \text{ of patients seen in emergency}$$

To estimate the total direct health-care costs of toxoplasmosis in Canada, we estimated both mild (i.e., those who did not visit an emergency room or hospital) and serious toxoplasmosis cases. To capture mild cases of toxoplasmosis, we used a previous Canadian estimate for the annual incidence (379 cases per 100,000).⁹ Subsequently, using percentages of infections associated with clinically significant cases of lymphadenopathy, we estimated that 5% of people infected with *Toxoplasma* would see a physician.²¹ Furthermore, using the incidence of ocular manifestations from a 1995 outbreak of toxoplasmosis in the province of British Columbia we estimated that 0.475% of infected individuals would see an ophthalmologist.²² The price of a general practitioner and ophthalmologist visits were derived from the 2015 Alberta Medical Procedure Price List for physicians.²³ We calculated the total costs for each type of serious toxoplasmosis using the following equation:

$$(\text{DAD average cost per case}) \times (\text{number of cases in DAD}) + (\text{NACRS average cost per case}) \times (\text{estimate of number of NACRS cases nationally based on Ontario NACRS}) + (\text{DAD average cost per case}) \times (\text{estimate of number of DAD cases in Quebec})$$

We subsequently combined the cost and incidence estimates for all serious toxoplasmosis cases in the CIHI databases as well as the mild case estimates⁹ to calculate the total health-care cost for congenital, adult-acquired, and HIV-associated cases of *T. gondii*-related disease per year. All costs are presented in 2015 Canadian dollars (C\$).

Ethics. This project was reviewed and approved by the University of Saskatchewan Biomedical Ethics Review Board (REB 13-51), which adheres to Canadian national standards set out by the Tri-Council Policy Statement for research involving humans.

RESULTS

Risk factor analysis. The annual incidence rates for serious toxoplasmosis and toxocariasis were 0.257 (95% CI: 0.254–0.260) and 0.010 (95% CI: 0.007–0.014) cases per 100,000 persons, respectively. The ratio of serious to mild toxoplasmosis cases was approximately 1:74. The proportion of people hospitalized for toxoplasmosis varied significantly between provinces (Table 1, Figure 1). The higher proportion of toxoplasmosis in males versus females was significant at the national level and for two provinces (British Columbia and Ontario). Congenital toxoplasmosis was diagnosed in 48 newborn infants and 12 infants aged over 1 day and under 24 months, for an annual incidence rate of 1.7 per 100,000 births (Table 2). Congenital toxoplasmosis was also noted

for 12 patients aged 2–84 years. Among adult-acquired cases, the mean age was 40 years (42 years for HIV-positive cases). Toxoplasmosis was diagnosed most frequently in residents older than 14 years from urban core areas; however, the difference in cases per capita between urban versus rural areas was not significant.

Noncongenital toxoplasmosis presented most frequently as meningoencephalopathy or oculopathy, and far less frequently with pulmonary, cardiac, or hepatic involvement (Table 2). Mortality occurred for 9% of clinical cases overall (8% congenital, 4% adult-acquired, and 15% HIV-positive). HIV was reported as a comorbidity in 40% of toxoplasmosis cases overall, most commonly in those with meningoencephalopathy and least commonly in congenital cases. By age group, HIV as a comorbidity occurred in 1% (1/89) of those under 15 years, in 51% (203/401) of those aged 15–64 years, and in 15% (5/33) of those aged 65 years and older. Among toxoplasmosis cases, HIV occurred in significantly more males (49% of 293) than females (28% of 230; $P < 0.001$).

Toxocariasis occurrence was not significantly different ($P = 0.22$) between males and females (12/19 and 7/19, respectively). Three cases of toxocariasis occurred in infants younger than 24 months (all male) and four occurred in children (2–14 years). The mean age for the remaining 12 cases was 27 years with a range of 2–56 years, and the proportion of toxocariasis cases was significantly higher in children (0–14 years) than for adults (> 14 years; $P = 0.03$). Both toxocariasis and toxoplasmosis

TABLE 1
Description of acute and emergency care patients diagnosed with toxoplasmosis in Canada from 2002 to 2011

Descriptor	Cases, <i>N</i> (%)	Proportion cases/capita $\times 10^6$	<i>z</i> -Score†	<i>P</i> value
Gender				
Female	230 (44)	14	3.2	0.001
Male	293 (56)	19		
Age (years)				
0–14	89 (17)	16	–1.3	0.21
15–64	401 (77)	18	Reference	Reference
≥ 65	33 (6)	7	–5.1	< 0.001
Urban/rural‡				
Rural	38 (10)	12	1.9	0.06
Urban core	322 (82)	17	Reference	Reference
Urban fringe	10 (3)	13	0.9	0.35
Urban area outside CMA/CA	23 (6)	15	0.6	0.54
Missing	41	–	–	–
Neighborhood income quintile§				
C\$14,800	178 (35)	–	–	–
C\$25,800	86 (17)	–	–	–
C\$35,300	86 (17)	–	–	–
C\$46,900	82 (16)	–	–	–
C\$78,800	72 (14)	–	–	–
Missing	19	–	–	–
Province of residence				
British Columbia	58 (16)	14.1	–0.83	0.41
Alberta	55 (15)	16.7	0.31	0.76
Saskatchewan	11 (3)	11.4	–1.1	0.27
Manitoba	6 (2)	5.2	–2.8	0.005
Ontario	194 (52)	16.0	Reference	Reference
Québec	5 (1)	–	–	–
Newfoundland and Labrador	4 (1)	7.9	–1.4	0.16
Nova Scotia	14 (4)	15.3	–0.15	0.89
New Brunswick	23 (6)	31.5	3.1	0.002
Yukon, Northwest Territories, and Nunavut	4 (1)	39.5	1.9	0.06

CA = census agglomeration; CMA = census metropolitan area.

*Percent of cases where descriptor data are available.

†*z*-score compares cases/capita for each risk factor.

‡Urban/rural status only reported for patients > 14 years.

§Average adjusted after-tax income for individuals calculated for 2006 in 2009 constant dollars (<http://www.statcan.gc.ca/pub/75-202-x/2009000/analysis-analyses-eng.htm#a2>).

||Inpatients only (Discharge Abstract Database); only Québec residents who received medical care out of province.

FIGURE 1. Total cumulative toxoplasmosis inpatient cases per 100,000 people for the years 2002–2011 reported by the Discharge Abstract (except QC = Québec; BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; NL = Newfoundland and Labrador; NS = Nova Scotia; NB = New Brunswick; YT = Yukon Territories; NT = Northwest Territories; NU = Nunavut). * Québec cases treated in Ontario hospitals.

were diagnosed most frequently in patients who resided in the lowest neighborhood income quintile. No patients receiving care for toxocariasis were coinfected with HIV, and no patients died as a result of their infection. Length of stay and cost estimates were unavailable for toxocariasis patients.

Economic analysis. On average, patients with both toxoplasmosis and HIV required longer inpatient and emergency room visits than those with congenital or adult-acquired toxoplasmosis (Table 3). Annual treatment costs per infected individual were significantly different between the three case presentations, with noncongenital toxoplasmosis being least costly and HIV-associated toxoplasmosis being most costly. Most congenital and HIV-related cases of serious toxoplasmosis were treated in hospital (76% and 95%, respectively)

rather than emergency clinics, whereas, only 31% of serious adult-acquired toxoplasmosis cases were hospitalized.

Overall, toxoplasmosis cost the Canadian health-care system C\$1,686,860 per year based on 2010/2011 CIHI data (Table 4). While adult-acquired toxoplasmosis had the highest number of cases, HIV-associated toxoplasmosis had the highest economic burden on the health-care system in Canada, accounting for 53% of total costs in 1 year. In comparison, adult-acquired and congenital toxoplasmosis cases accounted for 20% and 11% of the total toxoplasmosis costs per year, respectively. Finally, although mild toxoplasmosis cases were most common (18.95 per 100,000 persons per year), each case cost on average only C\$41.60 per year. Therefore, overall mild toxoplasmosis had a relatively small

TABLE 2
Frequency and description of human toxoplasmosis cases in Canada (2002–2011)

ICD-10 code	Description	Frequency	% Of cases	HIV comorbidity frequency	HIV (% of toxoplasmosis cases)
B58.0	<i>Toxoplasma</i> oculopathy	77	14.7	4	5
B58.1	<i>Toxoplasma</i> hepatitis	5	1.0	3	60
B58.2	<i>Toxoplasma</i> meningoencephalopathy	84	16.1	71	85
B58.3	Pulmonary toxoplasmosis	12	2.3	9	75
B58.8	Toxoplasmosis (other organs)	86	16.4	46	53
B58.8 + I41.2	Toxoplasmosis + myocarditis	3	0.6	2	67
B59.9	Toxoplasmosis (unspecified)	184	35.2	73	40
P37.1	Congenital toxoplasmosis*	72	13.8	1	1
Total		523	100	209	40

HIV = human immunodeficiency virus; ICD = International Classification of Diseases.

*Including hydrocephalus.

TABLE 3
Annual toxoplasmosis costs per patient for inpatient and emergency care in Canada

	Congenital toxoplasmosis	Adult-acquired toxoplasmosis	Toxoplasmosis + HIV comorbidity
Inpatient LOS (days)			
Median	5	7	20
Mean	17	17	37
Range*	1–98	1–123	1–441
Emergency LOS (days)			
Median	0.3	0.2	0.7
Mean	0.4	0.2	0.9
Range*	0.08–1.1	0.04–1.1	0.2–2.1
Cost/patient/year† (C\$ 2015)			
Median	1,971	763	5,744
Mean	9,561	3,781	16,926
Range*	585–52,124	210–52,163	1,684–130,234

LOS = length of stay in hospital or clinic.

*Range is based on maximum and minimum values for inpatient LOS (days), emergency LOS (days), and the costs per patient per year (\$) provided in the Discharge Abstract Database and National Ambulatory Care Reporting System (NACRS) databases.

†Cost estimates calculated by extrapolating Ontario NACRS incidence and costs to all other provinces and territories in Canada.

health-care burden, costing a total of C\$271,526 per year or 16% of the total cost of treating toxoplasmosis.

DISCUSSION

Although clinical cases severe enough to require emergency or hospital care are relatively rare, our study suggests that toxoplasmosis and toxocarasis can result in significant burdens for individual patients and the health-care system. As well, our findings suggest that these parasites should be considered neglected diseases, as they reflect social inequities even within a resource-rich country with robust public health and veterinary systems.

Herein, we report incidence rates for congenital and adult-acquired toxoplasmosis that are lower than previous estimates, likely because we did not adjust for undiagnosed infection and because we restricted case identification to recorded diagnoses rather than laboratory surveillance data or extrapolation from serological data.^{5,9} Also, we did not have access to data from the northern part of Québec (Nunavik), which has the highest seropositivity nationally and where outbreaks of clinical toxoplasmosis have been reported.²⁴ In Canada, human exposure to *T. gondii* has been associated with gender, drinking water source, ethnicity, and education level. Immigrant populations are considered high risk, which may explain why urban core areas in this study reported higher incidence rates than areas

with fewer new immigrants.^{5,25} In contrast to serological surveys in northern Canada, which found that more females had been exposed than males,¹⁰ our analysis found that a significantly higher proportion of males developed serious toxoplasmosis than females. HIV infection, a risk factor for the development of serious toxoplasmosis disease, is more prevalent among men than women in Canada (0.32% among men, 0.096% among women).²⁶ However, in our analysis, the association between gender and serious toxoplasmosis was independent of whether HIV was present as a comorbidity. The prevalence of HIV among toxoplasmosis patients in this dataset was 40% (49% among men, 28% among women), which is high compared with the 0.2% HIV prevalence in the general population.²⁷ Comorbidities or other risk factors for developing severe toxoplasmosis, including causes of impaired cellular immunity, should be explored in further research.

Toxoplasmosis is an opportunistic infection among individuals with immune compromise, and occurs due to newly acquired acute infection or reactivation of chronic infection, causing potentially fatal encephalitis, as well as chorioretinitis or pneumonitis.²⁸ According to our economic analysis, HIV-associated toxoplasmosis accounts for the majority (53%) of the total toxoplasmosis-related health-care costs, with both the highest incidence of hospitalization cases and the highest treatment cost per case. We could not dissociate treatment costs for HIV from that of toxoplasmosis, which may have resulted in an overestimation of the relative impact of HIV-associated toxoplasmosis. Regardless, this work demonstrates the public health and economic importance of targeting prevention programs to groups with immune compromised and to groups at highest risk of exposure. Serological testing for *T. gondii* is recommended for all people living with HIV.²⁹ As well, prophylactic antibiotic treatment to prevent toxoplasmosis is recommended for severely immunocompromised patients with serological evidence of exposure and for all HIV patients with a previous diagnosis of toxoplasmosis.²⁹

Direct contact with domestic cat stool is often cited as the primary source of toxoplasmosis, although unsporulated oocysts in fresh cat feces are not immediately infective for people. However, water- and food-borne routes (e.g., consuming undercooked meat containing tissue cysts or fresh produce contaminated with oocysts) are more common sources of human infection in Canada and abroad.^{5,9,17,24,30} Our cost estimates for toxoplasmosis appear low compared

TABLE 4
Total annual costs of toxoplasmosis by case presentation

	Total cost per year (C\$ 2015)	Range*	% Of total cost
Congenital toxoplasmosis	191,122	11,783–1,046,165	11.3
Adult-acquired toxoplasmosis	336,115	18,829–4,633,098	19.9
Toxoplasmosis + HIV	888,097	88,469–7,599,103	52.7
Mild toxoplasmosis	271,526	33,619–2,945,908†	16.1
Total	1,686,860		

HIV = human immunodeficiency virus

*The ranges for cases of serious toxoplasmosis were calculated with the minimum and maximum cost and length of stay estimates provided in the Discharge Abstract Database and National Ambulatory Care Reporting System database.

†The range for cases of mild toxoplasmosis were calculated by varying the number of infections according to high and low estimates provided by Thomas and others⁹ and by varying the percentage of those who would see a general practitioner between 3% and 7%.²¹

with those of other pathogens because we only measured direct health-care costs and did not measure indirect medical costs (e.g., travel to medical clinic) and nonmedical costs (e.g., loss of productivity for both patients and caretakers). We could not estimate the total economic burden of toxoplasmosis in Canada. This was largely due to a lack of data on the incidence of toxoplasmosis sequelae and the long-term effects of the disease in Canada. Also, our analysis did not include medical costs from toxoplasmosis-related miscarriages or the costs of pharmaceuticals outside the inpatient setting. Other models integrating both direct and indirect costs, as well as adjusting for underreporting, identify toxoplasmosis as having one of the highest burdens of disease compared with other food-borne pathogens.^{31,32} In the United States, extrapolation from serological data suggested that food-borne toxoplasmosis (assumed to be 50% of total cases of toxoplasmosis) costs approximately US\$12,145–72,669 per case, with a total economic burden of US\$1,019–6,606 million annually.³¹ Most estimates of toxoplasmosis costs demonstrate a wide degree of uncertainty, especially for adult-acquired and mild cases, which are most likely to be underreported and underdiagnosed. Improved knowledge of the proportion of symptomatic cases both seeking and not seeking medical attention, could produce more accurate estimates of the economic burden of disease and risk factors for infection in Canada.

Our study suggests that congenital toxoplasmosis has a small impact on direct health-care costs in Canada, in comparison with other toxoplasmosis presentations; however, this does not imply a small economic burden as congenital cases incur significant costs for long-term care and education, along with productivity losses.³³ Most women who acquire toxoplasmosis during pregnancy do not experience symptoms or report epidemiological risk factors for infection, creating challenges for detection during a period when treatment could prevent congenital infection.³⁴ Screening programs to detect recently acquired infection exist in many jurisdictions, including Austria, Denmark, France, several American states, and northern Québec, and should be increased among pregnant women in Canada.^{35,36} The implementation of systematic screening for toxoplasmosis, as with any screening program, should be considered in the context of factors including local burden of disease, local risk factors for disease, availability and acceptability of testing, availability of treatment, and costs.³⁷ As well, printed materials or health-care provider advice describing key practices to prevent exposure to *T. gondii* may reduce rates of infection among pregnant women, although a systematic review of such interventions found existing research on the topic to be generally of poor quality.³⁸ A Canadian randomized controlled trial observed mixed results regarding behavioral changes following a program combining educational materials and prenatal counseling.³⁹ Further research to identify efficacious and cost-effective interventions for primary prevention of toxoplasmosis is needed.

Our estimate of toxocariasis incidence for the Canadian population based on hospital discharge records confirms that this condition is rare (0.010 cases/100,000/year). However, because of underreporting, underdiagnosis, and data limitations during the study period, the incidence for both toxoplasmosis and toxocariasis are likely underestimated. In the United States, toxocariasis is now considered to be the most

common helminthiasis in people, and is closely linked with poverty.^{17,40} The most common form, covert toxocariasis, is characterized by nonspecific asthma-like symptoms, presenting challenges for diagnosis.^{13,40} Overall, 1.3–2.8 million Americans are estimated to have toxocariasis, and OLM incidence is estimated at 10 cases per 100,000 people annually.⁴⁰ No estimates are available for VLM incidence or prevalence.^{18,41} Previously, young age was reported to be a risk factor for toxocariasis, and this is supported by our dataset.^{13,15,40} The cases we observed in older age groups could be explained by the recent increase in meat-borne transmission among adults.¹⁷ Other previously reported risk factors such as gender, socioeconomic status, and rural residence were not confirmed by this dataset, likely due to small sample size and limitations in nationally reported census data. In our study, toxocariasis did occur most frequently in low-income and urban core neighborhoods, which is consistent with high seroprevalence in poor inner-city neighborhoods in the United States.⁴⁰ This suggests that poverty may also be an important risk factor for exposure in Canada.

The economic burden of toxocariasis remains unknown, largely because disease frequency estimates have not been calculated.^{13,17,18} According to Torgerson and MacPherson, toxocariasis is an important burden for both individuals and society, especially as children are most frequently affected.¹⁷ Diagnosis and treatment of toxocariasis is costly, and long-term effects such as delayed cognitive development, asthma, and vision impairment decrease opportunities for employment as well as increasing health-care costs. Prevention of human toxocariasis is largely linked with decreasing patent infections in definitive hosts through deworming dogs and cats for roundworms (canids for *Toxocara canis*, felids for *Toxocara cati*), preventing high-risk behaviors such as pica, and cooking meat to destroy encysted larvae in tissues.

Toxocariasis and toxoplasmosis are preventable zoonotic infections, with potentially serious long-term health effects for infected individuals. Our analysis suggests that interventions with input from both human and animal health professionals, and targeted to high risk groups such as children and those with immune compromise, are most likely to reduce parasitism and its associated health-care costs. Our work calls for enhanced human and animal surveillance, as well as policies that facilitate improved access to veterinary and medical services in underserved remote and northern regions.

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REFERENCES

- Barry MA, Weatherhead JE, Hotez PJ, Woc-Colburn L, 2008. Childhood parasitic infections endemic to the United States. *Pediatr Clin North Am* 60: 471–485.
- Lee R, Moore L, Bottazzi M, Hotez P, 2004. Toxocariasis in North America: a systematic review. *PLoS Negl Trop Dis* 8: e3116.
- Tenter A, Heckeroth A, Weiss L, 2000. *Toxoplasma gondii*: from animals to humans. *Int J Parasitol* 30: 1217–1258.
- Hill D, Dubey J, 2002. *Toxoplasma gondii*: transmission, diagnosis and prevention. *Clin Microbiol Infect* 8: 634–664.
- Carter A, Frank J, 1986. Congenital toxoplasmosis. *Can Med Assoc J* 135: 618–623.
- Roberts T, Murrell K, Marks S, 1994. Economic losses caused by foodborne parasitic diseases. *Parasitol Today* 10: 419–423.
- Montoya J, Remington J, 2000. Toxoplasmosis. Mandell G, Bennet J, Dolin R, eds. *Principles and Practices of Infectious Diseases*. Philadelphia, PA: Churchill Livingstone, 2858–2888.
- Jones J, Roberts J, 2012. Toxoplasmosis hospitalizations in the United States, 2008, and trends, 1993–2008. *Clin Infect Dis* 54: e58–e61.
- Thomas M, Murray R, Flockhart L, Pintar K, Pollari F, Fazil A, Nesbitt A, Marshall B, 2013. Estimates of the burden of foodborne illness in Canada for 30 specified pathogens and unspecified agents, circa 2006. *Foodborne Pathog Dis* 10: 639–648.
- Messier V, Levesque B, Proulx J-F, Rochette L, Libman M, Ward B, Serhir B, Couillard M, Ogden NH, Dewailly E, Hubert B, Dery S, Barthe C, Murphy D, Dixon B, 2009. Seroprevalence of *Toxoplasma gondii* among Nunavik Inuit (Canada). *Zoonoses Public Health* 56: 188–197.
- Jenkins E, Castrodale L, de Rosemond S, Dixon B, Elmore S, Gesy K, Hoberg E, Polley L, Schurer JM, Simard M, Thompson RCA, 2013. Tradition and transition: parasitic zoonoses in people and animals in northern North American and Greenland. *Adv Parasitol* 82: 33–204.
- Jones J, Kruszon-Moran D, Won K, Wilson M, Schantz P, 2008. *Toxoplasma gondii* and *Toxocara* spp. co-infection. *Am J Trop Med Hyg* 78: 35–39.
- Smith H, Holland C, Taylor M, Magnaval J-F, Schantz P, Maizels R, 2009. How common is human toxocariasis? Towards standardizing our knowledge. *Trends Parasitol* 25: 182–188.
- Embil J, Tanner C, Pereira L, Staudt M, Morrison E, Gualazzi D, 1988. Seroepidemiologic survey of *Toxocara canis* infection in urban and rural children. *Public Health* 102: 129–133.
- Won K, Druszon-Moran D, Schantz P, Jones J, 2008. National seroprevalence and risk factors for zoonotic *Toxocara* spp. infection. *Am J Trop Med Hyg* 79: 552–557.
- Schurer J, Ndao M, Skinner S, Irvine J, Elmore S, Epp T, Jenkins EJ, 2013. Parasitic zoonoses: One Health surveillance in northern Saskatchewan. *PLoS Negl Trop Dis* 7: e2141.
- Torgerson P, Macpherson C, 2011. The socioeconomic burden of parasitic zoonoses: global trends. *Vet Parasitol* 182: 79–95.
- Torgerson P, Budke C, 2006. Economic impact of *Toxocara* spp. Holland C, Smith H, eds. *Toxocara: The Enigmatic Parasite*, 1st edition. Wallingford, United Kingdom: CABI, 281.
- Statistics Canada, 2009. *Urban Core, Urban Fringe and Rural Fringe*. Available at: <https://www12.statcan.gc.ca/census-recensement/2006/ref/dict/geo050a-eng.cfm>. Accessed June 21, 2014.
- Statistics Canada, 2006. *2006 Census of Population*. Available at: <https://www12.statcan.gc.ca/census-recensement/2006/index-eng.cfm>. Accessed June 17, 2014.
- Advisory Committee on the Microbiological Safety of Food, 2012. *Risk Profile in Relation to Toxoplasma in the Food Chain*. Available at: <http://www.food.gov.uk/sites/default/files/multimedia/pdfs/committee/acmsfrtaxopasm.pdf>. Accessed December 10, 2015.
- Burnett A, Shortt S, Isaac-Renton J, King A, Werker D, Bowie W, 1998. Multiple cases of acquired toxoplasmosis retinitis presenting in an outbreak. *Ophthalmology* 105: 1032–1037.
- Government of Alberta, 2015. *Medical Procedure List as of 01 April 2015*. Available at: <http://www.health.alberta.ca/professionals/SOMB.html>. Accessed January 26, 2016.
- McDonald J, Gyorkos T, Alberton B, MacLean J, Richer G, Juranek D, 1990. An outbreak of toxoplasmosis in pregnant women in northern Québec. *J Infect Dis* 161: 769–774.
- Jones J, Kruszon-Moran D, Wilson M, McQuillan G, Navin T, McAuley J, 2001. *Toxoplasma gondii* infection in the United States: seroprevalence and risk factors. *Am J Epidemiol* 154: 357–365.
- Public Health Agency of Canada, 2014. *HIV/AIDS Epi Updates: National HIV Prevalence and Incidence Estimates for 2011*. Available at: <http://www.phac-aspc.gc.ca/aids-sida/publication/epi/2010/1-eng.php>. Accessed October 5, 2015.
- Public Health Agency of Canada, 2011. *Estimates of HIV Prevalence and Incidence in Canada*. Available at: <http://www.acch.ca/resources/Summary%20HIV%20Prevalence%20and%20Incidence%20in%20Canada,%202011.pdf>. Accessed February 23, 2015.
- Montoya J, Liesenfeld O, 2004. Toxoplasmosis. *Lancet* 363: 1965–1976.
- BC Centre for Excellence in HIV/AIDS, 2009. *Opportunistic Infections Therapeutic Guidelines*. Available at: <http://www.cfenet.ubc.ca/therapeutic-guidelines/opportunistic-infection>. Accessed September 22, 2014.
- Cook A, Gilbert R, Buffolano W, Zufferey J, Petersen E, Jenun P, Foulon W, Semprini AE, Dunn DT, 2000. Sources of *Toxoplasma* infection in pregnant women: European multicentre case-control study. *BMJ* 321: 142–147.
- Scharff R, 2012. Economic burden from health losses due to foodborne illness in the United States. *J Food Prot* 75: 123–131.
- Mangen MJ, Bouwknegt M, Friesema I, Haagsma J, Kortbeek L, Tariq L, Wilson M, van Pelt W, Havelaar AH, 2014. Cost-of-illness and disease burden of food-related pathogens in The Netherlands, 2011. *Int J Food Microbiol* 196: 84–93.
- Roberts T, Frenkel J, 1990. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. *J Am Vet Med Assoc* 196: 249–256.
- Boyer K, Holfels E, Roizen N, Swisher C, Mack D, Remington J, Withers S, Meier P, McLeod R, 2005. Risk factors for *Toxoplasma gondii* infection in mothers of infants with congenital toxoplasmosis: implications for prenatal management and screening. *Am J Obstet Gynecol* 192: 564–571.
- Lavoie E, Levesque B, Proulx JF, Grant J, Ndassebe A, Gingras S, Hubert B, Libman M, 2008. Evaluation of the efficacy of the *Toxoplasma gondii* screening program among pregnant women in Nunavik, 1994–2003. *Can J Public Health* 99: 397–400.
- Montoya J, Remington J, 2008. Management of *Toxoplasma gondii* infection during pregnancy. *Clin Infect Dis* 46: 554–566.
- Wilson J, Jungner G, 1968. *Principles and Practice of Screening for Disease*. Report no: 34. Geneva, Switzerland: World Health Organization, 163.
- Gollub E, Leroy V, Gilbert R, Chene G, Wallon M, European Toxoprevention Study Group (EUROTOX), 2008. Effectiveness of health education on *Toxoplasma*-related knowledge, behaviour, and risk of seroconversion in pregnancy. *Eur J Obstet Gynecol Reprod Biol* 136: 137–145.
- Carter A, Gelmon S, Wells G, Toepell A, 1989. The effectiveness of a prenatal education programme for the prevention of congenital toxoplasmosis. *Epidemiol Infect* 103: 539–545.
- Hotez P, Wilkins P, 2009. Toxocariasis: America's most common neglected infection of poverty and a helminthiasis of global importance? *PLoS Negl Trop Dis* 3: e400.
- Lim J, 2008. Toxocariasis of the liver: visceral larva migrans. *Abdom Imaging* 33: 151–156.