

2020-08-21

Understanding the Heterogeneity of the Echinococcus multilocularis transmission patterns, processes, and mechanisms: an agent-based modeling approach

Mori, Kensuke

Mori, K. (2020). Understanding the Heterogeneity of the Echinococcus multilocularis transmission patterns, processes, and mechanisms: an agent-based modeling approach (Doctoral thesis, University of Calgary, Calgary, Canada). Retrieved from <https://prism.ucalgary.ca>.
<http://hdl.handle.net/1880/114123>

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UNIVERSITY OF CALGARY

Understanding the Heterogeneity of the *Echinococcus multilocularis* transmission patterns, processes, and mechanisms: an agent-based modeling approach

by

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE

DEGREE OF DOCTOR OF PHILOSOPHY

GRADUATE PROGRAM IN GEOMATICS ENGINEERING

CALGARY, ALBERTA

AUGUST, 2020

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ABSTRACT

Epidemiological models are essential in managing disease risks. However, the traditional epidemiological models are less applicable with complex life-cycle parasites. *Echinococcus multilocularis* (*Em*) is a parasite with complex life-cycle that is naturally present among wildlife and a cause for a serious zoonosis. One of the notable patterns of *Em* epidemiology was the spatial heterogeneity in prevalence. To explain the heterogeneity, we proposed three hypotheses, namely 1) intermediate host hypothesis, 2) definitive host hypothesis, and 3) metapopulation hypothesis.

Its natural presence in wildlife makes the eradication of *Em* impractical and thorough understanding of its epidemiology through observation and experiments impossible. In order to understand the transmission processes and test the hypotheses, modeling is essential. Because the parasite's transmission is indirect (through predation of intermediate hosts by definitive host), hosts display territoriality and distinct home ranges, the landscape is heterogeneous, and hosts display high diversity in the parasite load, we decided to develop a spatially-explicit agent-based model (ABM).

Small mammal data from the urban parks in the City of Calgary was statistically analyzed for their statistical association to the environmental variables, and to the observed prevalence of *Em* among wildlife hosts. The association of small mammal community to the environmental variables were used to develop a map of small mammal communities. Fecal data of dogs and coyotes were analyzed for spatial patterns, association to the environmental variables, and to the park management. These analyses were used to develop the virtual urban landscape of the ABM, allowing the development of Calgary *Echinococcus Multilocularis* Coyote Agent-based model (CEMCA). While the CEMCA was successfully calibrated on coyote behaviors, the validation using the epidemiological patterns deviated from observation in some of the epidemiological patterns. However, we believe the deviations provide insights on what is unknown or important in the system. The CEMCA was used to conduct experiments on the hypotheses on spatial heterogeneity, and indicated that the intermediate host and metapopulation hypotheses are likely to be true. The CEMCA is a novel work of ABM of trophically-transmitted parasites with complex life-cycle using a complex landscape, and has many more potential use for assessing *Em* and epidemiology in general.

PREFACE

The work in chapter 3, 4 and 5 is the result of a multi-author collaboration.

The chapters 1 and 2 are not published. Chapter 5 was submitted but since been revised, and chapter 3 has been accepted for publication. Chapter 4 is being revised for submission to urban planning.

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ACKNOWLEDGEMENTS

Thanks to Chris Manderson and Jenna Cross from the City of Calgary Parks for financial and technical support through direct funding and through the Urban Alliance initiative with the University of Calgary. We thank Department of Geomatics Engineering, Faculty of Graduate Studies, University of Calgary and Alberta Innovates Health Solutions for studentships. We thank Karina Lamy, S. Gingerick, Sabrina Colquhoun, Joanna Deunk, Heather Gordon, Megan Hart, Fabien Labelle, Sultana Majid, Abraham Munene, Holly Shaw, Francois Patard, Kaitlyn Varga and Monica Viapiana for their precious contribution in field collection and laboratory analysis. We are grateful to June Au Yeung, Courtney Cavinet, and Monica Freeman, for their generous and friendly support, as well as Susan McKee and Quazi Hassan for their constant availability. Special acknowledgments to James Wang and Claudia Klein.

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LIST OF ABBREVIATIONS

ABM: Agent-based model

AE: Alveolar echinococcosis

CEMCA: Calgary Echinococcus multilocularis Coyote Agent-based model

DH: Definitive host

Em: *Echinococcus multilocularis*

IH: Intermediate host

LIST OF NOMENCLATURE

Assemblage: Phylogenetically related groups within a community (Fauth et al., 1996). In this study, the term is used to indicate the species composition and relative abundances of the assemblage

Canids: Family of mammals that includes dogs, wolves, foxes, and coyotes.

Cestode: a parasitic tapeworm from class *Cestoda*. In this study the term cestodes is used as an adult stage of the *Cestoda*.

Community (ecological community): Collection of species that co-occur in the same location at the same time (Fauth et al., 1996).

Definitive host: The host in which the sexual stages of the parasite mature.

Embryonated eggs: In parasitology the embryonated eggs indicate nematode eggs with a developed larva inside, ready to hatch.

Intensity: Also known as worm loads. In epidemiology, the term intensity indicates the number of parasites infecting a host.

Intermediate host: The host in which the parasite develop before being transmitted to the definitive host.

Lagomorphs: Order of mammals that includes rabbits and hares.

Metacestode: Metacestodes are fluid-filled vesicles that the larval stage of the tapeworm forms in the infected organ of the intermediate host.

Metapopulation: A metapopulation consists of a group of spatially separated populations of the same species which interact and exchange individuals at some level.

Oncosphere: The larval stage of a tapeworm that emerges from the embryonated eggs after it was ingested by an intermediate host.

Parasite: General term for organisms that live on or within other living organisms (host) to obtain nutrients at the expense of the host.

Parasite with complex life-cycle: Parasites that require two different host species and free living stage outside of host in its life cycle.

Prevalence: In epidemiology, the prevalence indicates the proportion of the hosts that are infected with the parasites.

Protoscoleces: The larval stage of *Echinococcus* species that forms inside metacestode in the intermediate host. When the protoscoleces are ingested by the definitive host, the protoscoleces attach to the intestinal walls of the definitive hosts.

Rodents: Order of mammals that include mice, rats, voles, and beaver.

Small mammal: In this study the small mammals are the group of animals that take the role of prey items for coyotes, usually rodents but include squirrels, shrews, and lagomorphs.

Zoonosis: Human diseases caused by infection from animals.

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CH 1: BACKGROUND/GENERAL INTRODUCTION

Echinococcus multilocularis (*Em*) is a species of parasitic tapeworm that can cause alveolar echinococcosis (AE) in humans, a most serious liver disease caused by parasites in regions outside of the tropics (Massolo et al., 2014). The parasite is naturally present among wildlife, and transmitted orally through predator-prey interactions (Craig, 2003; Romig, 2003; Vuitton et al., 2003). The parasite is widely distributed across the northern hemisphere, including the north central region of North America where the City of Calgary, Alberta, is located (Deplazes et al., 2017; Massolo et al., 2014; Romig et al., 2017a). Although historically there has been little record of AE in Calgary (Massolo et al., 2014), there is a concern that the city and its surrounding area will face increased risk of the parasite in the future (Massolo et al., 2019). The city population is rapidly growing (The City of Calgary, 2016) and developed areas are expanding. With the spread of the urban areas and associated changes in the wildlife habitats, people and wildlife are often found in close proximity to each other. Among the wildlife species now found in urban areas, one of the most notable is the coyote (*Canis latrans*). Its potential as wild host of *Em* (Catalano et al., 2012) has raised serious concerns. The prevalence of the parasites among the coyotes in urban areas of the City of Calgary has been found to be more than 20% (Liccioli et al., 2014), just as high as some areas in Europe where the parasite is causing significant health problems (Craig, 2003).

The number of dogs owned by Calgary residents is also rapidly increasing (National Canine Research Council, 2011). Dogs can become infected by the parasite and can in turn transmit to humans, acting as a bridge for the parasite between wildlife and humans (Romig, 2003; Romig et al., 2017a). Calgary contains several recreational parks with off-leash areas for dogs that wildlife also uses as habitat. It is known that some dogs capture wild small mammals in those parks, which are potentially infected with the parasite (Massolo et al., 2014).

Because AE is highly fatal, Craig (2003) considers the disease public health significance at an incidence rate of 0.1 per 100,000. Although historically the disease has not been considered a serious threat in North America, there are many indications that the disease is becoming more significant in North America (Massolo et al., 2019). An improved understanding of the dynamics of the parasite transmission is required for effective surveillance and preparation against the disease. However, the natural reservoir of the parasite among the wildlife hosts makes the parasite very difficult and expensive to survey, and conducting an experiment at the community or population level is practically impossible. To solve such a problem, simulation models are required.

1.1. THREATS AND TRENDS OF ECHINOCOCCOSIS

Echinococcus is a genus of tapeworms that can cause a zoonotic infection referred to as human echinococcosis. The parasite requires more than one species of mammalian hosts to complete its life cycle; it needs a mammalian prey species as intermediate host and canid mammalian predator as definitive host. A definitive host is infected by *Echinococcus* when it preys on infectious intermediate hosts and ingests their infectious organs, usually the liver. Once in a definitive host, the larva of *Echinococcus* spp. attaches to the intestinal walls and develops to reach maturity. Adult worms produce embryonated eggs, which are subsequently released into the environment with the host feces. An intermediate host will in turn become infected when it accidentally ingests the eggs in the environment, thus completing the cycle. A human can be infected as an “accidental” intermediate host when he accidentally ingests the eggs of *Echinococcus* or has frequent contacts with infected definitive hosts (Thompson, 2017).

Although several species of *Echinococcus* are known and are all potentially zoonotic, two species are of the most concern for human health (Romig et al., 2017a). *E. granulosus* (*Eg*) is the most common cause for human echinococcosis (cystic echinococcosis), while human infection by *Em* is relatively rare but is considered the most serious of the parasitic zoonosis where it occurs (Craig, 2003; Romig, 2003; Romig et al., 2017a). In most cases, the life cycle of *Eg* is solely based on domestic animals. Because of its proximity to humans, cystic echinococcosis can be common in some areas (Romig, 2003). In contrast, a typical life cycle of *Em* involves wild animals. Their typical intermediate hosts are small mammals such as rodents and lagomorphs, and definitive hosts are various fox species and, in the case of North America, coyotes. Their distribution is confined to temperate and cold regions of the northern hemisphere (Deplazes et al., 2017). The presence of the parasite is often correlated with grassland and open agricultural fields because the intermediate hosts are typically grassland species. However, in Hokkaido, Japan, the parasite’s life cycle is completed through small mammal species inhabiting forested areas (Ito et al., 2003; Romig, 2003).

Human infection to *Em* is considered to occur through contamination of food by wild definitive hosts or domestic dogs becoming a definitive host to the parasite. People who work on gardens or farms frequently visited by wild definitive hosts are at increased risk of infection. Domestic dogs can become a definitive host by preying upon infected small mammals, which in turn can infect humans through close contact. There are reports that cats can also become definitive hosts, potentially leading to human infection (Romig, 2003). However, an experimental infection of cats resulted in much smaller number of egg production than dogs and foxes (Kapel et al., 2006). Children’s playground may become contaminated with the eggs of the parasite where wild hosts are present in urban environment (Atkinson et al., 2013b; Vuitton et al., 2003). It is often difficult to define the exact cause of infection because there

is a period of 5 to 15 years between contracting the parasite and the appearance of the symptoms (World Health Organization, 2017).

Although occurrences of AE are rarer than occurrences of cystic echinococcosis, the symptoms of AE are more serious. If a patient with AE is untreated the mortality can be more than 90% within a 10-15 year following infection. Available treatments for the disease are removal of the infected portion of the liver through surgery and medication, though these treatments only prevents relapse and does not cure the patients (Craig, 2003; World Health Organization, 2017). Only in very rare occasion the patients are known to fully recover (Vuitton et al., 2003).

Globally, cases of AE are on the increase in number and in areas (Figure 1; Massolo et al., 2014). The eggs of *Em* are well adapted to cold temperatures while being vulnerable to heat and desiccation (Veit et al., 1995). However, climate change may result in an increase in precipitation and temperature, causing an expansion of the potential host species distribution and increase of the parasites in some regions (Atkinson et al., 2013b). Landscape changes can also have a significant effect on the parasite's host population and distribution. Deforestation and over-grazing are known to cause an increase in the parasite's intermediate host species and in the number of the disease around the world (Atkinson et al., 2013b; Vuitton et al., 2003). Foxes, the definitive hosts of the parasite, are increasing in number and distribution in Europe, most likely due to rabies control program (Vuitton et al., 2003) and also possibly due to the removal of larger predators, availability of anthropogenic food source, and decrease in hunting pressure. The number of countries with infected foxes in Europe has increased from 4 to 21 since 1980 (Geszy et al., 2013). There is also a concern that expanding human settlements and increasing urbanization of the parasite's host species are causing increased exposure of people to the parasites eggs in Europe and Japan (Atkinson et al., 2013b; Vuitton et al., 2003). It should be noted that a similar increase and expansion of foxes and coyotes accompanied with expanding human settlements are observed in North America (Lukasik & Alexander, 2011a).

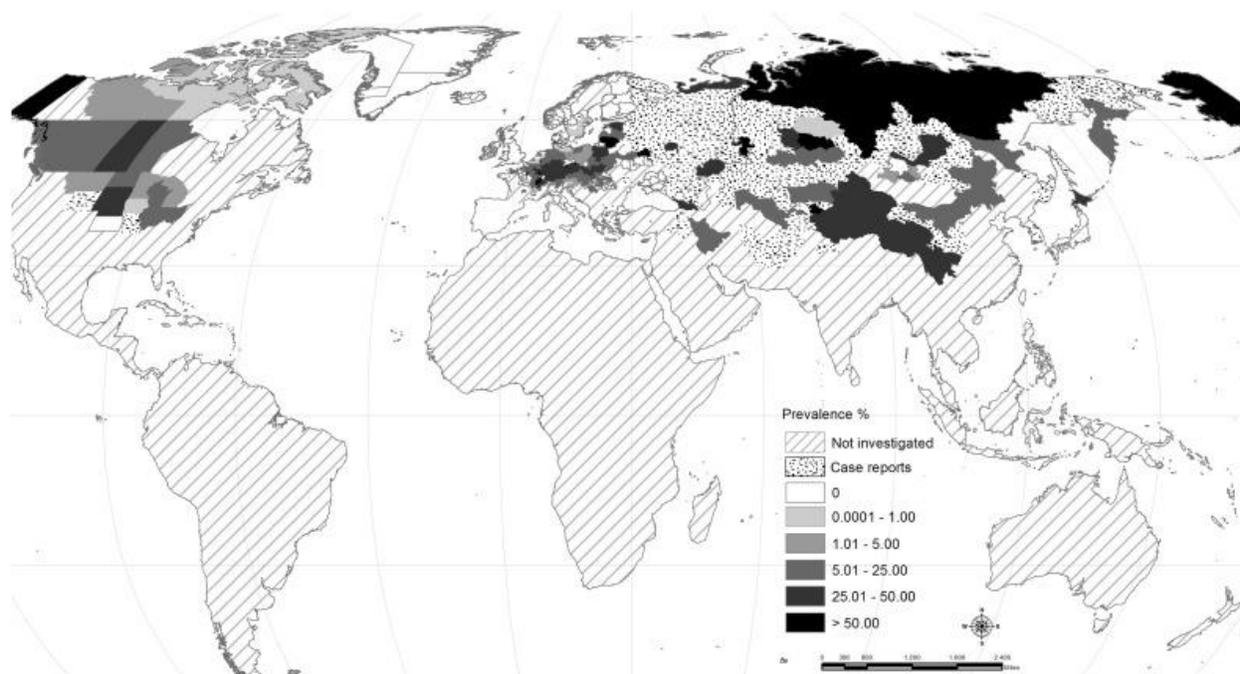


Figure 1. Map showing the global distribution of *Echinococcus multilocularis*. Figure taken from Deplazes et al. (2017)

In central North America, even though *Em* is endemic and prevalent in wild species, prior to 2016 only three cases of AE have been reported that are considered to have local source of infection (Massolo et al., 2014). However, since 2016 six more cases of AE have been identified, indicating a potential increase in the region (Massolo et al., 2019). It was assumed that the reason behind this much lower number of cases of AE in North America is the particular genotype of the parasite of the region being less infectious to people (Vuitton et al., 2003). The recent discovery of European strain of *Em* among wild coyotes and foxes in North America therefore is a grave concern (Geszy et al., 2013; Massolo et al., 2019).

1.2 EPIDEMIOLOGY AND ECOLOGY OF *EM*

The life cycle of *Em* in the context of Calgary is portrayed in the conceptual diagram in Figure 2. It can be mainly divided into three stages: a free-living egg stage, a larval stage in intermediate hosts, and an adult stage in definitive hosts.

1.2.1. THE EGG STAGE

Embryonated eggs of the *Echinococcus* are released into the environment from the definitive hosts along with feces of the hosts. The parasite's eggs are known to survive for 240 to 478 days in the optimal temperature of -18 to 4 °C, with a poor survival rate at temperatures above 25 °C or below -83 °C (Veit et al., 1995). A study of *E.granulosus* found that the eggs survived for 41 months in the field exposed to

environmental conditions of large thermal amplitude (-3 to 37 °C) with warm summers, cold winters, and low precipitation (Atkinson et al., 2013b). Moisture and humidity also affect their survival. Eggs of *Em* suspended in water survived for 2 hours in 65 °C (Federer et al., 2015). Increase in precipitation may wash off the eggs from the field and reduce the infection of intermediate hosts, or may cause an increase in water-borne infection (Atkinson et al., 2013b). No researches have been conducted to compare the survival of eggs between different species or between different strains of *Em* to the best of our knowledge.

It is assumed that eggs released in the environment survive for long periods and accumulate over the winter, leading to high density of eggs in the spring (Eckert et al., 2001). Such accumulation of eggs over winter, along with the snow conditions and small mammal population fluctuations may lead to seasonal differences in infection rate of small mammals. For example, because small mammals typically live under layers of snow during the winter months, the parasite's eggs attached to the feces are unlikely to reach the intermediate hosts during a presence of snow cover unless they were deposited before the snowfall. In addition, in winter, feces are likely frozen and solid, locking in all the eggs. In the spring, small mammals' populations start to increase at the same time the feces breakdown and spread the eggs along with the snowmelt water, becoming accessible to the small mammals. In the summer, small mammals are more numerous and active, and are more likely to come in contact with the eggs under shorter periods of time (Getz et al., 2001).

1.2.2. INTERMEDIATE HOSTS

The intermediate hosts of the *Em* are infected by the parasite through accidental ingestion of the parasite's eggs. Once ingested by the intermediate hosts, the larvae of the parasite (oncospheres) emerge from the eggs in the small intestine of the host and invade the blood vessels. The oncospheres then typically migrate to the liver, though they are known to infect other organs as well (Craig, 2003). In the liver, oncospheres grow into tumor-like vesicles called metacystodes, within which they reproduce asexually. These asexually reproduced individuals are called protoscoleces. In one experimental study, the number of protoscoleces within an infected small mammal has reached 3,700,000 at 142 days after infection (Ishikawa et al., 2003).

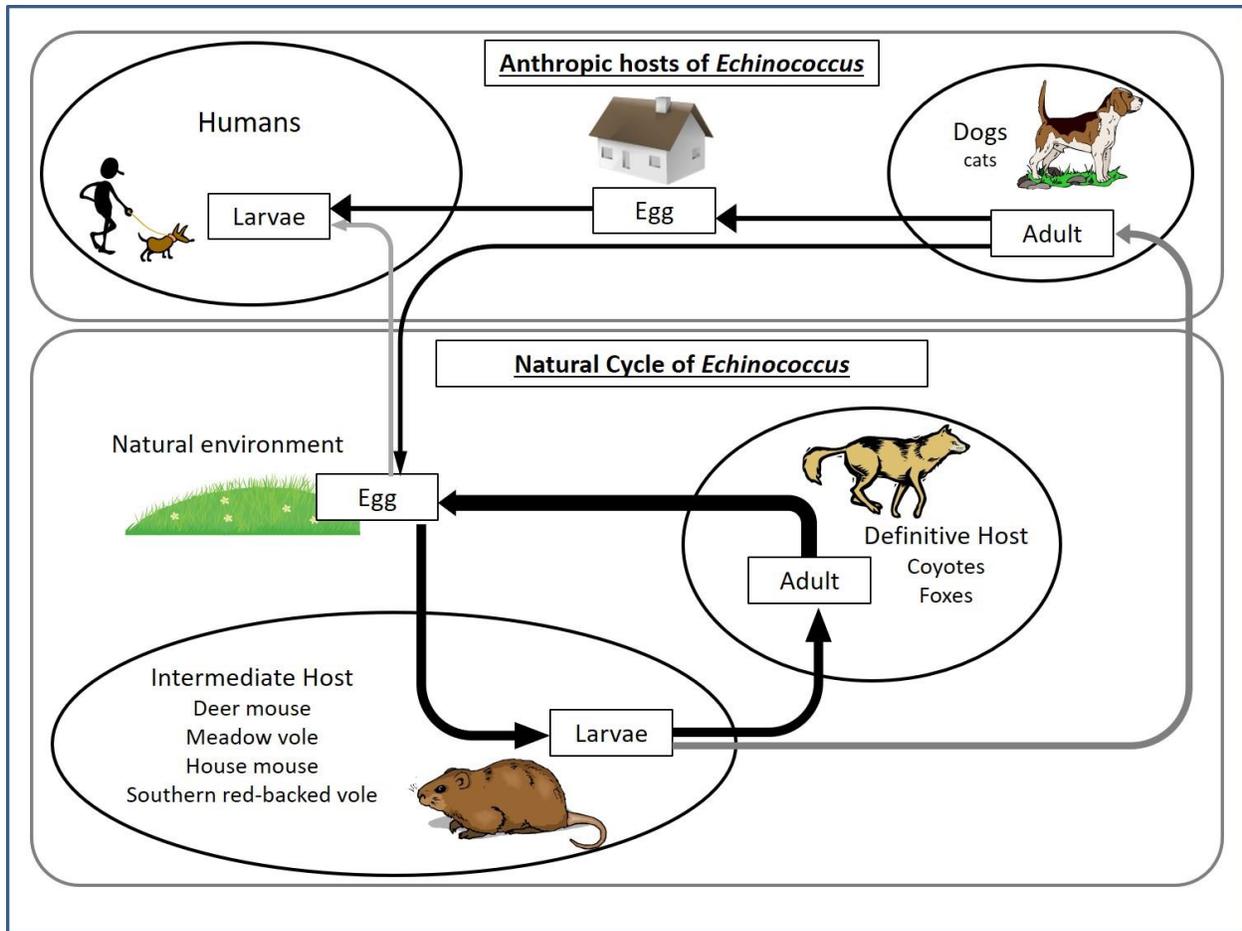


Figure 2. Conceptual diagram of the life cycle of *Echinococcus multilocularis* and its accidental human infection

While *E. granulosus* has less severe effect on the health of its intermediate host, the small mammals infected by *Em* are invariably killed within few months (Romig, 2003). However, in natural settings small mammals have a short life span and high mortality from various causes, while the prevalence of the parasites is generally limited to less than 5% (Craig, 2003). Therefore, it can be assumed that the disease effect on small mammal populations is small. A small mammal infected by *Em* starts producing protoscoleces within two to four months (Craig, 2003; Thompson, 2017). In contrast, it takes 5 to 15 years for the metacestodes to develop in humans, and they often fail to produce protoscoleces, indicating that the parasite did not evolve for continuation of its life cycle, and that human infection is completely accidental (Craig, 2003).

In endemic regions around the world, the prevalence of *Em* among intermediate hosts is very low (less than 5%) even in areas where there is a prevalence of 60% among definitive hosts (Craig, 2003).

However, there are indications that the *Em* manipulates the behavior of IH. In a study in Calgary coyotes, far higher prevalences were detected among small mammals extracted from coyote stomach than those found in the field (unpublished study).

The oncospheres of *Echinococcus* are subject to the host's immune system, and ingestion of an egg by small mammals does not always lead to development of metacestodes (Vuitton & Gottstein, 2010). The immune response is probably one of the main reasons why many species of small mammals that live in the areas of endemic *Em* are never found with metacestodes, and why the development of metacestodes in humans is rare and slow. The probability of infection, or the egg viability, also varies with the conditions to which the eggs are exposed to (Veit et al., 1995).

In areas around Calgary, the known species of intermediate hosts are deer mouse (*Peromyscus maniculatus*), meadow vole (*Microtus pennsylvanicus*), house mouse (*Mus musculus*), and possibly bushy tailed woodrat (*Neotoma cinerea*) though there is no evidence that they inhabit Calgary urban areas (Smith et al., 1993; Vuitton et al., 2003). However, Liccioli et al. (2013) report a southern red-backed vole (*Myodes gapperi*) that was infected and infectious with *Em*; this species may also play an important role in the life cycle of *Em* in North America. Muskrats (*Ondatra zibethicus*) are also known to be intermediate hosts (Bartel et al., 1992).

1.2.3. DEFINITIVE HOSTS

The definitive hosts are infected by the *Em* by preying on an infected intermediate host and ingesting the protoscoleces in their livers. Once the definitive hosts ingest the protoscoleces, the parasites mature into adult tapeworms (cestodes) in 28-35 days in the small intestine of the new hosts (Craig, 2003). The cestodes in turn reproduce sexually, releasing eggs into the environment along with the host's feces. Experimental infection of foxes with *Em* reports the number of eggs to be 27 per worm per day on average, but the number varies over the lifetime of the cestodes (Nishina & Ishikawa, 2008). Heinzmann et al. (2011) state that the number of eggs in feces of infected dogs is not correlated with the number of worms, but do not cite the source of this information.

The cestodes of *Em* live in the definitive hosts for 6 to 12 months (Craig, 2003). The number of the cestodes carried by a single definitive host is highly variable and over-dispersed, from a few to hundreds of thousands. The highest number of worms (infection intensity) found from a survey of urban coyotes in the Calgary and Edmonton areas was 258,888 while the median was 2,188 (Massolo, unpublished data). A similar over-dispersion in intensity was found in foxes of Europe (Guislain et al., 2008; Hofer et al., 2000) and in Japan (Yimam et al., 2002). A definitive host with a greater intensity of infection will consequently release a greater number of eggs into the environment, likely leading to a greater number of

infections to intermediate hosts. Because most worms are found within few individual definitive hosts, it is possible that those few individuals are responsible for most of the transmission of the parasite (Hofer et al., 2000).

The intensity of the infection in a definitive host is determined by the number and frequency of infectious intermediate hosts the animal eats, and the number of protoscoleces in the ingested intermediate hosts (Nishina & Ishikawa, 2008). The number of protoscoleces in the intermediate host is in turn determined by the length of time since it was infected. Definitive hosts' immune systems are also known to react against *Em*, though its significance and quantitative effect on the prevalence and intensity are either unknown or limited (Nishina & Ishikawa, 2008). Some surveys report that sub-adult had significantly greater number of worms than adults (Hofer et al., 2000), while other surveys found no such relationship (Guislain et al., 2008; Yimam et al., 2002). Coyotes infected to clinical mange, a disease that causes hair loss, were found to have a significantly higher prevalence and intensity of *Em* (Massolo, unpublished data).

The definitive hosts can be dewormed with anthelmintic baits, though applications of this treatment on wild hosts have generated mixed results (Nishina & Ishikawa, 2008; World Health Organization, 2017). Unlike the intermediate hosts, definitive hosts infected by the parasite seem to have little health problems. However, there are reports of domestic dogs (typically a definitive host) being infected as intermediate hosts, in which case the health effect is severe (Massolo et al., 2014).

In north-central North America (including areas around Calgary), the natural definitive hosts are coyotes (*Canis latrans*), and possibly foxes (red fox *Vulpes vulpes* and grey foxes *Urocyon cinereoargenteus*; Massolo et al., 2014; Vuitton et al., 2003). Domestic dogs and cats can also become definitive hosts and release eggs into the environment (Massolo et al., 2014; Romig, 2003).

Dogs are known to play a major role as a definitive host in the transmission of *Em* in some communities (Massolo et al., 2014). In the City of Calgary, while the main hosts are coyotes, at least one dog was found to be infected with the parasite with the estimated prevalence of 0.46 % (Massolo et al., 2014). Although the prevalence among the dogs are low, the total number of dogs in the city is far greater than that of coyotes (estimated as 122,325; National Canine Research Council, 2011); an estimated prevalence of 0.46 % means that there is more than 550 dogs that are releasing eggs into the environment. In addition, the movements by dogs are not bound by the same territoriality and movement behavior as coyotes, and can spread the *Em* in ways and over distances that coyotes cannot.

1.3 HOST SPECIES ECOLOGY AND BEHAVIORS

The natural hosts of *Em* also interact with each other and with dogs and people ecologically and behaviorally in various ways besides the transmission of parasites. It is highly conceivable that these interactions influence and complicate the epidemiology of *Em* and their risks to people.

1.3.1 COYOTES

Coyotes are known to be social animals. They form groups called packs, and form territory to be defended against coyotes of other packs (Andelt & Gipson, 1979; Sacks et al., 1999). Typically a pack consists of a breeding pair and their pups, and sometimes extra members that are often pups from previous years or closely related individuals (Hennessy et al., 2012). As other canids, coyotes are known to mark their territories by urines and feces. Coyotes, and particularly the breeding pairs, are known to urinate more often at periphery of their territories and trails they often travel. Compared to urines, feces are less important in marking the territory, deposited in the interior of the territories just as often as the peripheries (Gese & Ruff, 1997). However, feces are still used as territorial markings, and when they are deposited they tend to be along trails and at crossroads (Barja & List, 2014). Coyotes may also consider dogs as territorial rivals, and try to mark their territories along trails that dogs frequent (Lenth et al., 2008). There are also non-territorial, non-breeding individuals known as transients that may travel wide areas (Sacks et al., 1999).

Coyotes are highly omnivorous. Plant materials constitute a fair portion of their diet, and they are known to prey upon ungulates, birds, insects, and domestic animals as well as upon small mammals (Gese et al., 1996a; Lukasik & Alexander, 2011b; Sacks et al., 1999). Grasslands provide better hunting grounds for coyotes than shrubs or forests (Gese et al., 1996b). In Calgary, meadow voles constitute the major portion of the small mammals they eat (Liccioli et al., 2015a).

Coyote behaviors and movements change with season. Andelt and Gipson (1979) divided their yearly activity into six seasons: breeding, gestation, nursing, pup training, adolescence, and pre-breeding. Their home range increases during the adolescence, pre-breeding, and breeding seasons (autumn and winter), while their activity becomes more concentrated around their dens during the gestation, nursing, and pup training seasons (spring and summer, Andelt & Gipson, 1979). Their diet also varies with the season, as the availability of foods including the small mammals fluctuate widely. For instance, snow cover shelters small mammals from predation during winter (Gese et al., 1996b), while deer would be slowed down by the snow and become an easier prey. In addition, the coyote behavior and diet are known to change by the infection to clinical mange. Coyotes infected with mange have larger home ranges, are more active during the day, and rely more on anthropogenic food (Murray et al., 2015b).

In general, coyotes avoid human presence. They are observed to live in proximity to people and utilize manmade trails for movements, but they prefer to remain hidden and become active after sunset. Although coyotes are naturally crepuscular (Andelt & Gipson, 1979), the presence of humans and artificial light sources shift the time of their activity (Ditchkoff et al., 2006). However, some individuals become habituated to human presence and can cause problems (Lukasik & Alexander, 2011a). Presence of dogs may enhance their avoidance response, but they are also known to be attracted by dogs as potential territorial rivals or as preys (Lenth et al., 2008).

1.3.2 INTERMEDIATE HOSTS

The small mammal species of intermediate hosts in Calgary each have habitat preferences that influence their distribution. Meadow voles are known to prefer dense grass covers and moist environments (Iverson & Turner, 1972; Snyder & Best, 1988). Deer mice are known to prefer shrub covers and presence of coarse woody debris (Lee, 2004; Stapp & Van Horne, 1997). Southern red-backed voles tend to prefer shrub and forest covers (Iverson & Turner, 1972). However, many individuals of these species are found outside of their preferred habitat.

Small mammals' presence in a habitat is influenced by various factors besides their preferences. For example, the females of these species are known to become territorial during the breeding season, excluding other females of the same species and other species from their territory. During the winter season, on the other hand, the territoriality disappears, and they congregate into groups to reduce heat loss (Madison, 1980). Iverson and Turner (1972) observed that meadow voles and southern red-backed voles congregate in winter, while they disperse into their preferred habitats during the breeding season.

Small mammals are also known to have highly fluctuating populations, with both seasonal and multi-annual cycles (Hansson & Henttonen, 1988). Many factors are suggested as the cause for the multi-annual population fluctuation, including the corresponding fluctuation of predator populations, food abundance, disease, and weather. Predators specialized at hunting a particular species is hypothesized to increase the fluctuation of the prey population, while a generalist predator will likely reduce the fluctuation (Hansson & Henttonen, 1988). In Calgary urban areas, the primary predator to the intermediate hosts is the coyote, which is known to be a generalist predator, and likely to be a stabilizing factor of the population of intermediate hosts population. Heisler et al. (2014) suggest that weather, and particularly snow depth during the winter, could be an important factor in causing the population fluctuation. Snow cover provides small mammals both insulation from cold air and shelter against predators, allowing the small mammals to conserve energy and quickly reproduce in the following breeding season. When the population is at its peak, the preferred habitats are occupied by strong individuals, while weaker

individuals are chased out into less preferred habitats. In such situations, the less preferred habitats would have higher population densities, while the preferred habitats tend to have relatively constant population densities.

When the population density is high, the chance of transmission of *Em* to intermediate hosts and therefore the density of infected intermediate hosts may increase. However at the same time the chance of the transmission from intermediate hosts to definitive hosts may decrease from the dilution effect (Randolph & Dobson, 2012). However, it is possible that coyotes will preferably hunt species with higher density, counteracting the dilution effect.

The small mammal distribution is also highly influenced by the presence of predators. Experiments have shown that they are less active at edge habitats on nights when the moon light is bright (Bowers & Dooley, 1993). In urban environments, densities of small mammals have been observed to be negatively impacted by the presence of cats (Baker et al., 2003). Small mammals avoid mowed grass (Bowers & Dooley, 1993). Preliminary sampling of mowed grass area in Calgary has failed to capture any small mammals except for a single shrew in 600 trap-nights (Unpublished data). They are also known to avoid trails frequented by dogs (Lenth et al., 2008).

While house mice (*Mus musculus*) are also known to be an intermediate host species of *Em*, they are rarely observed in natural areas (Liccioli et al., 2014).

1.4. COYOTES AND *EM* IN THE CITY OF CALGARY

The studies on urban coyotes were initiated after two coyote incidents with children occurred in the City of Calgary in 2005 (Canada Broad Casting News, 2005). Citizen reports of incidents with coyotes from January 2005 to August 2008 were gathered to assess the frequency and seriousness of the incidents and conflicts occurring between the city residents and coyotes (Lukasik & Alexander, 2011a). In addition, their feces were collected for dietary analysis to assess how much anthropogenic food was included (Lukasik & Alexander, 2011b). The occurrences of coyote-resident conflicts and the presence of anthropogenic food in the feces were assessed for spatial correlation (Lukasik & Alexander, 2011b). It was found that serious incidents between coyotes and residents were rare, and anthropogenic food takes up a small portion of coyote's diet. Both occurrences of conflicts and anthropogenic food tend to be more frequent close to the city center and in small parks. Conflicts were more frequent during the breeding season (January to April) while the occurrence of anthropogenic food was more frequent during the dispersal season (September to December, Lukasik & Alexander, 2011a; Lukasik & Alexander, 2011b).

In 2009, the Calgary Urban Coyote Project (A.Massolo, <http://vet.ucalgary.ca/coyote/>) was initiated to study the coyotes in Calgary urban areas in cooperation with the City of Calgary. Two coyotes were captured and harnessed with a GPS collar to assess their spatial movements and behaviors in the urban environment. One collar stopped functioning after few months while the other remained functional for more than a year. The collected data were used to develop a coyote habitat connectivity map of the city landscape (Lamy, 2015). However, because the coyote traps raised concerns among dog owners after a dog was caught accidentally, the study was terminated. In addition, several coyote dens in the city were located and monitored to collect data of the coyote reproduction (unpublished data).

Through the studies of coyotes in the City of Calgary, concerns were raised that they host parasites that may be transmitted to domestic animals or to humans. In response to this concern, a study on the gastrointestinal parasites hosted by coyotes in the city was conducted (Watts & Alexander, 2011). Coyote feces were collected in the Calgary city parks and rural areas surrounding the city from July 2009 to June 2010. Gastrointestinal parasites were identified and their diversity was used as indicators of the coyote's exposure to the parasites. The study identified 15 species or genus of parasites in total and found that the parasite diversity was highly variable between geographic areas. Rural areas tended to have a higher number of species of parasites. Watts and Alexander (2011) suggest that rural areas have a greater variety of parasite hosts as prey, while within the city, limitation of natural prey and availability of anthropogenic food may reduce the coyote's exposure to parasites. However, some urban areas had just as many parasite species as the rural areas. Watts and Alexander (2011) suggested that the interactions amongst the coyotes due to the presence of riparian travel routes and concentration of food sources, and in some areas domestic dogs, could have introduced more parasites (Watts & Alexander, 2011).

Watts and Alexander (2011) focused on investigating the diversity of parasite species, and therefore did not identify *Em* at the species level. Instead, they used a category *Taenia*-like species that can include the genus *Echinococcus* and other tapeworm species, partially because they are difficult to distinguish from each other at the egg stage in the feces. Catalano et al. (2012) conducted a targeted study of *Em* among coyotes in Calgary and Edmonton area. They studied the intestines of hunted or road-killed coyotes from urban and surrounding areas of Calgary and Edmonton from October 2009 to July 2011. They discovered *Em* to be highly prevalent among coyotes in those areas. The overall prevalence was found to be 23% (23 out of 91). The Edmonton areas have a higher prevalence (62.5%, n=7) than the Calgary area (20.5%, n=83). In the Calgary area, a higher prevalence was found in rural fringes (27.3%, n=33) compared to urban areas (14.8%, n=27). Male coyotes have a higher prevalence (34.19%, n=44) than females (15.2%, n=46). The number of worms (intensity) has a highly skewed distribution, ranging from 4 to 258,888 with a median of 2036 (unpublished data).

Reflecting the public health concern raised by Catalano et al. (2012) and Liccioli et al. (2012), an additional study was conducted on the wild hosts of *Em* inhabiting urban parks in the City of Calgary to investigate the spatiotemporal patterns of the parasite infections in both coyotes and the intermediate hosts and assess the association of these patterns with small mammal assemblages (Liccioli et al., 2014). The study was conducted in Nose Hill Park (NHP), Bowmont (BM), Weaselhead (WSH), Southland lowlands (SL), and Fish Creek Provincial Park (FCPP,

Figure 3). In these five parks, small mammals were trapped from June 2012 to July 2013, mostly using Woodstream Museum Special Traps placed in rectangular grids of 200 traps set at regular intervals of 7 to 10m. Traps were checked and reset every morning for three days, generating the maximum trapping efforts of 600 trap-nights. Caught small mammals were necropsied for the presence of *Em* cysts (Liccioli et al., 2014). In addition, coyote feces were collected in the same parks along the trails. The feces were inspected for the presence of *Em* eggs, and the constitution of the coyotes' diets (Liccioli et al., 2015a; Liccioli et al., 2014).

With the above trapping scheme, 982 small mammals were caught. *Em* was detected among deer mice (2/305), meadow voles (2/267), and southern red-backed voles (1/71). BM had the highest estimate of prevalence (2.13%), followed by NHP (1.22%) and SL (1.06%). No small mammals with cysts were found in WSH and FCPP. The estimated prevalence by season was highest in winter (December to February, 3.33%), followed by autumn (September to November, 0.68%), summer (June to August, 0.46%), while no cysts were found in spring (March to May). Due to the small number of cases with cysts, the differences in the estimated prevalence between sites and seasons were not statistically significant (Liccioli et al., 2014).

In addition to the trapping of small mammals, 385 coyote feces were collected; 95 (21.42%) of them were found containing *Em* eggs. The fecal prevalence was significantly higher in BM (63.07%), with no significant differences detected among the other four parks (NHP = 17.28%, FCPP = 6.23%, WSH = 6.22%, SL = 5.42%). The fecal prevalence was the highest in spring (43.47%), followed by autumn (21.8%), winter (19.4%), and summer (10.52%). Fecal prevalence in spring was significantly higher than the other three seasons (Liccioli et al., 2014).

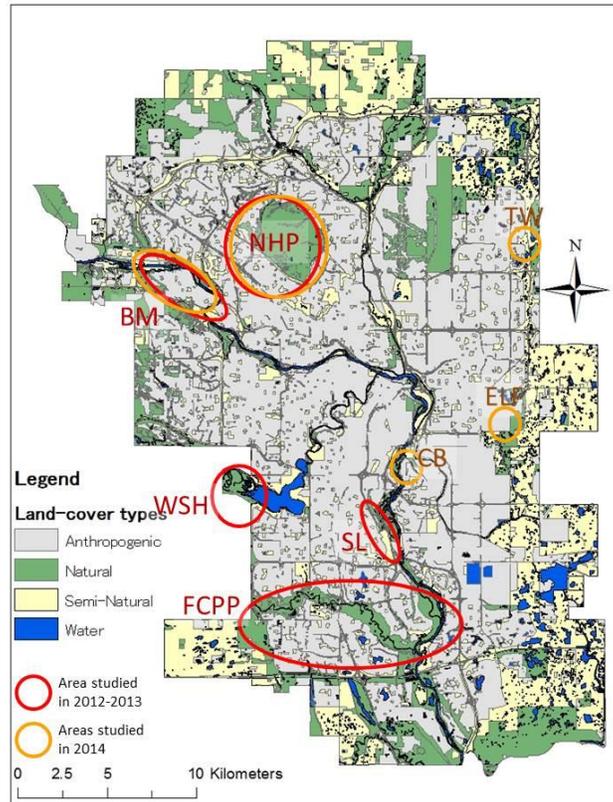


Figure 3. Location of the studies of small mammals conducted in the City of Calgary.

The coyote feces were further analyzed for genotyping to account for the multiple sampling of the same individual coyotes. From the total of 425 feces, 33.4% were successfully genotyped to 60 individual coyotes (NHP = 15, BM = 17, WSH = 13, SL = 5, FCPP = 11). When the genotypes were accounted for, the prevalence of *Em* among coyotes in the City of Calgary was 25%, similar to prior estimates. The rate of coyotes becoming re-infected with the parasite was estimated to be 57.1% (Liccioli et al., 2015a).

Liccioli et al. (2014) suggested that the proportion of susceptible small mammals may be the key factor determining the prevalence of *Em* among coyotes. BM had the highest proportion of susceptible species of intermediate hosts caught (0.77) while SL had the lowest (0.36), though the overall capture rate was not significantly different between the areas. The proportion of adult small mammals was higher in winter (0.99) and spring (0.95), and lower in summer (0.77) and autumn (0.76).

Small mammals were found most frequently in coyotes' diet (found in 57.15% of the feces), followed by hares (20.6%) and deer (17.5%). Fruits (52.8%) and plant materials (81%) were found in most of the

coyotes' feces, but often only in small amounts. Small mammals were found in feces most often in summer (65.1%) and the least in winter (39.4%), while deer was found most often in winter and the least in spring and hares were most often found in spring and the least in summer (Liccioli et al., 2015b).

Among the small mammals consumed, meadow voles constitute the largest portion, occurring in feces more than expected from their availability estimated from the trapping. Deer mice were consumed significantly less than expected. The proportion of each species consumed by a coyote varied across a season, such that the proportion of susceptible small mammals consumed were highest in winter. Combined with the estimated prevalence of *Em* by season (Liccioli et al., 2014), the estimated probability of infection of coyotes by the parasite was found to be highest in winter (Liccioli et al., 2015a).

Another study of the small mammals in the urban parks of the City of Calgary was initiated in June 2014 with the objective of assessing the temporal patterns of *Em* infection over multiple years. The study included three new parks and natural areas in addition to BM and NHP: a natural area between Taradale and Stoney Trail NE and the neighboring Tarrington Woods Park (TW), Carburn Park and Quarry Park (CB), and natural areas in the East Landfill (ELF,

Figure 3). Unfortunately, the study was paused unexpectedly at the end of July 2014 due to some changes in the policy on the trapping of wild animals in the parks.

In the two months period of June-July 2014, 288 small mammals were caught and necropsied. The prevalence of *Em* estimated from this study was higher than in the previous study, resulting in 2.93 % (6/205) among meadow voles and 1.22% (1/82) among deer mice. It was again highest in BM (2.63%, 5/190). All the caught small mammals were susceptible to *Em*.

The collected field data consistently indicated a higher prevalence of *Em* in BM, both for intermediate hosts and for coyotes. Similar clustering of the parasite is found in studies around the world, indicating that the spatial heterogeneity in the prevalence of the parasite hosts appears to be a characteristic of the parasite (Hansen et al., 2004; Liccioli et al., 2014). Liccioli et al. (2014) inferred that the reason for the higher prevalence in BM is due to the assemblages of intermediate hosts. However, the inference was made from samples of small mammals trapped at three representative habitats of the park; they did not account for the proportion of each habitat types in the park, and the resulting differences in the overall availability of the small mammal assemblages. The samples from 2012-2013 were also limited to five parks that are located on the western side of the city, and did not capture the pattern of the overall prevalence in the city. It also did not account for the coyote preference on prey species and hunting grounds. Other factors in the park may facilitate the transmission of the parasites. The park is a relatively

narrowly shaped natural area along the Bow River located close to the rural fringe of the city, with a rather high concentration of trails used by people, bikes, and dogs as well as coyotes. The concentration of trails may lead to a concentration of fecal markings by coyotes. Riparian habitats are likely used by transient coyotes to travel through, leading to a greater exposure for the resident coyotes to pathogens and parasites. The park includes areas with relatively poor drainage, offering favorable environment for the parasite's eggs to survive. Although these factors are not unique to BM, combined with the complex behavior of coyotes and the stochastic process of parasite transmission may lead to the observed spatial heterogeneity in the prevalence of the parasite among the host species.

1.5. NEED FOR FURTHER STUDIES TO UNDERSTAND THE TRANSMISSION OF *EM*

The natural reservoir of *Em* among wildlife makes the parasite impossible to eradicate (Ito et al., 2003). There is currently no human vaccine available, and the detection of the disease without an expensive screening is difficult until it is used at an advanced stage (Atkinson et al., 2013b). Available treatments are both expensive and ineffective, often leading to either lifelong treatments or mortality (Craig, 2003). Although there have been few reported cases in interior North America historically, there has been increase in the reported cases since 2016 and many indications of emergence in North America (Massolo et al., 2019; Massolo et al., 2014). Before any public health actions against the parasites can be taken, its epidemiology and transmission dynamics must be understood, especially in an urban setting where large numbers of people are potentially at risk. The natural reservoir of *Em* among wildlife also makes the parasite very difficult to study. The transmission of *Em* is a highly complex process involving the interactions of numerous factors. Field studies alone cannot determine how the observed spatial pattern of prevalence developed. In order to understand its epidemiology among wildlife, a model is needed.

To understand the epidemiology of *Em*, a spatially-explicit agent-based model (ABM) is proposed. ABM is a process-based model that simulates the behavior and interactions of each individual referred to as agents. ABM is suited for modeling a system where complex interactions of individuals can significantly influence the whole system. ABM is spatially-explicit, and simulates movements of animals through complex landscapes. Because of its properties, ABMs have been used in numerous studies of systems similar to the system of our interest (Conner et al., 2008; Hansen et al., 2004; Heinzmann et al., 2011; Jiang et al., 2012; Nishina & Ishikawa, 2008; Nunn et al., 2011; Pitt et al., 2003).

1.6. THESIS RESEARCH OBJECTIVES

The overarching objective of this study is to understand the processes and mechanisms that produce the observed patterns in the transmission of *Em* using the system of the parasites and the host wildlife in the City of Calgary as a case study. Observed patterns such as spatial and temporal heterogeneity in the

prevalence of the parasites and heterogeneity in the intensity of the parasite infection among individual definitive hosts are difficult if not impossible to be understood with the use of traditional epidemiological models. An ABM that simulates coyote and small mammal habitat use, movements and interactions will be developed to test hypotheses about the parasite transmission that may explain the observed patterns of the parasite.

We formulate three hypotheses to explain the observed patterns of *Em* among host species.

1. The first hypothesis (referred to as the *intermediate host hypothesis*) is that the patterns are caused by the differences in the intermediate host assemblages. A small mammal assemblages that have higher proportion of susceptible hosts would facilitate the transmission of *Em*, as suggested by Liccioli et al. (2014). The intermediate host assemblages and their spatial distribution are in turn determined by processes occurring at the spatial scale of small mammal home range, or approximately 100~300m (Madison, 1980).
2. The second hypothesis (referred to as the *definitive host hypothesis*) is that the behavior such as habitat preference, prey selection, and territorial markings of definitive hosts cause the observed patterns. In order for *Em* to complete its life cycle, it is required that the habitats of susceptible intermediate hosts must overlap or occur in proximity of where the definitive hosts defecate and hunt (Guislain et al., 2008). The behavior of definitive hosts (coyotes) is in turn determined by various processes such as their territoriality, seasonality, and availability of habitats within their home ranges, occurring at the spatial scale of coyote home ranges over several kilometers (Harrison & Gilbert, 1985). With this hypothesis, it is predicted that two areas with similar small mammal assemblages will still have different patterns in the transmission of the parasite.
3. The third hypothesis (referred to as *meta-population hypothesis*) is that the patterns are caused by social grouping and territoriality of coyotes. Each coyote pack can act like an “island” for the parasites (Nunn et al., 2011). The parasites can be transmitted within a pack easily, but transmission between packs is limited, leading to a high prevalence in areas with infected packs, but a low prevalence in areas where the parasite is not established. The overall pattern is determined by the rate of infection relative to the rate of local extinction of the parasite in each pack, like a meta-population system. In a city landscape, the patterns of the parasite transmission is then determined by the proximity and connectivity of the parks and natural areas that form the coyote habitat at the spatial scale of the entire city.

Understanding the processes and mechanisms behind the observed patterns of *Em* among its host species will provide key insights on how the parasites may be managed or the risks from the parasites may be controlled. The knowledge of the key mechanisms and processes that cause the patterns in the parasite

transmission may open possibilities for effective management of the parasite. It will allow the prediction of “hotspots” or “super-spreaders” that are disproportionately important in the transmission of the parasite, allowing public health workers to monitor or apply anthelmintic baits more effectively.

CH 2: REVIEWS ON MODELING THE TRANSMISSION OF *ECHINOCOCCUS MULTILOCULARIS*:

The natural reservoir of the *Echinococcus multilocularis* (*Em*) among wildlife makes the parasite very difficult to eradicate or control effectively. The specific requirements for hosts by the parasite and complex ecological interactions among species can cause unintended results to an intervention. While we can prepare the medical and veterinary facilities against the parasite, because of the rarity of alveolar echinococcosis (AE) and their severe treatment, unplanned preparation against the disease by the medical facilities would be costly and inefficient (Ito et al., 2003).

In order to control the risks of AE effectively, it is essential to understand the mechanisms and processes of *Em* transmission and how they produce the patterns at the community and population levels. Many studies *Em* in the past conducted experiments at individual levels to decipher the mechanisms of the development of the parasites (e.g. see Veit et al., 1995). Many studies observed patterns of *Em* at community/population levels, such as prevalence and their association with other factors (e.g. see Liccioli et al., 2014). However, connecting these studies conducted at different organizational levels and spatial scales are practically impossible without using an epidemiological model.

Reflecting the needs for efficient and effective control of *Em*, several models have been developed by researchers around the world. These models can be broadly categorized into several categories:

statistical models, compartmental models, network models, and agent/individual based models (ABMs). The characteristics of each category of these models are summarized in [Error! Reference source not found.](#)

In this chapter, the models applied to *Em* or similar epidemiological systems are reviewed, outlining the pros and cons of each modelling approach. The features of *Em* epidemiological systems that needs to be explicitly represented in the model for our purposes are described. Finally, the modelling approach for this study is proposed.

2.1 STATISTICAL MODELS

Table 1. Summary of the types of epidemiological models applicable to the epidemiology of *Echinococcus multilocularis*.

Statistical models rely on statistical correlations between occurrences of AE with various factors, such as

<u>Model type</u>	<u>Characteristics</u>	<u>Advantages</u>	<u>Limitations</u>	<u>Examples</u>
Statistical Model	<ul style="list-style-type: none"> Statistical correlation of the disease occurrence with various factors 	<ul style="list-style-type: none"> Simple statistics No need for detailed understanding of the transmission process Model outputs are easy to interpret 	<ul style="list-style-type: none"> Requires extensive data Often difficult to develop the model for fine spatial resolution Cannot be used for extrapolation 	<p>Giraudoux et al. (2013)</p> <p>Danson et al. (2006)</p>
Compartmental Model	<ul style="list-style-type: none"> Process-based Processes at population level Usually concerned with temporal pattern of the disease 	<ul style="list-style-type: none"> Can be developed without local data Can be analyzed mathematically 	<ul style="list-style-type: none"> Spatial components difficult to be included Assumes large population that mix evenly Potential errors on parameters and bias on selection of factors 	Ishikawa et al. (2003)
Network Model	<ul style="list-style-type: none"> Process-based model Systems described into nodes and edges 	<ul style="list-style-type: none"> Able to represent complex structure and relationships 	<ul style="list-style-type: none"> The structure must be known to build a model Model outputs can be difficult to interpret Uncertainties in model building Computationally demanding 	N/A
Agent-based Model	<ul style="list-style-type: none"> Process-based model Individual level Complex model Usually stochastic 	<ul style="list-style-type: none"> Highly flexible Able to represent spatial and individual variations Intuitive structure of the model Can be modelled with spatial processes with various scales 	<ul style="list-style-type: none"> Model outputs can be difficult to interpret Large uncertainties Computationally demanding 	<p>Nishina and Ishikawa (2008)</p> <p>Heinzmann et al. (2011)</p> <p>Jiang et al. (2012)</p> <p>Lane-deGraaf et al. (2013)</p>

land cover or the life style of people. Several statistical models have been developed for China (e.g. see Danson et al., 2006; Giraudoux et al., 2013) where the AE is most frequent, but also in Europe and central Asia (e.g. see Miterpáková et al., 2006; Tolnai et al., 2013). These models are generally aimed at identifying people or areas at high risk of the disease. Many of them use spatial data as predictors and

produce maps of the gradient of infection risks. The findings from these models can guide policy makers in concentrating the resources and efforts for medical services at areas of high risk, or change the policy to prevent the disease.

One of the most often studied factors for predicting the occurrence of AE is the land cover. The life cycle of *Em* depends on the presence of wild hosts, and the land cover that can be used to predict the presence of host species can also be used to predict the occurrence of the disease. Particularly, the land cover of the past 5-20 years (general latent periods of AE in human body) was found to be important predictors of the disease (Giraudoux et al., 2013). Other predictors often used in these models are climates and people's life styles. Climate can influence the survival of the parasite's eggs in the environment as well as the presence of the host species, and are known to be correlated to the frequencies of the disease. Farmers can be at higher risk of infection to the disease because they work with the soils that are contaminated with the eggs of the parasites. People who own free ranging dogs, for herding livestock for example, are also known to be at higher risk of the infection (Giraudoux et al., 2013). The method of kriging has also been used for modelling the risk of the infection (Danson et al., 2006; Giraudoux et al., 2013).

These statistical models have advantages over other kinds of models. First, statistical models are based on simple statistical relationships and require no understanding of the causal relationships between the predictors and the occurrence of *Em*. The statistical models also produce results that are easy to interpret. A map indicating the regions of high risk of AE is easily understandable for people who have little knowledge of the biology or the epidemiology.

However, the statistical models have limitations. First, they require accurate and extensive medical records of *Em* presence or patients with AE to produce valid results. In regions of the world where no such records exist, no statistical relationships can be established. For example, in the endemic regions of interior North America AE was traditionally considered very rare with only two reported cases of AE , but since 2016 six new cases were reported, suggesting either a recent emergence or frequent misdiagnosis and lacks comprehensive data (Massolo et al., 2019; Massolo et al., 2014). The spatial resolution of the data is also an issue. Because it would be impossible to identify the exact occasion of the acquisition of the disease with several years of latent periods, the medical record of the patients may not be able to identify the specific location where the patients have contracted the disease (Danson et al., 2006). Similarly, the presence of intermediate hosts to the *Em* can be predicted at the landscape level using land-cover data, but at finer resolution their presence is often patchy and depend on microhabitats that are too small to be identified on land-cover maps (Danson et al., 2006).

Second, the statistical models cannot be used for prediction or extrapolation. The statistical models rely on past data, and cannot make predictions on situations where no data exists (Cuddington et al., 2013). It cannot make prediction of “what-if” scenarios such as application of anthelmintic baits to remove *Em* from definitive hosts (Ishikawa et al., 2003).

2.2 COMPARTMENTAL MODELS

Compartmental models or mathematical models have been used in epidemiology for a long time (Anderson & May, 1982). These models represent the transmission and spread of a disease mathematically. These models are often also called process-based (or mechanistic) models because they are built upon the processes and mechanisms underlying the system and phenomenon.

While most studies using statistical models are concerned with the spatial pattern of *Em*, studies using compartmental models are typically concerned with temporal patterns of the disease and its influence on the population size. The compartmental models generally assume that there is a distinct population that mixes uniformly and with little or no migration with other population. The populations are then divided into groups or compartments, such as infected or susceptible, and their interactions or transfers from one compartment to another are represented as mathematical equations that represent the aggregates of all the individual interactions as sum of averages. The model results can show how quickly the infection spreads through a population, whether the disease will remain as epidemic or eventually disappear, and whether the disease will drive the population to an extinction or to an equilibrium.

One of the most classic mathematical models in epidemiology is called SIR model, where a population is divided into three classes of “susceptible (S),” “infected (I),” and “recovered (R)” (Figure 4; Anderson & May, 1982). The model assumes the rate of contacts, and therefore the rate of infection, simply depends on the number/proportion of S and I, while the certain portion of I cures from disease and turn into R, and R loses immunity and becomes S at a constant rate. The SIR model is often utilized for estimating the number of vaccines to be distributed to the population to reduce the infection rate to below a certain level, or estimating the stability of a wildlife population with an infectious disease (Anderson & May, 1982). Although the model can be arranged to accommodate more complex systems, the SIR model generally assumes a case of simple, directly-transmitted infectious disease in a single, homogeneously mixing population.

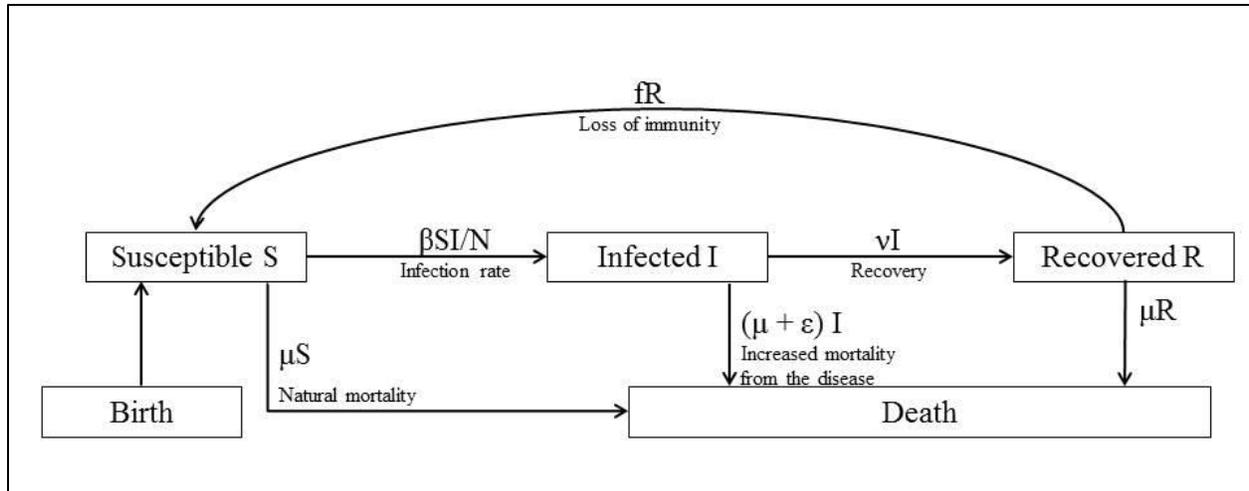


Figure 4. Conceptual diagram of a typical SIR model with population dynamics and loss of immunity.

In the case of echinococcosis, the transmission is indirect and involves a complex life cycle and transmission mechanisms, making compartmental model difficult to be applied. However, there have been several studies that attempt to model the epidemiology of echinococcosis mathematically. Ishikawa et al. (2003) developed an extended version of the SIR model to study the transmission of *Em* among foxes (*Vulpes vulpes*) and gray-sided voles (*Clethrionomys rufocanus*) in Hokkaido, Japan. In the model, foxes were divided into “susceptible,” “infected but not infectious,” “infectious,” and “infectious with low egg production” while the voles were divided into “susceptible,” “infected but not infectious,” and “infectious.” The “infected” were divided into “infected but not infectious” and “infectious” to simulate the period between the contraction of the disease and the production of the eggs or the protoscoleces by the parasite, while “infectious with low egg production” was added to simulate the known reduction in egg production of the parasites in definitive hosts after some time. The “Recovered” class was not in the model because voles do not recover from the disease; foxes recover from the disease and but becomes “susceptible” again because the immunity was difficult to quantify.

Further details were incorporated in the model of Ishikawa et al. (2003). The foxes were divided into juveniles and adults while the voles were divided into five age groups to take into account the different survival rates of each age group. Reflecting the complexities of the *Em* epidemiology in the model, the susceptible foxes were infected by infectious voles, and susceptible voles were infected by infectious foxes. The rate of infection of the foxes depended on the number of susceptible foxes and the number of infectious voles, while the rate of infection of the voles depended on the number of susceptible voles and infectious foxes. The infection rate of the voles also depended on the longevity of the eggs of *Em* in the environment, which was calculated based on the temperature. The model also calculated the seasonal

population dynamics of voles and foxes, based on breeding season for foxes, and seasonally different birth rates and breeding rates for the voles.

The models such as the one by Ishikawa et al. (2003) have advantages over the statistical or agent/individual based models in several aspects. The compartmental model can be developed qualitatively without quantitative data. Data are required to set the model parameters such as the infection rate, as well as to validate the model results. However, frequently in wildlife studies detailed quantitative data are difficult to obtain and the only available information may be qualitative. In those situations, compartmental models can still be developed as an experimental model and test range of plausible parameters. The parameters can often be derived from reasonable assumptions. While a model developed without enough data cannot provide reliable predictions, such a model would still be useful for pattern analysis.

Compartmental models are fairly flexible. They can incorporate factors that influence the process with relative ease. The models can be also be used to make simulations of various scenarios. For example, deworming of foxes (changing Infectious into Susceptible) can be implemented in the model by Ishikawa et al. (2003) to see how much effect such intervention has. The results of such simulations can be used to advise policy makers in selecting the effective or efficient methods of control of the parasite.

A major limitation of compartmental models compared to the statistical or individual/agent-based models is the difficulty they have in representing the spatial component. Most compartmental models assume a population that inhabits a uniform landscape, and any parts of that population have on average the same density of the hosts and prevalence of the parasite as everywhere else in the population. However, such landscapes do not exist in reality. Space plays an important role in any process including the transmission of disease. Diseases are more likely to be transmitted between individuals that are near each other than those that are far from each other. Simple proportion of infected and susceptible individuals cannot predict transmission rate if the infected are close to each other and far from the susceptible. In many wildlife hosts, the habitable areas are often mingled with non-habitable areas, and the movement of hosts are restricted by various barriers such as rivers, roads and other man-made structures. The compartmental models also have difficulty incorporating movement and behavior patterns of the host species. Wildlife hosts behaviors often determine their interactions with each other, such as territorialities, and yet compartmental models assume homogenous population with and equal interaction, and any individual difference would average out.

Compared to the statistical models, the process-based models make far more parameter estimates. While there are several methods for making the estimates, they are not perfect and contain uncertainties. As the

models become more explicit and detailed, the number of estimates and the uncertainties in the estimates accumulate, reducing the confidence in the predictions of the model. The models with uncertainties are still useful for pattern analysis, but interpreting the results will be less intuitive and more difficult.

Including every factor and process into the model would be impossible. Therefore in the process-based models, the model developers must select factors and processes to be included in the model for the purpose of the model. There is always a possibility that the model is missing a key factor.

2.3 COMPLEX MODELS

While compartmental models are useful in understanding epidemiological systems, they can be overly simple and miss many of the complexities that are inherent in the system (Lanzas & Chen, 2015). The assumption of homogenous population that interact with every other individual can miss important patterns in the interactions among the individuals that determine the transmission (Duan et al., 2015). For addressing the complexities in the systems, models like network models and agent-based models has been used in epidemiology (Craft & Caillaud, 2011; Duan et al., 2015; Lanzas & Chen, 2015). These models can represent more realistic and detailed mechanisms and processes of epidemiological systems, spatial aspects, and population structure. In return, the results of these models are difficult to analyze, and typically requiring multiple simulations to learn about the systems, in turn requiring computation powers (Lanzas & Chen, 2015).

Network models are models that represent system as networks of nodes and edges, where nodes represent entities or components of the systems and the edges represent the interactions and relationships between nodes (Craft & Caillaud, 2011). While this type of modeling can represent more realistic and complex epidemiological contact patterns, these models must be built upon known contact patterns, and therefore cannot be built on systems where the structures of transmission is unknown or is itself a question. Perhaps because of this, to the best of my knowledge no study has been conducted on the *Em* or similar epidemiological systems using a network model. Therefore, I will not delve into network models further here, and review the agent-based models.

2.3.1 AGENT-BASED MODELS

Individual-based or agent-based models (ABM) are also process-based models like mathematical models. While a typical compartmental model would describe process as a sum of the entire population, the individual or agent-based model would describe the processes and interactions of each individual in the population. Similar to compartmental models, the ABMs capture the temporal patterns. At a given time

step, the ABM would model activities of each individual agent and become infected by the disease, recover from the disease, or remain susceptible. Unlike compartmental models, ABMs can capture spatial patterns easily. Agent-Based Models that explicitly represent spatial components are called spatially-explicit ABM. In most ABMs, because many of the processes of each individual are probabilistic, a model with the same set of parameters does not lead to the same results. While most of the compartmental models are called deterministic because a model always leads to a single result, these probabilistic models are called stochastic. Because the model results are not always the same, studies using ABMs typically repeat several simulations and use the distribution of results for analysis.

Nishina and Ishikawa (2008) developed an ABM largely based on the previous work of Ishikawa et al. (2003), to model the transmission of *Em* in Hokkaido, Japan. Each individual fox was modelled with probabilities of survival, reproduction, and infection. Voles and the parasites in the environment (eggs) in the intermediate hosts were modelled deterministically. The number of worms within each fox was also modelled deterministically, though the number of foxes that carry the worms was stochastic. The model was not spatially-explicit and assumed a uniform landscape where every fox in the population has equal chance of preying on every vole in the landscape. Nishina and Ishikawa (2008) used the model to experiment on the distribution of anthelmintic baits that would remove worms from foxes, and determined that the application of the baits had little effect in winter and most strong effect on early summer.

Heinzmann et al. (2011) developed an ABM of *Echinococcus granulosus* transmissions between domestic dogs and sheeps in Kazakhstan. In the model, infection and survival of each individual dog and sheep were modelled stochastically. Unlike the wild population of foxes and voles modeled by Nishina and Ishikawa (2008), Heinzmann et al. (2011) assumed the population size of the domestic dogs and sheep constant, and any death of an individual was associated with the reproduction of a new individual. When an infectious sheep dies, it has certain probability of infecting one dog in the population. An individual sheep has a chance of being infected based on the prevalence of infection among the dogs. The parasites were not modelled individually, but the development and recovery of disease were modelled stochastically. The model was also not spatially-explicit, and an infectious sheep had equal chance of infecting every dog in the model. Heinzmann et al. (2011) used the model to determine how quickly the parasites can be removed from the population by the use of anti-parasitic drug on dogs every 6 weeks.

Jiang et al. (2012) created an agent-based model of the transmission of *Toxoplasma gondii*, a parasite with a complex life cycle that generally requires two different species of hosts for the completion of its life cycle similar to the *Echinococcus*, between cats and mice in a farm. In the model, survival, reproduction,

infection, and movement of each individual cats and mice were modelled stochastically. The model by Jiang et al. (2012) was spatially-explicit, and the locations and movements of each individual cats and mice were modeled explicitly. A cat in the model could only prey on a mouse nearby. An infectious cat shed oocysts (equivalent of eggs in *Echinococcus*) at the location of where the cat was, and those oocysts could only infect a mouse in that location. However, the model still assumed a uniform landscape, and each cats and mice could move to any part of that landscape and only limited by its own movement speed.

Lane-deGraaf et al. (2013) developed an ABM of *Entamoeba histolytica* and *E. dispar* transmissions among long-tailed macaques (*Macaca fascicularis*) in Bali, Indonesia. Though the two parasites modelled were not *Echinococcus* or have complex life-cycles, this system was similar to *Em* in that they are transmitted fecal-oral routes and requiring use of same space at different time. More importantly, the model by Lane-deGraaf et al. (2013) was spatially-explicit and represented a real landscape with habitats and non-habitats, and the land-use of the host animals, leading to spatial variation in the transmission patterns that are otherwise missed.

These ABMs are advantageous over the statistical or compartmental models in several ways. First, ABMs have very flexible structure. The population structures and transmission patterns can emerge from the model based on the behaviors of the individuals, instead of being designed by the model developers from the known structure and transmission patterns as in network models. It can integrate data and processes at multiple scales, and is useful when there are significant individual and spatial variations in the system (Lanzas & Chen, 2015).

Second, the ABMs can model processes at finer spatial resolution than the statistical or the mathematical models, and incorporate various data and processes occurring at various spatial scales (Lanzas & Chen, 2015). The ABMs do not have to be the model for the entire population like in the compartmental model. Instead, it can model any group of individuals within a population. A spatially-explicit ABM can in theory be designed at any spatial resolution and level of organization as it needs to be.

Finally, the spatially-explicit ABMs would be able to capture both the temporal and spatial patterns of the disease. The spatially-explicit ABMs would be able to predict when and where the disease risk will be high. Such information can be highly valuable to the policy makers or public health workers.

There are several limitations to the ABMs. First, the model results can be difficult to interpret. The ABMs would be far more detailed than compartmental models, and while the ABMs can be more realistic their results lack generality and its inferences may be restricted to the specific case (Lanzas & Chen, 2015). In

addition, because of the stochastic nature of the model, an outcome of a model simulation is different every time, requiring analysis of multiple results to see patterns in the output.

Another problem with the ABMs is its long computational time (Lanzas & Chen, 2015). Because the ABMs are more detailed and involve many calculations and processes, and because they typically need to be repeated several times to interpret the results, they are more computationally demanding and time consuming than the statistical or compartmental models. Very long computational time, in turn, can restrict the number of scenarios to be simulated.

One of the major concerns for the ABMs is the uncertainties in the model. Like the compartmental models, the ABMs are process-based models, and require their parameters to be estimated (Messina et al., 2008). Because the ABMs are detailed and require estimation of many more parameters than the compartmental models, the uncertainties in the ABMs are greater. Studies using ABMs often focus on the analysis of the patterns in the results rather than making specific predictions on the outcome such as the prevalence.

2.4. MODELING THE TRANSMISSION OF *ECHINOCOCCUS MULTILOCULARIS* IN CALGARY

The overarching objective of this study is to understand the processes and mechanisms that produce the observed patterns in the transmission of *Em* using the system of the parasites and the wildlife host in the City of Calgary as a case study. Observed patterns such as spatial and temporal heterogeneity in the prevalence of the parasites and heterogeneity in the intensity of the parasite infection among individual definitive hosts are difficult to be understood with the use of field and laboratory studies, and models are required. For this objective, the model must meet several requirements.

First, the model must be spatially-explicit at the scale of within city landscape. One of the pattern of interest is the spatial heterogeneity, and the model must be able to represent and predict that spatial heterogeneity. It is known that addition of spatial components in a model can lead to different conclusions for otherwise same models (Durrett & Levin, 1994; Shaw et al., 2019). For the coyotes and rodents in urban Calgary that are potential hosts to *Em* do not form a single uniformly mixing population. The landscape is not a uniform habitable space but rather a landscape of habitable patches among less suitable habitats. The movements of hosts between the habitable patches would be limited by several barriers such as roads, fences, and rivers. The coyotes can be territorial and for packs (Gese et al., 1996a). The home range sizes of the small mammals' are very small compared to that of the coyotes and rarely travel long distances (Gese et al., 2012; Madison, 1980), and therefore even in a connected homogenous habitat the small mammals can hardly be considered a single population that mix homogeneously if they are

separated by several kilometers. All these factors will influence the transmission of *Em* and comes from the spatial aspect of the system.

Second, the model must be process-based. The interest of the study is the mechanisms and processes and they must be represented in the model. While statistical studies have been conducted on *Em* in the City of Calgary to explain the observed patterns (Liccioli et al., 2015a; Liccioli et al., 2014; Liccioli et al., 2015c; see chapter 3), statistical associations cannot explain the mechanisms that are causing the patterns.

Third, the model must be able to represent individual heterogeneities. The infection intensity of *Em* hosts are known to be widely variable, and few individuals are suspected to contribute disproportionately to the transmission (Catalano et al., 2012; Massolo et al., 2014). Several causes are suspected for these variations, including differences in individual coyote's behaviors and locations leading to the different diet and the use of landscape (Gese & Ruff, 1997; Gese et al., 1996a, 1996b), infection to other diseases that affect their behaviors and immune responses (Murray et al., 2015b), and past experiences and history of each individual.

Above requirements leads to a spatially-explicit ABM as an answer. A spatially-explicit ABM can represent spatial-components, processes and mechanisms of the system, and individual differences of the hosts. More traditional compartmental models would be able to model processes and add some spatial components, they are simply not good at spatial and individual representation. While network models can represent processes and mechanisms that connect the individuals of the system, it is not very good at predicting how these connections form.

CH 3: A COMMUNITY ANALYSIS APPROACH TO PARASITE TRANSMISSION IN MULTI-HOST SYSTEMS: ASSEMBLAGES OF SMALL MAMMAL PREY AND *ECHINOCOCCUS MULTILOCULARIS* IN AN URBAN AREA IN NORTH AMERICA

3.1. ABSTRACT

Background: *Echinococcus multilocularis* (*Em*) is a parasite with a complex life cycle whose transmission involves a predator-prey interaction. Accidental ingestion of *Em* eggs by humans may cause alveolar echinococcosis, a potentially fatal disease. Although previous research suggested that the composition of the assemblage of prey species may play a key role in the transmission, the relation between *Em* presence and the prey assemblages has never been analyzed. Herein, we propose a community analysis approach, based on assemblage similarity statistics, clustering, non-metric dimensional scaling and GLM modelling to analyze the relationships between small mammal assemblages, environmental variables, and the prevalence of *Em* in intermediate and definitive hosts in an urban area.

Results: In our study areas within the City of Calgary, Alberta (Canada), we identified three main small mammal assemblages associated with different prevalence of *Em*, characterized by a different proportion of species known to be good intermediate hosts for *Em*. As expected, assemblages with higher proportion of species susceptible to *Em* were observed with higher prevalence of parasite, whereas the total abundance *per se* of small mammals was not a predictor of transmission likely due to dilution effect. Furthermore, these assemblages were also predicted by simple environmental proxies such as land cover and terrain.

Conclusions: Our results indicated that the use of a community analysis approach allows for robust characterization of these complex and multivariate relationships, and may offer a promising tool for further understanding of parasite epidemiology in complex multi-host systems. In addition, this analysis indicates that it is possible to predict potential foci of disease risk within urban areas using environmental data commonly available to city planners and land managers.

3.2. BACKGROUND

Echinococcus multilocularis (*Em*) is a parasitic tapeworm that can cause human alveolar echinococcosis (AE), currently considered among the most serious zoonotic diseases outside of the tropics (Massolo et al., 2014). The parasite is endemic across the northern hemisphere, and its distribution is expanding (Davidson et al., 2012; Massolo et al., 2014). The disease has high fatality rate (i.e. > 90%) if not treated, and often requires life-long treatments (Craig, 2003). In 2010, it was estimated that globally there were 18,235 human cases of AE annually (Torgerson et al., 2010) with an increasing trend. Only few cases were reported in North America outside of Alaska, but there are indications that the risk of AE may be increasing (Massolo et al., 2014).

Echinococcus multilocularis is a trophically transmitted parasite with a complex life cycle that involves two different hosts and a free-living stage. The parasite typically infects canid predators such as foxes *Vulpes* spp. and coyotes *Canis latrans* (but also domestic dogs) as definitive hosts (DH). The adult parasite, in the DH intestine, produces embryonated eggs which are released in the environment with feces. More than 40 small mammal species (usually rodents) act as intermediate hosts (IHs) by accidentally ingesting these eggs (Liccioli et al., 2013; Vuitton et al., 2003) and developing the final infectious larval stage in the target organ (often the liver). The life cycle is completed when infectious IHs are predated by DHs. Although climate conditions likely determine the limit of the parasite distribution at the global scale, at more local scales the presence and relative abundance of the IH species plays a key role in the parasite distribution and transmission intensity (Giraudoux et al., 2004; Liccioli et al., 2013; Romig et al., 2017b). In the southern edge of its European distribution, for example, *Em* spread was deemed to be limited by the presence of single species of small mammal IH (Guerra et al., 2014). Landscape and environmental characteristics that define the distribution of small mammals (e.g., the proportion of the landscape composed by optimal habitat for the susceptible small mammal species) can be important predictors of where the intensity of the parasite transmission is high (Giraudoux et al., 2004; Raoul et al., 2015).

However, the influence of susceptible small mammal species on the transmission of *Em* is made complex by interactions among small mammal species and between predator and prey. Higher population density of DH is expected to increase the transmission rate (Raoul et al., 2015). Even in an area inhabited by susceptible small mammal species, parasite transmission is unlikely if their relative abundance within the prey ensemble is low. The presence of other species that are not susceptible to the parasite but preferred as prey by DHs will reduce the probability of *Em* transmission (Baudrot et al., 2016; Guerra et al., 2014). Our previous research on the distribution of small mammals and *Em* in the City of Calgary suggested that the proportion of susceptible species within the small mammal community may be a key factor in determining the prevalence of the parasite (Liccioli et al., 2014).

Despite these recent findings, so far researchers have only analyzed the effects of single intermediate species variations on transmission of *Em*, and speculated on or modelled the effects of the small mammal assemblages as a whole. Following up on our previous study (Liccioli et al., 2014), we wanted to explore in more detail the association between small mammal assemblages and *Em* transmission using an analytical approach typical of community ecology. In addition, we analyzed environmental features associated with the prevalence of the parasite, which may allow us to predict areas of high risks.

In particular, we aimed to

- A. characterize the composition and structure of the various types of small mammal prey assemblages in the study area;
- B. explore the association between the various types of prey assemblages and *Em* infection in both definitive and intermediate hosts;
- C. identify the environmental proxies that are associated with the various assemblages, and the environment where *Em* transmission is more likely to occur, using geographical data commonly available for city planners.

3.3. METHODS

3.3.1 STUDY AREA AND DATA DESCRIPTION

The samples were collected in the City of Calgary (AB, Canada; 51°5'N, 114°5'W; Figure 5), located in the southeastern region of Alberta in the foothills of the Canadian Rocky Mountains, from June 2012 to July 2013. The city encompasses an area of 848 km² and has a population of 1,235,171 (The City of Calgary, 2016). The city ranges in elevation from 965 to 1304 meters a.s.l., and encompasses many streams and water bodies with riparian habitats that are often designated as parks and natural areas. The climate is relatively dry (annual precipitation of 412.6 mm) and cold, with an average annual high temperature of 10.5 °C and low temperature of -2.4 °C (Statistics Canada, 2017). Common habitats in parks and natural areas are grasslands in dry areas, aspen forests in moderately well-drained areas, and willow shrublands in imperfectly drained areas (The City of Calgary, 2014).

Common mammals in the city area are snowshoe hares (*Lepus americanus*), white-tailed jack rabbit (*Lepus townsendii*), Richardson's ground squirrels (*Urocyon richardsonii*), gray squirrels (*Sciurus carolinensis*), southern red-backed and meadow vole (*Myodes gapperi*; *Microtus pennsylvanicus*), deer mouse (*Peromyscus maniculatus*), muskrat (*Ondatra zibethicus*), coyote, beaver (*Castor canadensis*), mule deer (*Odocoileus hemionus*), white-tailed deer (*Odocoileus virginianus*), and less commonly red fox (*Vulpes vulpes*; The City of Calgary, 2014). Of these, only southern red-backed vole, meadow vole, deer

mouse, beaver and muskrat are currently described as IHs for *Em* (Liccioli et al., 2013), but beaver and muskrats were rarely reported in the diet of urban coyotes in the City of Calgary (Liccioli et al., 2015a).

We used data on small mammal relative abundance per site collected for the study of Liccioli et al. (2014) between June 2012 and July 2013 in sites within Calgary urban parks and natural areas. Specifically, these sites were located in Nose Hill Park (site NHP1 ~ NHP3), Bowmont (BM1 ~ BM3), Weaselhead (WSH1 ~ WSH3), Southland lowland (SL1 & SL2), and Fish Creek Provincial Park (FCPP1 ~ FCPP3; Figure 5). Samples collected in June and July 2013 were not used in the study by Liccioli et al. (2014) because of their interest in seasonal pattern, but were included in this study in order to increase the sample size, whereas the first trapping session in June 2012 included in Liccioli et al. (2014) was removed from this study because it was conducted with a different protocol (i.e. trappings were conducted for 4 nights in row instead of 3 due to weather condition causing most traps to misfire on the first night). The small mammals sampled within these sessions totaled 1223 small mammals of 9 different species (Liccioli et al., 2014).

We used DH prevalence estimated from 385 coyote feces collected by Liccioli et al. (2014) in the same five areas between May 2012 and July 2013 (Table 2: Liccioli et al., 2014). For more details on the small mammal and fecal collection methods and data analysis methods, see Liccioli et al. (2014).

3.3.2 ASSEMBLAGE ANALYSIS

The trap catch-rate of small mammals caught at each site were standardized by aggregating all captures for each site and then divided by number of trap-nights, not counting misfires and traps that caught other species (e.g. a trap that caught a deer mouse could not have caught a meadow vole that same night) to represent the relative abundances of each species (Table 2). Differences between species composition at each trap site were measured using the Bray-Curtis statistic (Bray & Curtis, 1957), treating each trap site as statistical unit and the relative abundance for each species as variable. The relative abundances were log-transformed ($\log(x+1)$) before calculation of the similarity matrix (Beals, 1984)

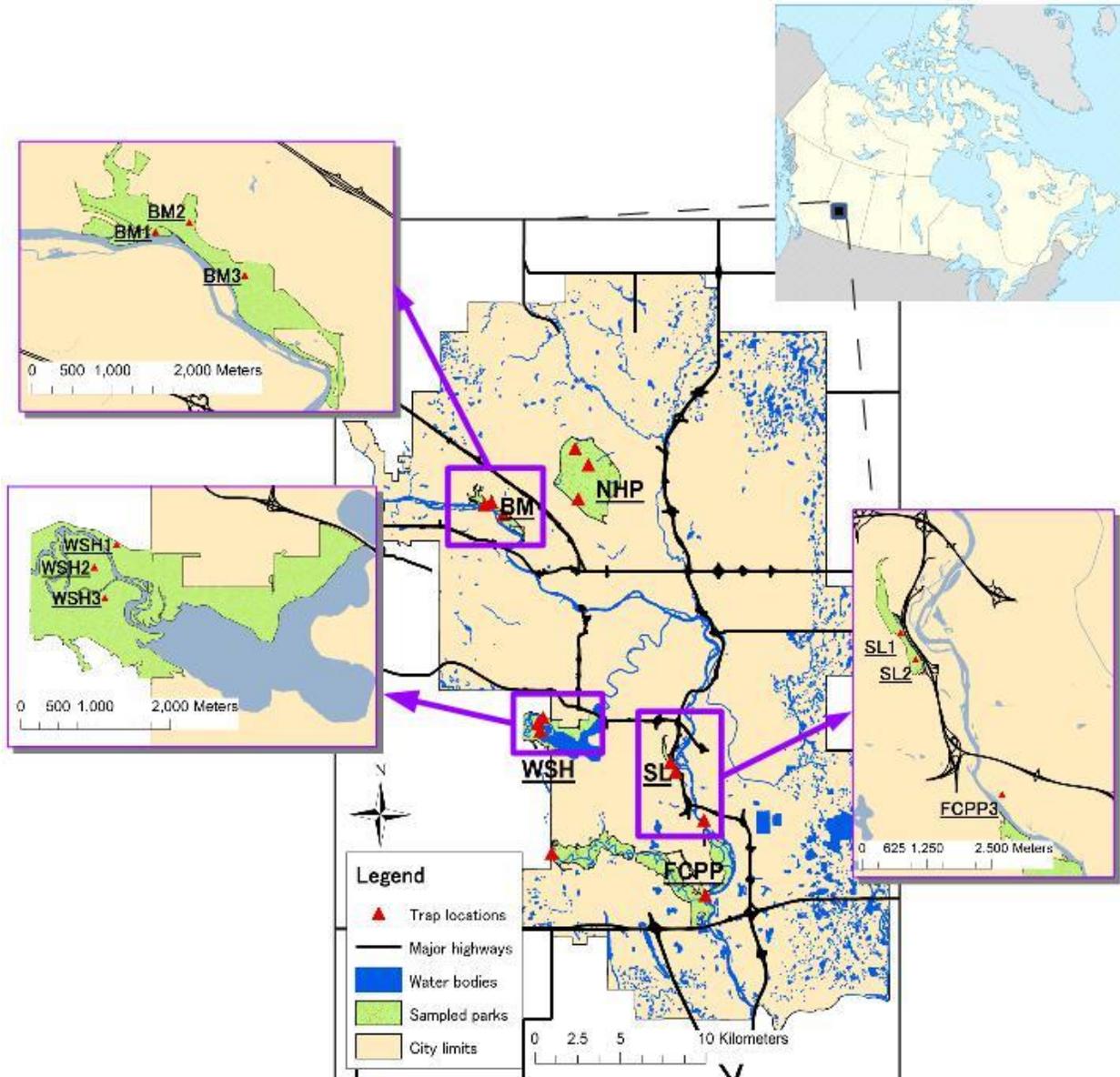


Figure 5: Study sites for the characterization of the small mammal assemblages in urban Calgary, AB, Canada in 2012-2013, showing the location of five areas in Urban Calgary and detailed map of Bowmont, Southland Lowlands, and Weaselhead. Bowmont (BM), Fishcreek Provincial Park (FCPP), Nose Hill Park (NHP), Southland Lowlands (SL), and Weaselhead (WSH).

The Bray-Curtis similarity was visualized through hierarchical agglomerative clustering dendrogram, using group average algorithm to calculate the distance between clusters (Field et al., 1982). To test the robustness of the cluster structures, clustering with single-linkage and complete-linkage algorithms were also performed. In addition, hierarchical agglomerative clustering was performed on data transformed to percentage of each species before calculation of Bray-Curtis similarity, again using group average, single-

linkage, and complete-linkage. Resulting cluster structures were compared for consistency. Significance of the clusters were tested using similarity profile (SIMPROF) tests (Clarke et al., 2008). The association between clusters and presence of *Em* infected small mammals were statistically tested using Fisher's exact test (Sokal & Rohlf, 1995).

To identify the general characteristics of each cluster type, we performed Canonical Correlation Analysis on the principal coordinates (CAP) procedure (Anderson & Willis, 2003). This procedure displays cloud of multivariate points with reference to a hypothesis set a priori by finding axes that maximize the difference among groups. The procedure also tests the significance in the difference among groups using permutation tests and "trace" statistics, equivalent to Pillai's trace statistics in traditional multivariate analysis of variance test. Pearson correlation coefficients between the abundance and proportion of each species to the CAP axes were calculated and their vectors overlaid on the plot.

A pooled *Em* prevalence was calculated for each small mammal assemblage for each site as the number of infected animals divided by the total number of small mammals caught. This pooled prevalence was a simple estimate of the likelihood for a coyote to become infected by preying on a specific assemblage.

We associated the DH prevalence estimates for the five areas to the trap sites in each area, which is a reasonable assumption considering the distance between each area and territoriality of coyotes. The possible exception was the FCPP3 site which was close to SL. However, because SL and FCPP had similar estimate of DH prevalence, FCPP3 could be either associated with DH of FCPP or SL with little difference.

3.3.3 ENVIRONMENTAL ANALYSIS

The environmental proxies surrounding each trap site were identified using ArcGIS Desktop (Release 11. Redlands, CA: Environmental Systems Research Institute). We hypothesized that combination of land cover types, distance to water, and terrain features would allow us to identify habitats associated with small mammal assemblages. Land cover types and distance to water were obtained from a Land Cover map (updated at 2014) with 5 meter resolution (Fiera Biological Consulting Ltd., 2014). Terrain features (the average aspect, slope, and "ruggedness" or the standard deviation of the slope) of each trap site were calculated from a digital elevation model with resolution of 0.75 arc-second, or approximately 18 meters (Natural Resources Canada, 2012).

Table 2: This table summarizes the data on small mammal assemblages composition extracted from (Liccioli et al., 2014) collected in 2012-2013 in city parks and natural areas in the City of Calgary (Alberta, Canada). In table are reported the catch rate for each species (indicated by genus names) for every hundred trap-nights, the presence of *Echinococcus multilocularis* (1= present, 0 = absent) and prevalence (%) among intermediate hosts (IH), and prevalence among definitive hosts (DH) at each site. The species of small mammals are: Deer mouse (*Peromyscus maniculatus*), Meadow vole (*Microtus pennsylvanicus*), Shrews (*Sorex* sp.), Southern red-backed vole (*Myodes gapperi*), Western jumping mouse (*Zapus princeps*), Thirteen-lined ground squirrel (*Spermophilus tridecemlineatus*), Least chipmunk (*Tamias minimus*), Northern pocket gopher (*Thomomys talpoides*), and House mouse (*Mus musculus*).

<u>Site</u>	<u>Peromyscus</u>	<u>Microtus</u>	<u>Sorex</u>	<u>Myodes</u>	<u>Zapus</u>	<u>Thomomys</u>	<u>Spermophilus</u>	<u>Tamias</u>	<u>Mus</u>	<u>IH presence (Prevalence %)</u>	<u>DH Prevalence (%)</u>
BM1	2.9530	0.1030	0.1545	0.1545	0	0	0	0	0.1545	1 (1.43)	
BM2	1.2318	0.0462	0.2304	0	0.3682	0	0	0	0	1 (2.44)	63.07
BM3	0.8246	0.0462	0.5969	0	0.0923	0	0	0	0	0	
FCPP1	0.8836	3.8810	0.7804	0.0524	0	0	0	0	0	0	
FCPP2	0.1284	0.7653	0.5963	0	0.2138	0	0	0	0	0	6.23
FCPP3	0	0.3745	0.8696	0	0	0	0	0	0.0626	0	
NHP1	2.0658	3.2526	1.6213	0	0	0	0	0	0	1 (0.93)	
NHP2	1.4470	2.4053	0.8836	0	0.4178	0	0	0	0	1 (1.00)	17.28
NHP3	1.5603	1.9081	0.2874	0	0.4304	0	0	0	0	0	
SL1	1.6618	4.0874	3.4752	0	0	0.0367	0	0	0.0367	1 (0.38)	5.42
SL2	0.4288	1.0230	2.4780	0	0	0.0861	0	0	0	0	
WSH1	0.9620	0.7610	0.6098	0.1021	0.2041	0	0.3058	0	0	0	
WSH2	2.0045	1.1976	0.9752	2.5111	0.9009	0	0	0.1513	0	0	6.22
WSH3	2.0101	3.2258	1.5980	2.6622	0.3407	0	0	0.1706	0	0	

A multinomial logistic regression (MLR) model (Fox, 2008; Hosmer et al., 2013) associating the environmental variables to assemblage types was developed. We built a set of alternative models based on what we considered biologically relevant combinations, such as land cover types of forest, grassland, and shrub lands and terrain features. We used focal statistics with circle of 200 meter radius to standardize the way we measure surrounding environment, assuming that areas within 200 meter were sufficient for identifying the habitats influencing the small mammals based on their home ranges while also approximating the areas covered by trap grids (Madison, 1980; Madison et al., 1984). We used total numbers of raster cells within 200 meter radius for each land cover type as predictor variables. We used the mean value of the cells within 200 meter radius for the terrain variables after resampling each terrain raster to 5 meter resolution. The models were then compared using the corrected Akaike Information Criteria (AICc) scores and weights (Burnham & Anderson, 2002). The best performing MLR model was then applied to develop a predicted distribution map of the small mammal assemblage for the entire area of the City. Because we did not sample small mammals from agricultural areas, and because the agricultural areas were at the periphery of the city, we removed agricultural areas from the final map. Similarly, because small mammals are known to avoid mowed grass (Bowers & Dooley, 1993), and because in one experimental trapping we found no small mammal in a field of mowed grass adjacent to a naturally wooded area, we also removed areas classified as manicured grass. Final map was resampled to 50 meters resolution to be used for an agent-based simulation of the transmission of *Em* in future study.

All the statistical analysis, except for the MLR were performed using software Primer ver.6 with PERMANOVA+ add-on (Anderson et al., 2008). MLR was performed using SPSS ver.24 (IBM Corps. 2016).

3.4 RESULTS

3.4.1 ASSEMBLAGE ANALYSIS

To reduce the noise on the community analysis, least chipmunk, northern pocket gopher, and house mice were removed from relative abundance data prior to the calculation of the Bray-Curtis similarity matrix because of their minimal abundance in the data. The hierarchical clustering of the small mammal assemblage identified three major assemblage types using an arbitrary cut-off line of 45% similarity, although SIMPROF test failed to detect significance ($p=0.678$, Figure 6a).

Cluster 1 consisted of three BM sites, where Liccioli et al. (2014) found two IHs positive for *Em*, and estimated highest prevalence among DH. Cluster 2 consisted of three NHP sites, FCPP1, SL1, WSH2 and WSH3. Liccioli et al. (2014) found positive IHs in three sites and estimated moderately high prevalence

among DH in NHP. The remaining sites WSH1, SL2, FCPP2, and FCPP3 constituted cluster 3. Liccioli et al. (2014) found no positive IH in these sites and estimated low prevalence of DH in these areas (Table 2). Fisher's exact test on the *Em* positive cases of small mammals and the three clusters could not detect any significant difference ($p = 0.136$).

Clustering with complete-linkage algorithm also grouped trap sites into the same three clusters ($p = 0.695$, Figure 6b). The same pattern was not observed with single-linkage, where trap sites successively joined groups instead of grouping into distinct clusters (not shown, $p = 0.718$). Similar, but slightly different cluster patterns were observed when group-average and complete-linkage clustering algorithms were performed on percentage of species ($p = 0.144$ and 0.136 respectively, result of group-average shown in Figure 6c). With percentage of species, cluster 3 was smaller and consisted of only two sites, but BM still formed a single cluster. Clustering percentage data with single-linkage algorithm showed less distinct a pattern, but BM sites still grouped into a single cluster ($p = 0.127$). All the following analyses are based on relative-abundance data and clusters based on group-average algorithm.

Conversely, CAP procedure of the small mammal assemblages, using the three clusters identified as grouping factors (Figure 7), highlighted the significant difference between the three clusters (trace statistics 1.6536, $p = 0.001$). Vectors representing the correlation between the CAP axes and the abundances of each species overlaid in Figure 7a indicated that all the species were more abundant in cluster 2. Vectors indicating the correlation of the CAP axes to the proportion of each species and (Figure 7b) indicated that cluster 1 assemblages (particularly BM 1 and BM2) were dominated by deer mice, whereas cluster 3 sites (SL2 and FCPP2) were characterized by shrews.

3.4.2 ENVIRONMENTAL PROXIES FOR ASSEMBLAGES

The best MLR model selected by AICc used north-south aspect and ruggedness as predictor variables, with AICc of 18.722 and classified 13 out of 14 trap sites correctly (Table 3). When this model was applied to the natural areas of the City of Calgary, 1209 ha (6.96%) were predicted to be habitat for cluster 1, 8164 ha (47.02%) for cluster 2, and 7991 ha (46.02%) for cluster 3 (Figure 8; see supplementary material for parameter estimates).

3.5. DISCUSSION

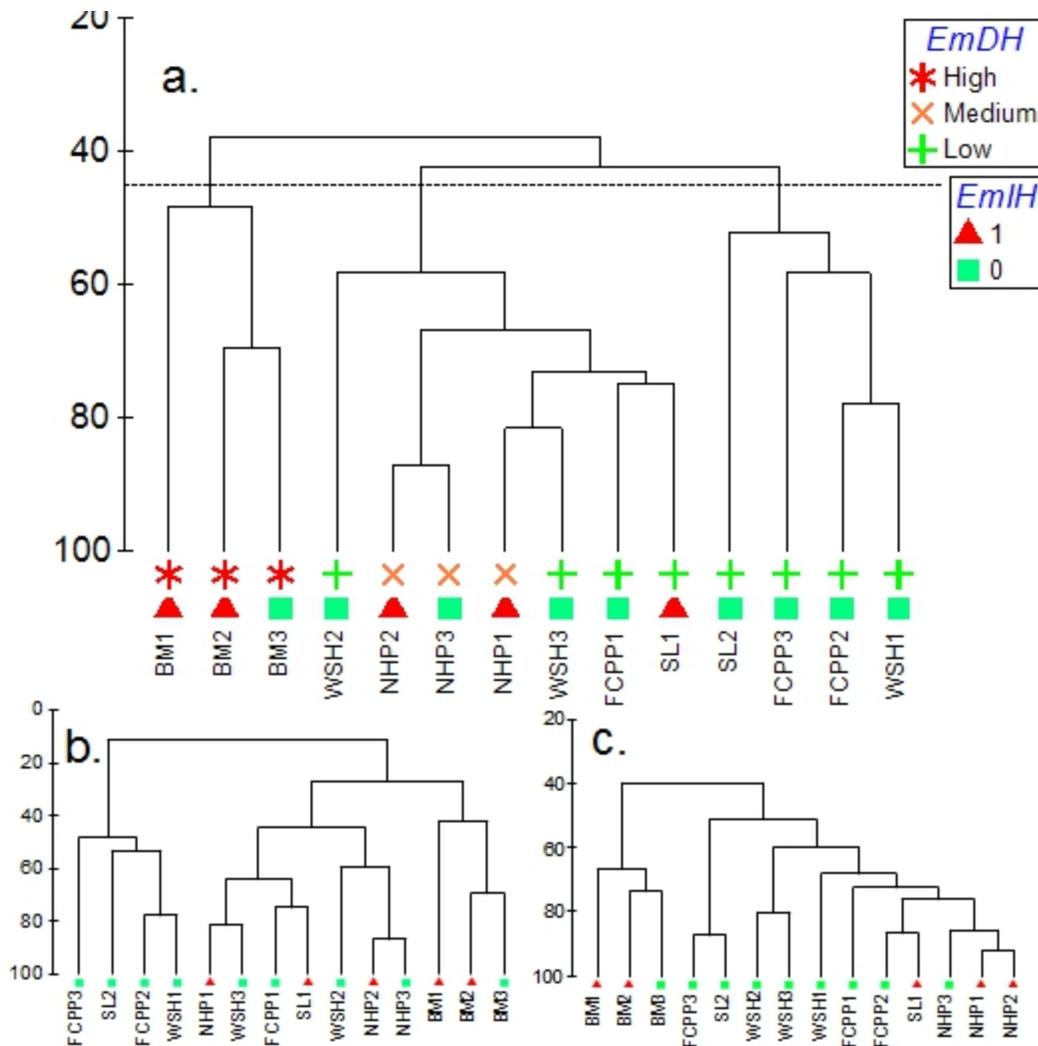


Figure 6: Dendrograms derived from the Bray-Curtis similarity of small mammal assemblages in five parks and natural areas in urban Calgary, AB, Canada, 2012-2013. a) Dendrogram using abundance data and group-average clustering algorithm. The dashed line indicates the cluster cut-off line of 45% similarity. Symbols for each site indicate the prevalence of definitive hosts (EmDH) and presence (1) or absence (0) of infected small mammals (EmIH). b) Dendrogram using abundance data and complete-linkage clustering algorithm. Note how it is similar to the dendrogram using group-average algorithm. c) Dendrogram using proportion data and group-average clustering algorithm. Note how all BM sites are in single cluster and all NHP sites and most sites are in another cluster, similar to the dendrogram using abundance data.

Using a community ecology analytical approach, we identified three assemblage types of small preys of coyotes, the main carnivore species in urban settings in Calgary, Alberta (Canada). More importantly, we highlighted an association between these assemblages and the presence of *Echinococcus multilocularis* in wild hosts. Finally, we identified potential environmental proxies calculated from land use data readily available for urban settings that could be associated with parasite within this sylvatic cycle. Our results

provided evidence to support recent theoretical models that emphasized the role of complexity of host community in transmission of trophically transmitted parasites (Baudrot et al., 2016).

3.5.1 SMALL PREY ASSEMBLAGES AND *ECHINOCOCCUS MULTILOCULARIS*

Our clustering analysis using Bray-Curtis similarity identified three clusters. Although the clusters structures were not statistically significant by SIMPROF test possibly due to small sample size, similar structure were observed in both relative abundances and percentage of species, and with different clustering algorithms, providing some confidence in classifying the small mammal assemblages to the three assemblage types. Assemblage 1 consisting of BM sites seemed to be highly susceptible to the transmission of *Em*, while assemblage 3 seemed to be least susceptible to *Em* transmission.

Table 3: Comparison of multinomial logistic regression models predicting various types of assemblages of small mammals developed from data collected in 2012-2013 in city parks and natural areas in the City of Calgary, (Alberta, Canada). The values k , Δ_i , and w_i indicate number of parameters estimated, difference in AICc, and relative weights of AICc, respectively. Although the model with north-south aspect and ruggedness performed best in terms of AICc, N-S aspect and slope model, N-S aspect, slope, and ruggedness model performed comparably well.

<u>Model</u>	<u>k</u>	<u>-2 * log likelihood</u>	<u>Classification accuracy (%)</u>	<u>AICc</u>	<u>Δ_i</u>	<u>w_i</u>
N-S Aspect & Ruggedness	3	4.322	92.9	18.722	0	0.4857
N-S Aspect & Slope	3	5.616	92.9	20.016	1.2940	0.2543
N-S Aspect & Ruggedness & Slope	4	0	100	20.4444	1.7224	0.2053
N-S Aspect only	2	14.06	78.6	23.1509	4.4289	0.0530
Slope only	2	22.887	57.1	31.9779	13.2559	0.0006
Ruggedness & Slope	3	18.586	64.3	32.9860	14.2640	0.0004
Intercept only	1	29.805	50	33.3023	14.5803	0.0003
Ruggedness only	2	24.532	50	33.6229	14.9009	0.0003

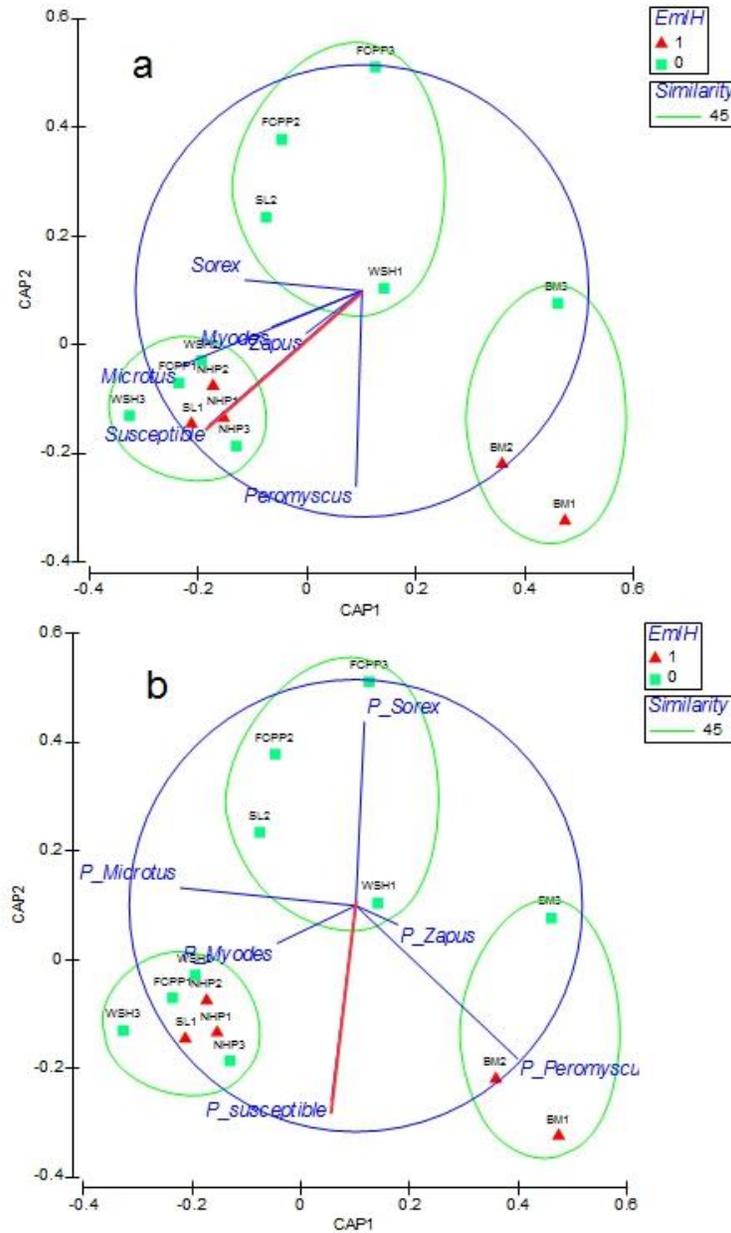


Figure 7: Plot of the Canonical Correlation Analysis on the principal coordinates (CAP) of small mammal assemblages in five parks and natural areas in urban Calgary, AB, Canada, 2012-2013, using the cluster as a grouping factor. The cluster 1 is on the lower right corner, cluster 2 is on the lower left corner, and cluster 3 is on the center to the top of the plot. The 45% similarity contour line is drawn based on the dendrogram in Figure 5a. a) Vectors were overlaid showing the correlation with the abundances of each species to each cluster. The red vector shows the correlation with the abundance of all the susceptible species combined. b) Vectors were overlaid showing the correlation with the proportion of each species to each cluster. The red vector shows the correlation with the proportion of all the susceptible species.

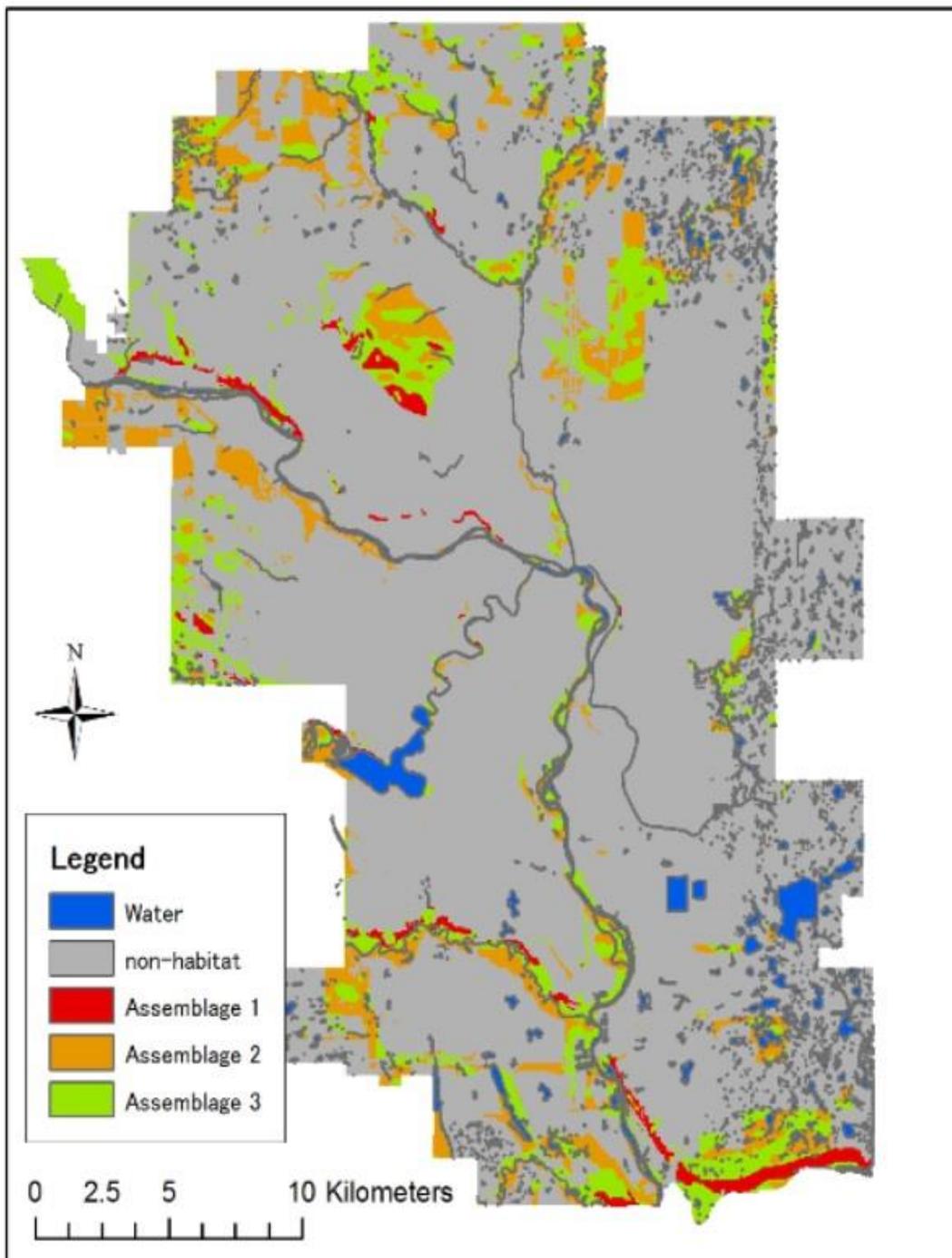


Figure 8: Map showing the geographic distribution of three small mammal assemblage types predicted for the City of Calgary area by a multinomial logistic regression (MLR) model associating the environmental variables to assemblage types, developed from data collected in 2012 and 2013 (Liccioli et al., 2014). Note how large portion of BWM and NHP were classified as assemblage 1 as expected, but also large portion of FCPP, where it was not expected.

In our study area, the three small mammal species of most interest due to their known susceptibility to *Em* are deer mice, meadow voles, and southern red-backed voles (Liccioli et al., 2013a). Particularly interesting was the correlation of proportion of deer mice to assemblage 1, where the prevalence among DH was high (Figure 7b). This is consistent with conclusions drawn by Liccioli et al. (2014) that proportion of susceptible species is the key factor in the transmission of the parasite. However, even though assemblage 1 and 2 had about same proportion of susceptible species, assemblage 1 was associated with higher prevalence in both DH and IH. Compared to assemblage 1, assemblage 2 had higher abundance of most species of small mammals (Figure 7a). Therefore we suspect that higher abundance of small mammals in general, both susceptible and non-susceptible, led to dilution of exposure and reduced transmission (Baudrot et al., 2016).

Any inference drawn from this cluster analysis is limited by the samples size - an issue associated with the low prevalence at which the parasite occurs in intermediate hosts, which likely caused the lack of statistical significance for the Fisher's exact test on the assemblage types and the presence of positive IHs. However, the patterns observed were in agreement with the theoretical studies (Baudrot et al., 2016; Raoul et al., 2015).

3.5.2 THE URBAN SMALL MAMMAL ASSEMBLAGES AND THEIR LANDSCAPE PROXIES

In our study, the terrain features (north-facing aspect and ruggedness) turned out to be better predictors of assemblage types than land cover types and were selected for the best MLR model. This was probably because the land cover classification was too coarse for the habitats of small mammals. While land cover types were good indicator of where the natural land covers were (because we collected samples only from natural areas), terrain features were probably better indicators of subtle differences in habitats (Franklin, 1995). For example, assemblage 2 seemed to be associated positively with north-facing aspect and negatively with ruggedness (Appendix 1). These terrain features may be better predictors of vegetation types that prefer moist environment. Distance to water was not selected in the model, probably because most sites were close to water, and the only site that differed for this variable (NHP3) had species composition resembling other sites.

Interestingly, the predicted distribution of the small mammal assemblage type 1 was characterizing most of BM and a fair portion of NHP (Figure 8). The prevalence of *Em* in these two areas were higher than the other three areas (Liccioli et al., 2014) and in agreement with our inference that assemblage 1 contributed most to the transmission of the parasite, and possibly explains why NHP had higher prevalence even though all three NHP sites were in assemblage 2. However, the predicted distribution of assemblage 1

also covered large area of FCPP, where the prevalence of *Em* was estimated to be low, both in DH and IH (Liccioli et al., 2014).

Another possible explanation for the observed pattern of *Em* prevalence would be the availability to coyotes of food sources other than small mammals, which was not quantified in our study. Coyote diet in our study area includes deer and lagomorphs, fruits and vegetable matters, and anthropogenic food sources (Liccioli et al., 2015a). Abundance of deer in the area is expected to be particularly important in winter, when they are more frequently consumed and the parasite prevalence in IH is highest (Liccioli et al., 2015a; Liccioli et al., 2014). Large and/or connected parks such as NHP, FCPP, and WSH would likely be used by deer more frequently than smaller, less connected parks such as BM and SL.

The feeding and marking behavior of coyotes (i.e., DHs) can also be important for the transmission of the parasite. Although the small mammal assemblages and environmental proxies in and around each site may provide some clues on the parasite transmission, coyotes are known to have wide home ranges and readily travel through urban areas (Gehrt, 2007; Lamy, 2015). To estimate transmission of parasites and their spatial patterns, analysis of small mammal assemblages alone is not sufficient. Studies on spatial behavior of coyotes, using simulations such as agent-based models, would provide further understanding of the spatial patterns of *Em* transmission. Such studies would also allow testing if changes in small mammal assemblages could exert significant effects on parasite transmission.

CH 4: FECAL CONTAMINATION OF URBAN PARKS BY DOMESTIC DOGS AND COYOTES: ANOTHER EXAMPLE OF TRAGEDY OF THE COMMONS?

4.1 ABSTRACT

Contamination of public parks by dog and wildlife feces is potential sources of conflict among park users, causing “tragedy of commons” problems. Besides the social conflict, feces can pose serious health risks to both dogs and people. In this study we analyzed the extent and patterns of the distribution of dog and coyote feces in the urban parks of the City of Calgary. We estimated 1,423 kg of dog feces are left unpicked in city parks in total every week. As expected, dog feces were found more often and in greater amount in off-leash parks, and near park entrances and parking lots. Coyote feces were found in rather small quantity of 0.42 per km of trails and pathways. These results suggest that feces of both dogs and coyotes are likely to be exposed to public park visitors and would likely have negative consequences to their experiences and to their health.

4.2 INTRODUCTION

Urban parks are important in increasing the quality of life in large metropolitan areas, providing place of recreation and physical activity for residents, and habitats for wildlife (Rock et al., 2016). Parks are also important for dog-owners as places for walking their dogs. However, use of urban parks by dog owners can cause various conflicts with other users of the parks (Weston et al., 2014). Dogs might defecate near children’s playground, cause injury to children, or interfere with outdoor activities such as fishing, cycling, and other sports. Dogs can prey on or scare away native wildlife, which can reduce the values of the parks to some users (Lenth et al., 2008).

Dog fecal contamination of public parks can be particularly concerning. Not only do dog feces act as deterrent for other park users including other dog-owners, but their presence often leads to loss of trust in park managers (Rock et al., 2016; Teedon et al., 2014). Dog feces can also cause water contamination downstream (Garfield & Walker, 2008).

Wild canids such as foxes and coyotes are known to adapt well to the urban environment, often inhabiting the urban parks and sharing parasites with domestic dogs (Lukasik & Alexander, 2011a; Romig, 2003;

Romig et al., 2007). Fecal contamination poses risks of parasite transmission from dogs to wildlife and vice versa (Lowe et al., 2014; Smith et al., 2014; Wang et al., 2012).

Fecal contamination of parks could be considered as another example of what is known as “tragedy of the commons,” a type of environmental dilemma where there are finite resources that are shared by multiple groups, exclusion or regulation of the use of the resources are impossible or difficult, and the use of the resources by one will reduce the available resources for others (Hardin, 1968; Matisoff & Noonan, 2012). City parks can be considered a common, degradable resource shared by park users, that could be degraded by dog fecal contamination. A strict enforcement of the rules on dogs to the dog owners are difficult to implement and would reduce the values of parks to dog owners.

In Calgary, Alberta, a parasite of serious zoonotic concern, *Echinococcus multilocularis* (*Em*), has been detected with very high local prevalence (Catalano et al., 2012; Liccioli et al., 2015c). The parasite, the aetiological agent of Alveolar Echinococcosis (AE), is ranked as the third most relevant food-borne parasitic zoonosis (World Health Organization, 2014). The parasite is naturally present in wild coyotes, and at least one dog in Calgary was identified as infected (Massolo et al., 2014). Recently an outbreak of human cases of AE has been described in Alberta, apparently caused by an endemic strain of the parasite likely originated through the invasion of a European strain (Massolo, 2019; Massolo et al., 2019).

Infection of a dog can greatly increase the chance of zoonosis to dog owners and should be of great concern for policy makers, park managers, and dog owners. Furthermore, dogs often have far larger “home range” compared to coyotes, as dog owners can take their dogs to several parks far apart, allowing transmission of parasite over distances that are otherwise unlikely to occur with wild hosts alone.

In this study, we followed up on works by Rock et al. (2016) and focused on the fecal contamination of urban parks in Calgary by dogs and coyotes in relation to the park dog leash policy (no dogs, off-leash, on-leash, and mixed), and to the environments and landscapes of the park. The aim of our study was to understand the extent and spatial pattern of dog and coyote fecal contamination in urban parks, and to assess relationships between the amount of fecal contamination and park management, and environmental factors.

4.3 MATERIALS AND METHODS

4.3.1 STUDY AREA AND SAMPLE COLLECTION

Coyote and dog fecal samples were collected in the City of Calgary (AB, Canada; 51°5'N, 114°5'W), in south-eastern Alberta, near the Canadian Rocky Mountains. The city has an area of 848 km² and

population of 1,476,598 (Calgary Population Census, 2018). Elevation ranges from 965 to 1304 meters a.s.l. The climate is predominantly cold and dry (with an average annual high temperature of 10.5 °C and low temperature of -2.4 °C). The city encompasses several parks and natural areas where residents often walk their dogs. The habitat compositions of those parks are determined by drainage levels: grasslands in dry areas, forests in well-drained areas and willow shrublands in wet soils areas. The city also encompasses three landfill areas, most of which is old landfill mound covered by mowed grass, surrounded by natural grassland and natural or artificial wetlands with shrubs. Although the areas are open to the public and currently active landfill areas have high human activities, most of them have little human presence other than occasional trucks and cars of landfill personnel passing through. Several mammal species can be observed in parks, natural areas, and in the residential areas of the city, such as white-tailed deer (*Odocoileus virginianus*), muskrat (*Ondatra zibethicus*), beavers (*Castor canadensis*), coyotes (*Canis latrans*), and small mammals such as squirrels, voles, shrews, and hares (Smith et al., 1993).

In June and August of 2011 feces of dogs, coyotes and other animals (mostly Canada goose *Branta canadensis* and white-tailed deer) were collected from 16 parks in the city (Figure 9). The 16 areas were selected for being representative of the main habitat types and regions of the City. They were also representative of different dog management rules within the city. These parks included parks in which the presence of dogs was not allowed (“no dog”); the presence of dogs was only allowed if they have the leash on (“leash on”); the entry of dogs was allowed without leash (“leash off”), and parks that has both “leash on” and “leash off” areas (“mixed”). Within the 16 parks, assessment of park fecal contamination was carried out using stratified random sampling at points randomly selected using a random point generator of ArcGIS10 (ESRI®). We used the size of the park to determine the number of sampling points, with minimum of two sampling points, in each park. Fecal samples were collected inside circular areas of 10 meter radius around the selected points. In order to assess the rate of fecal deposition over time, we cleared the areas of any feces already present in situ and returned a week later to collect and record the amount of feces deposited in that week. We tagged each sample with a unique identifier and recorded the species and weight.



Figure 9: A map showing the City of Calgary, and the locations of sampling points in the fecal surveys in 2011 in the city of Calgary.

As coyotes are known to defecate in non-randomly manner (Barja et al., 2004; Barja & List, 2014), another sample collection was conducted in 2015 with a different protocol specifically designed to collect coyote feces. Coyote feces were collected in six parks and three landfill areas in the city, where the presence of coyotes was determined either through direct observation or through indirect means (i.e., presence of coyote feces, words of park users and landfill staff). The nine areas were also chosen to be representative of the city areas geographically as well as available habitats in the city area.

The 2015 sampling was also designed to study *Em*. Four of the parks and all three landfill areas were not surveyed in studies on the presence of the parasite (Catalano et al., 2012; Liccioli et al., 2014). Two parks in particular, Nosehill Park and Bowmont Park, were chosen because they presented a high prevalence of *Em* in a previous survey (Liccioli et al., 2014). The coyote fecal samples were collected from April to June, and from October to December, when the *Em* prevalence is deemed to be higher, to maximize the chance of detecting *Em* (Liccioli et al., 2014).

Coyote fecal samples were collected along trails and dirt roads instead of randomly selected locations, because coyotes were known to exhibit a tendency to mark territories by defecating and urinating in specific locations, like crossroads and landmarks along pathways (Barja et al., 2004; Barja & List, 2014). Standardized pathways for sample collection were developed that would cover various areas and terrain, zones and locations which coyotes were more likely to use for marking territories, such as gaps and interruptions in fences or other linear features, and locations where the presence of coyotes was observed. These pathways were adjusted when the park or landfill managers closed trails and roads, which occurred in Bowmont Park and East Calgary Landfill. During the sampling period, coyote feces were collected along the pathways every ten days (Figure 10).

The locations of each fecal specimen were collected, recorded using a Garmin GPS unit, and tagged with the date of collection and a unique identifier. The feces were brought to the lab and placed in a -80 °C freezer for 48 hours to inactivate any *Em* eggs. The feces were then weighed and kept in a -20 °C freezer for further analysis.

4.3.2 GEOGRAPHICAL DATA

We obtained the size of each parks from the City Parks website where we could. For areas that were not listed in the City Parks website, we calculated their sizes using ArcGIS10 (ESRI®). We obtained maps of areas managed by the City Parks Services and areas of “off-leash” areas, developed and obtained from the City in 2019. The environmental variables characterizing each sampling points of 2011 survey were analyzed using the ArcGIS10 software.

First, the land cover types characterizing each sampling points were identified. The land cover map of Calgary area was obtained from the City of Calgary, which was developed in 2015 and with a resolution of 5 meters. From this land cover map the proportion of each land cover types was calculated for each of the surveyed areas (i.e. circular area of 10m radius around each point).

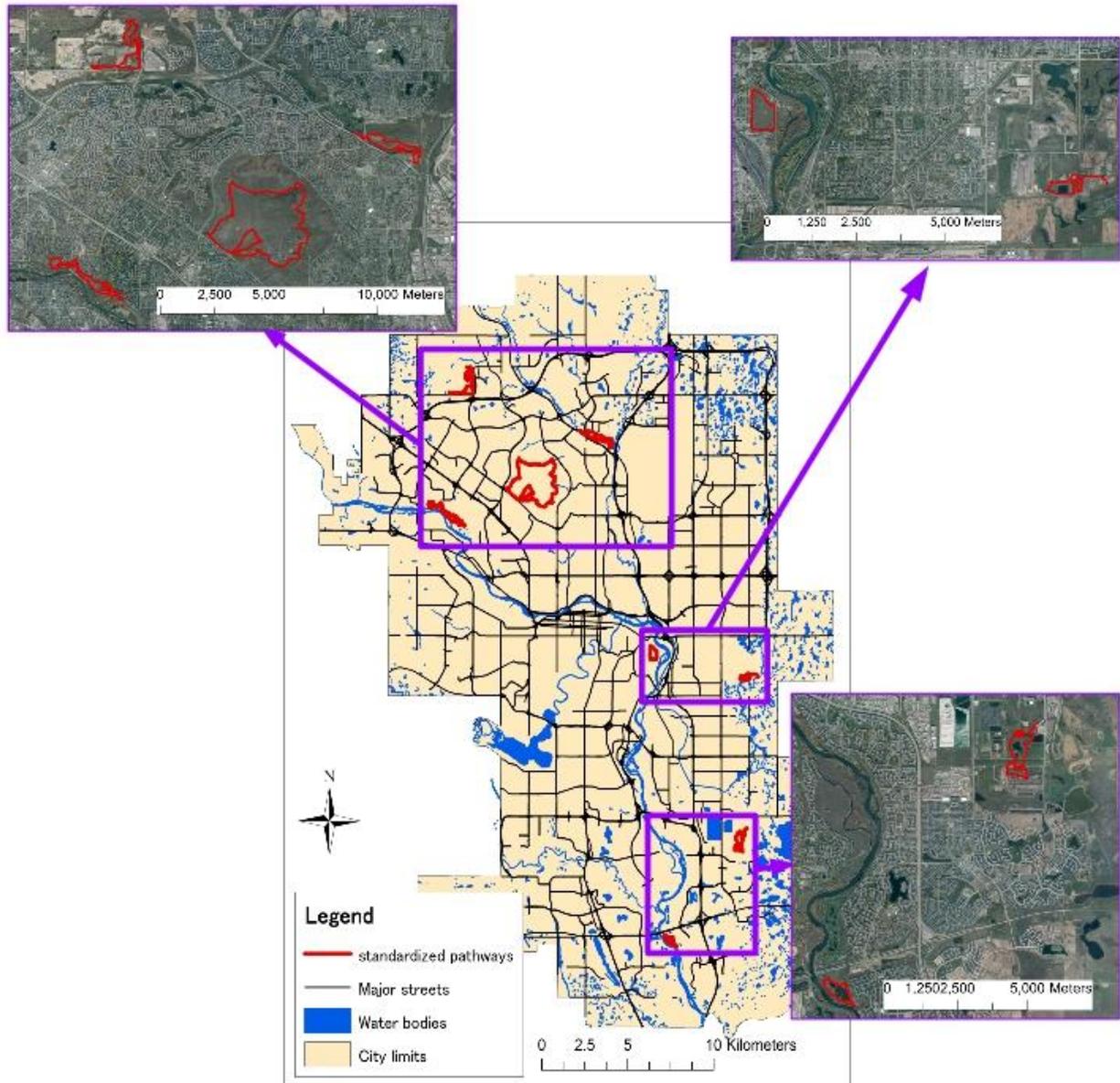


Figure 10: A map of the City of Calgary and the standardized pathways for coyote fecal surveys conducted in 2015.

To assess the ease of access to the sampling points by dog owners, which could also be related to the avoidance of the areas by wildlife such as coyotes, the distances to the nearest developed areas and trails from the sampling points were calculated. We defined the “developed area” as the land cover types of “roads/railroads” and “buildings/paved roads.” Maps of trails and footpaths inside the parks were obtained from the City of Calgary. The sampling points were also identified as whether they were within off-leash areas or not if they were in mixed park.

Terrain variables characterizing each sample point were calculated from a Digital Elevation Model (DEM) with a resolution of 0.75 arc per second, or approximately 18 meters (Natural Resources Canada, 2012). Terrain features of slope, aspect, and the ruggedness of the terrain (standard deviation of slope) were calculated from the DEM and the values at the sampling points were extracted.

To assess the environmental variables characterizing fecal samples from standardized pathways, the pathways were digitized by visually tracing the pathway using digital orthophotos of the Calgary area taken in year 2010 and prepared by the City of Calgary. Buffer zones of 10 m were generated around the pathways in order to assess the landscape that potentially influences the defecation behavior of coyotes. Because the standardized pathway survey consists of presence-only data, a same number of ‘pseudo-absence’ points as fecal samples were selected in this 10 m buffer area using the same random point generator used for the dog fecal matter sampling. The ‘pseudo-absence’ points were placed with a distance of at least 10 meters away from the presence points and from each other.

For each of the presence and ‘pseudo-absence’ point, the areas of each land cover type with a 10 m radius buffer zone, the characteristics of the terrain, and the distance from the nearest roads and buildings were calculated with the same procedure employed for random points. Because most of the standardized pathways were along trails, the shortest distance from the trail was not a meaningful variable and therefore was not included in the analysis on coyote feces. Instead of the distance from the trails and roads, distances from crossroads were calculated because coyotes are known to use as landmarks for territorial markings (Barja & List, 2014). Trail crossings were defined as points in which more than one segments of the trail map intersect.

4.3.3 DATA ANALYSIS

All the statistical analyses were conducted with R software, version 3.6.0. (Team, 2019).

4.3.3.1 Dog fecal contamination by leash law

The average density of fecal contamination was calculated as the number and gram of feces / ha / week from the survey in 2011. The differences in the average density of contamination between parks with different leash policy classes were tested using one-way ANOVA. Five parks were removed from the analysis because of the small number of sampling points (2 or 3). A Tukey test was performed to test the significance of pair-wise differences between the leash classes (Abdi & Williams, 2010).

Based on the average density of feces in off-leash areas and on-leash areas, the total amount of feces in the parks across the entire city was estimated. We assumed the survey in 2011 would be a reasonable representation of the snow-free period of approximately 6 months, as opposed to the entire year because

we expect somewhat different behaviors of dog/dog owners and the different detectability of feces in snow. The total area of parks in the city was also calculated using ArcGIS 10 from the map of the area the City Parks Services and map of off-leash area. Both maps were developed in 2019 and obtained from the City of Calgary. Although the map of the City Parks Services included “no-dog” areas, we assumed the “no-dog” areas were relatively small in sizes and therefore could be ignored in our estimate.

4.3.3.2 Dog feces distribution within parks

The spatial distribution of dog feces within the city parks were assessed by fitting a mixed effects Poisson distribution model to associate the number of dog feces found at each survey location (dependent variable) with independent environmental variables. The independent variables were: the dog allowance conditions (“no_dog”, “off”, “on” and “mixed”), the accessibility (distance from parking lots, roads, and trails), the area of each land cover types within the surveyed circular area of 10 m radius, and the terrain features (slope, average aspect, and ruggedness). The variability in the dog feces count was divided as within parks and in between parks. Model selection was performed by forward step-wise, and was based on the controlled Akaike Information Criterion, or AICc (Burnham & Anderson, 2002).

Analyses were carried out using the “*glmer*” algorithm in *lme4* package of R (Bates et al., 2014). The model goodness of fit was evaluated by assessing the R squared value (Nagelkerke, 1991) calculated using the function “*r.squaredLR*” of the *MuMin* package (version 1.40.4: Barton, 2009).

4.3.3.3 Coyote feces along trails

A logistic regression model with logit link function was used to assess the correlation between the presence of coyote feces along trails (dependent binary variable, with “0” defining the absence of feces and “1” for the presence) with independent environmental variables, comprising the terrain (slope, aspect, and ruggedness), land cover, and the distances from roads / buildings and from crossings of trails.

The final model was obtained using the “*dredge*” function of the package “*MuMin*” (version 1.40.4: Barton, 2009), which analyzes all the possible combinations of the explanatory variables and ranks the resulting models based on their corrected Akaike Information Criterion value (AICc; Fox, 2008). The model goodness of fit was evaluated by assessing the Nagdelkerke’s R squared value (Nagelkerke, 1991) and by comparing the full model with the null model through ANOVA (Fox, 2011) employing a Likelihood Ratio test.

4.4. RESULTS

4.4.1 CITY PARK FECAL CONTAMINATION

Total of 53 dog feces were found in 259 random point surveys of 2011. Dog feces were found on overall average of 0.2 per site in 2 weeks of survey (range: 0 ~ 6), which translates to 6.51 feces per ha per week. In terms of the mass, the overall average was 7.99 g of feces per site in 2 weeks (range 0 ~ 313.01 g), or 127.23 g per ha per week. Assuming that our surveys in June and August represent roughly the 6 months (~ 26 weeks) of the snow free times of the year, that leads to 169.26 feces and 3,307.98 g of feces per ha per 6 months. The highest density of the number of feces was found in Southland Park at 27.85 feces per ha per week, while the highest mass of feces was found in West Hillhurst at 1,362.37 g per ha per week (Table 4).

On average, “off-leash” parks were far more contaminated (4.4.2 DOG FECES DISTRIBUTION

The variable that explained the number of dog feces at each survey points with single variable best was the distance of the sampling points from parking lots followed by the leash policy. Most of the terrain and land cover variables resulted in little or negative improvements to the model. The final model included leash policy with a positive effect of off-leash policy, negative effect on on-leash policy, and strong negative effect for no-dog policy on the number of dog feces relative to mixed leash policy parks, and negative effects of distance to parking and distance to roads and buildings (

Table 7). The R-squared value of the model was 0.522.

4.4.3 COYOTE FECES DISTRIBUTION

Among independent variables assessed for the presence of coyote feces, the slope and ruggedness pair and Distance to trail crossings and grassland pair showed notable correlation of Pearson's correlation coefficient above 0.6 (0.788 and 0.705 respectively). The strongest predictor variables in the coyote feces model were the distance of the presence points from artificial structures such as roads and buildings and the environmental feature describing the percentage of soil devoted to agricultural practice. The best model included distance from crossroads with positive effects, distance from roads/buildings with positive effects, surrounding land cover (grassland with negative, agriculture with negative, manicured grass with positive, bare grounds with negative, roads/rails with negative), and all the terrain variables (slope with positive, ruggedness with positive, aspects of northing and easting with positive). Despite the statistical significance of the predictor variables, the goodness of fit of the model was low, with an R-squared value of 0.040.

4.5 DISCUSSION

For the extent of the fecal contamination, we found the rate of fecal contamination of the public parks in the City of Calgary was quite high. According to our calculations, more than 1.5 tons of dog feces can be washed into rivers and streams by a heavy rain, contaminating the water downstream of the city of Calgary every week. Because the dogs are in unnaturally higher density in those areas, the fecal contamination may have serious effects on local ecology and wildlife health.

Table 5). One-way ANOVA highlighted significant differences in density and amount of feces in these 4 types of parks ($df = 3$, $F = 14.02$, and $p = 0.0015$ for the number and $df = 3$, $F = 9.446$, and $p = 0.0053$ for the mass of the feces). Tukey-Kramer multiple comparisons test showed a significant difference between the off-leash and on-leash pair ($p = 0.001$), and between off-leash and no-dog parks pair ($p = 0.005$; Figure 11).

Based on the GIS map of the areas managed by the City Parks and the off-leash areas, and the size of Fish Creek Provincial Parks, there are total of roughly 13,133 ha of park areas in the City of Calgary, including 1,221 ha of the off-leash areas. Assuming the average of 642.10 g / ha / week in off-leash areas, the city would have total of 757.54 kg of fecal matter in the off-leash areas every week. Although the remaining 11,912 ha includes “no-dog” parks, assuming that “no-dog” areas are relatively small and average of 16.30 g per ha per week of “on-leash” areas are reasonable estimate, these remaining areas would have total of 665.79 kg of fecal matter every week, leading to 1,423.33 kg of fecal matter every week for the whole city. In other words, the city is contaminated by more than a ton of dog feces every week.

Total of 319 coyote feces were collected along the standardized pathways in the survey of 2015. Overall length of the standardized pathways was 46.87 km, which was surveyed 18 times, with the mean coyote feces of 0.42 per km per 10 days (Table 6). In general, there was a tendency to find coyote feces in higher density in the landfill areas ($N = 3$, mean = $0.67 / \text{km} / \text{day} \pm 0.014$) compared to the parks ($N = 5$, mean = $0.027 / \text{km} / \text{day} \pm 0.005$), though the difference was not statistically significant ($t = 2.61$, $df = 2.51$, $p = 0.095$).

Table 4. A table summarizing the leash law, area size, and number / mass of dog feces found in each of the area in the surveys in 2011. The number and mass of feces are show as found in survey, average rate per hectare per week, and the total feces estimated for the entire park in 6 months snow-free period

<u>Area</u>	<u>Leash law</u>	<u>Area (ha)</u>	<u>Number sampling point (x2)</u>	<u>Number dog feces found</u>	<u>Feces / ha/week</u>	<u>Total number in 6 months entire park</u>	<u>Total mass of feces found (g)</u>	<u>Mass / ha / week (g)</u>	<u>Total mass in 6 months entire park (kg)</u>
Bowmont Park	Mixed	164	25	6	3.82	407182.02	359.64	228.95	976.26
Edworthy Park Lower	On	108.28	12	1	1.33	3733.91	21.86	28.99	81.62
Edworthy Park Upper	Off	60.72	8	9	17.90	28266.82	397.89	791.58	1249.68
Fishcreek Provincial Park	On	1348	88	6	1.09	38030.58	291.57	52.73	1848.18
Inglewood Wildland	No dog	34	9	0	0.00	0.00	0.00	0.00	0.00
Inglewood Bird Sanctuary	No dog	36	4	0	0.00	0.00	0.00	0.00	0.00
Martindale	On	2.63	2	0	0.00	0.00	0.00	0.00	0.00
Meadowlark	On	1.39	2	0	0.00	0.00	0.00	0.00	0.00
Nose Hill Park	Mixed	1129	51	3	0.94	27481.21	56.74	17.71	519.77
Nosecreek	Off	18.04	3	0	0.00	0.00	0.00	0.00	0.00
Riverpark	Off	21	7	5	11.37	6207.04	117.42	266.97	145.77
Southland low	On	36.55	3	0	0.00	0.00	0.00	0.00	0.00
Southland park	Off	62	12	21	27.85	44897.62	654.16	867.61	1398.58
Stanley park	On	21	5	0	0.00	0.00	0.00	0.00	0.00
Taradale	Mixed	21.59	2	0	0.00	0.00	0.00	0.00	0.00
Weaselhead	On	237	24	0	0.00	0.00	0.00	0.00	0.00
West Hillhurst	On	1.11	2	2	15.92	459.32	171.20	1362.37	39.32

4.4.2 DOG FECES DISTRIBUTION

The variable that explained the number of dog feces at each survey points with single variable best was the distance of the sampling points from parking lots followed by the leash policy. Most of the terrain and land cover variables resulted in little or negative improvements to the model. The final model included leash policy with a positive effect of off-leash policy, negative effect on on-leash policy, and strong negative effect for no-dog policy on the number of dog feces relative to mixed leash policy parks, and negative effects of distance to parking and distance to roads and buildings (

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4.5 DISCUSSION

For the extent of the fecal contamination, we found the rate of fecal contamination of the public parks in the City of Calgary was quite high. According to our calculations, more than 1.5 tons of dog feces can be washed into rivers and streams by a heavy rain, contaminating the water downstream of the city of Calgary every week. Because the dogs are in unnaturally higher density in those areas, the fecal contamination may have serious effects on local ecology and wildlife health.

Table 5. A table summarising the dog fecal contamination of urban parks of the City of Calgary, classified into 4 categories based on the lease law of the park. The fecal contaminations are described using mean (\pm SE) number and mass (in gram) of feces found in each of the leash laws categories per hectare per week collected from random points within urban parks in the City of Calgary in the year 2011. “Off-leash” parks do not require dogs to be on leash, “On-leash” parks require dogs to be on the leash all the time, and “mixed” park has areas that are off-leash and on-leash. “No dogs” parks do not allow dogs at all.

	Off-leash	Mixed	On-leash	No dogs
Number of Feces (/ ha / week)	19.04 (\pm 2.77)	2.38 (\pm 1.02)	0.48 (\pm 0.13)	0
Fecal Mass (g / ha / week)	642.05 (\pm 109.01)	123.33 (\pm 7.47)	16.35 (\pm 4.78)	0

Table 6. A table summarizing the coyote fecal contamination of the urban parks and landfill areas in the City of Calgary in a survey conducted in 2015. The coyote feces were collected along standardized pathways, surveyed 18 times each. The length of the standardized pathways, the number of coyote feces found, and the overall average per km in each area are shown.

Area	Length (km)	Number of Coyote	
		Feces Found	Feces / km
Shepard Landfill	5.15	44	0.47
East Calgary Landfill	3.27	56	0.95
Inglewood wildland	2.09	10	0.27
Nose Hill Park	13.26	71	0.30
Bowmont Park	7.71	28	0.20
Fish Creek Provincial Park	2.37	19	0.44
Confluence Park	5.81	15	0.14
Spyhill Landfill	7.22	76	0.59

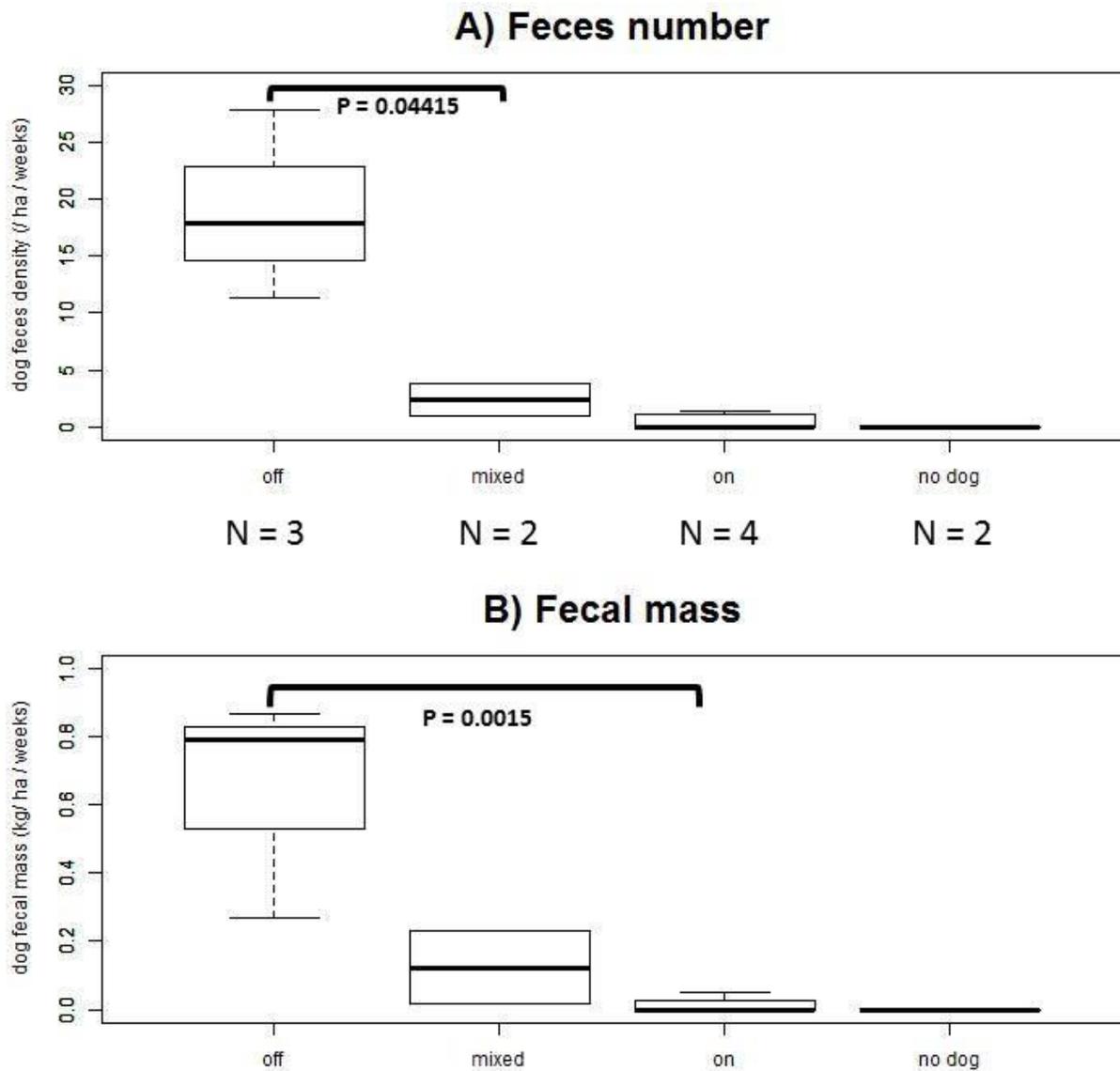


Figure 11. Dog fecal contamination in terms of the number (A) and mass in kg (B) in per hectare per week in the parks / natural areas in the City of Calgary (AB, Canada) in surveyed in summer 2011 in relation to their dog leash laws; “off” for parks where dogs are allowed off-leash, “on” for parks where dogs are allowed on-leash, “mixed” for parks containing both off-leash and on-leash areas, and “no dog” for parks where dogs are not allowed. The numbers of feces were significantly different between off leash parks and mixed parks, while the masses of feces were significantly different between off leash and on leash parks but not between off leash and mixed parks based on Tukey tests (p-value shown).

Table 7. A table details the results of the Poisson model for the number of dog feces in randomly selected survey locations. a), b) and c) Leash is a categorical variable indicating the leash law of the park, where no-dog is the parks where dogs are not allowed, off is where dogs are allowed off-leash, and on is where the dogs are allowed if they are on-leash; parks with both on-leash and off-leash areas were used as the base level; d) the distance of the points from artificial constructions such as roads and buildings; e) the points distance from the nearest parking lot in the parks. The p-values of variables with statistical significance (>0.05) are highlighted with bold fonts.

	Estimate	Std.error	Z value	Pr(> z)
Intercept	0.2421	0.4926	0.491	0.6232
Leash no-dog ^a	-28.19	491400	0	1
Leash off ^b	0.8078	0.4218	1.915	0.0555
Leash on ^c	-1.504	0.4993	-3.012	0.0026
Distance road & building ^d	-3.538e-03	2.009e-03	-1.761	0.0782
Distance parking ^e	-2.950e-03	7.445e-04	-3.963	7.4 e-5
AICc	217.7444			
R ² value	0.5224			

Off leash-laws seemed to significantly affect the amount of dog feces left unpicked by owners, indicating that dog owners usually pick the dog feces if they observe the dog defecation. For the park users the results of more concern may be that more dog feces were found near the park entrances and parking lots, which makes them more likely to be exposed to most park visitors. Defining and enforcing leash-laws for the parks would be an effective method for controlling fecal contamination. However, dog owners often find the ability to walk dogs off-leash to be an important quality of a park (Westgarth et al., 2014).

The fecal contamination of the public parks by coyotes was rather small, averaged slightly more than one feces in every 4 km of trails every ten days, or slightly less than one in every 2 km when landfill areas are included. However, despite the low contamination level coyotes' preference to defecate on trails makes their feces more exposed to park users, degrading the value of the parks to the park users (Teedon et al., 2014). It also makes the coyote feces more likely to be stepped on by people, ran over by the bikes, or sniffed at by dogs. Considering the potential for zoonotic, such contacts can be of grave concern. We recommend monitoring of

infection status of coyotes inhabiting public parks, as well as monitoring of dogs and people for possible spill-over by public health community.

We could not find clear patterns with coyote feces within parks or landfill areas, other than that they prefer to defecate along the trails. Coyotes are known to scent mark their territories using urine and feces (Barja & List, 2014; Barrette & Messier, 1980) and are expected to defecate in conspicuous locations (Barja et al., 2004). The fact that we could not find clear preferences on the defecation may indicate that trails are strong enough cue for coyotes that other factors have relatively weak effects, or utilize cues that are not represented in the geographical data we used in the modeling. Study by Barja and List (2014) indicate that coyotes use feces as scent markings, and place their feces on conspicuous places, crossroads, and near food source such as carcasses of a large animal. However, we found little effect of distance from trail crossings. Although we did not find correlation between coyote feces and trail-crossings, there are many other features that are likely used by coyotes and not described at the scale of most available spatial data. For example, there could be trails and paths that coyote and wildlife uses that are not present in the trail map we used. If the feces are deposited in crossings with such trails, our model would not be seeing any patterns. Wolves in Europe were found to use the height and diameter of plants in addition to species as cues for scent marking (Barja, 2009), something our geographical data of land cover are too coarse to capture.

Another possible pattern we missed in our coyote's fecal distribution model could be the location of the coyotes' dens and territories, around which the scent markings are made (Barja & List, 2014). It is also known that season and the structure of the local coyote packs can also influence the frequency and locations of the coyote's scent markings including the defecation (Gese & Ruff, 1997). Although the frequency of the defecation do not change by the season, the coyote activities are concentrated near the den during the breeding season and widespread during the dispersal season (Andelt & Gipson, 1979; Gese et al., 2012). However, obtaining data such as small game trails, plant sizes, and locations of coyote dens / territories require local and continuous studies, and are usually not available for most urban areas. For most park managers, it may be sufficient to know that coyotes tend to defecate along trails. Overall, we found the fecal contamination of public parks by dogs as potentially serious issue that requires attention by park

managers and public health workers. The fecal contaminations by dogs were quite high, and feces of both dogs and coyotes were likely placed at spots that expose them to park users.

4.6. CONCLUSION

Large quantity of dog feces are added to the public parks, estimated to be more than 1.5 tons for the entire City of Calgary every week. The feces were found in greater quantity in off-leash parks, and near park entrances and parking lots. Coyote feces were found in smaller quantity than dogs, and more frequently found along trails and pathways.

CH 5: MODELING THE EPIDEMIOLOGY OF TROPHICALLY TRANSMITTED PARASITES WITH COMPLEX LIFE-CYCLE IN AN URBAN LANDSCAPE: AN AGENT-BASED MODELING APPROACH

5.1 ABSTRACT

Epidemiological models are essential in managing disease risks. However, the traditional epidemiological models are less applicable to complex life-cycle parasites. *Echinococcus multilocularis* (*Em*) is such a parasite that is naturally present among wildlife and causes a serious zoonosis. Its transmission is indirect (through predation of intermediate hosts by definitive host), hosts display territoriality and distinct home ranges, often within a heterogeneous landscape, and they present high diversity in parasite load. In order to incorporate these important complexities, we developed the Calgary *Echinococcus multilocularis* Coyote Agent-based model (CEmCA). Using the CEmCA, we tested three mutually non-exclusive hypotheses that may explain an observed spatial heterogeneity of *Em* prevalence, deemed to be due to intermediate hosts communities, coyotes' behaviors, and separation of habitats. The simulations suggested that distribution of intermediate hosts and separation of habitats can cause spatial heterogeneity. The simulations also suggested other key information that can have serious influence on the transmission were missing. This study is a novel attempt to understanding the epidemiology of a trophically transmitted parasite with complex life-cycle, and notwithstanding our model requires further work, this approach holds many promises.

5.2 INTRODUCTION

Epidemiological models are essential in understanding, predicting, and managing disease risks. Traditional epidemiological models such as SIR models were based on mass transaction models (Anderson & May, 1982), which assess the transmission of a parasite at the population level. These models generally assume all the individuals interact with each other homogeneously, and any individuality will average out at the population level (i.e. mass action: McCallum et al., 2001). However, it is becoming increasingly known that for many epidemiological systems, the assumption of homogeneous population misses many of the important processes of the transmission that occur at an individual level (Lane-deGraaf et al., 2013; Lanzas & Chen, 2015).

Spatially explicit agent-based models (ABM) offer alternate methods to the traditional mass transaction models for the analysis of epidemiological systems (Duan et al., 2015; Willem et al., 2017). Agent-based

models simulate individual units in a system called agents as they interact with each other and with the landscape. Agent-based models allow researchers to model and assess heterogeneity among individual hosts and landscape, instead of the population average. In many epidemiological systems, such heterogeneities are key elements in understanding the processes and mechanisms (White et al., 2018a, 2018b).

Echinococcus multilocularis (*Em*) is a species of parasitic tapeworm that causes human alveolar echinococcosis, considered as one of the most serious zoonotic diseases in non-tropical regions (Massolo et al., 2014). In urban areas of the City of Calgary, *Em* has been detected among wild small mammals and coyotes at high prevalence (Catalano et al., 2012; Liccioli et al., 2012). In interior north America, where alveolar echinococcosis was considered very rare traditionally, there has been signs of emergence as new cases are being reported and is a cause of grave concern (Belga et al., 2017; Massolo et al., 2014). Within the city, there was large heterogeneity on the intensity of infection among individual hosts, and on the prevalence between different areas of the city and at different time of the year (Liccioli et al., 2014).

While many studies have analyzed *Em* epidemiology, they were usually conducted by isolating a component of the system, such as the survival of eggs in a natural environment (Veit et al., 1995), behavior or the spatial distribution of the host species (Guerra et al., 2014; Liccioli et al., 2014). However, there is a gap in the knowledge on how these components interact to create the patterns in the transmission. Understanding how these patterns emerge in turn allow managers to effectively allocate resources in reducing the risks of diseases to people (Nishina & Ishikawa, 2008), particularly in urban landscapes. In order to integrate various studies, epidemiological models are needed.

However, the *Em* transmission involves highly complex systems (such as the urban ones) that are difficult to be represented with traditional epidemiological modeling approaches. *Echinococcus multilocularis* is a trophically transmitted parasite with a complex life-cycle that involves two different hosts (canid predator definitive host, DH hereafter; small mammal intermediate host, IH hereafter) and a free-living stage. Multitudes of complexities in the system can interact and influence the transmission of *Em*, including social groups and territoriality (Conner et al., 2008; Nunn et al., 2008), complex landscape (Lane-deGraaf et al., 2013), and behavior (Barja & List, 2014; Liccioli et al., 2015a). In order to incorporate such complexities into a model, we developed a spatially-explicit ABM of *Em* epidemiology.

In this paper we describe a spatially explicit agent-based model of transmission of complex life-cycle parasites that are transmitted through a predator-prey interaction, using *Em* among wild coyotes in the city of Calgary urban areas (Calgary *Echinococcus multilocularis* Coyote Agent-based model or CEmCA for short). The purpose of CEmCA was to understand the epidemiology and mechanisms that result in the

spatial heterogeneity of *Em* prevalence in definitive hosts in an urban environment, using the City of Calgary as a case study.

In particular, we tested three hypotheses on how the spatial heterogeneities of DH prevalence were produced, namely:

Small mammal assemblages and the proportion of susceptible species determine the local prevalence among DH (IH hypothesis).

Configuration of the local landscape leads to concentration or diffusion of DH activities related to the transmission in smaller area, leading to difference in the prevalence among DH (DH hypothesis).

Separation between natural habitats in urban landscape limits transmission between these areas, forming a kind of metapopulation for the parasite. This leads to differences in local prevalence just by chance (metapopulation hypothesis).

5.3 MATERIALS AND METHODS

5.3.1 SIMULATION SPACE, EXTENT, AND LENGTH

The City of Calgary is located in southwestern Alberta, Canada (51°5'N, 114°5'W), in the foothills of the Canadian Rocky Mountains. It has a growing population of 1.24 million inhabitants and covers an area of 825.56 km². The city has several rivers and creeks, most notably Bow river and Elbow river that converge in the city. The surfaces of these major rivers usually do not freeze over completely in winter, making a significant barrier to the wildlife movements. The city has several parks with the total area of 13,133 ha (The City of Calgary, 2015), 50.6% of which is natural areas (Calgary, 2018). Common habitats in parks and natural areas are grasslands in dry areas, aspen forests in moderately well-drained areas, and willow shrublands in imperfectly drained areas (The City of Calgary, 2014).

We limited the spatial extent of our model and the number of coyotes simulated so the computation time of the model is kept manageable. We focused our model around Nose Hill Park (NHP) and Bowmont Park (BM) in north-west Calgary (Figure 12), areas that are utilized by resident coyotes and where the prevalence estimates of *Em* among coyotes showed high heterogeneity (63.07% in BM, 17.28% in NHP; Liccioli et al., 2014). The extent of the simulation space was designated as the rectangular areas that encompass NHP, BM, and 5 km buffer around the two parks. We considered the 5 km buffer as a reasonable buffer based on the literature report on their home range size and movement distance (Andelt & Gipson, 1979; Gese et al., 2012).

The simulation was designed to run for 5 years of actual simulation, with another year at the start as a spin-up to allow coyotes to learn the landscape. We considered the simulation length of 5 years a reasonable length for epidemiological pattern of emerge after several transmission life-cycles of *Em*, whose generation time can be estimated as roughly 4 to 12 months (Ishikawa et al., 2003).

5.3.2 MODEL DESCRIPTION

The CEmCA was developed using NetLogo software (Wilensky, 1999). This software allowed us to visually assess coyote movements in the simulation, where and how it moved through the landscape of Calgary and compare them with our understanding of coyote movements (Figure 13). For a detailed description of the model mechanisms and its sub-models, see the supplementary material (Appendix 2).

5.3.2.1 Input data

The simulated landscape was represented as a rectangular space discretized into raster cells. The raster cells have the resolution of 50m by 50m square based on the resolution of the map of coyote permeability map (Lamy, 2015). The size of each cell was considered a reasonable size to be used as a home range of small mammals (Madison, 1980). Each cell was assigned a set of state variables that indicate the land cover type (The City of Calgary, 2015), permeability for coyote movement (Lamy, 2015), and whether there are any trails running through the cell (The City of Calgary, 2017). Assemblages of small mammal (species composition, density of each species) in the City of Calgary were classified into three types, and each natural land-cover cells were assigned to one of these types (Mori et al., 2019). The areas of the natural land-cover were also divided into patches of contiguous and homogenous land-cover as units of land the coyotes perceive (Figure 14).

Weather data and time of sunrise-sunset were included in the CEmCA for the simulation of *Em* epidemiology. The average temperature and snow depth for each day of the simulation were obtained from Natural Resources Canada (2018) and used to model the change in infectivity of *Em* eggs in coyote feces. The sunrise-sunset times were obtained from National Research Council of Canada (2016) which influenced behaviour of coyotes in the model.

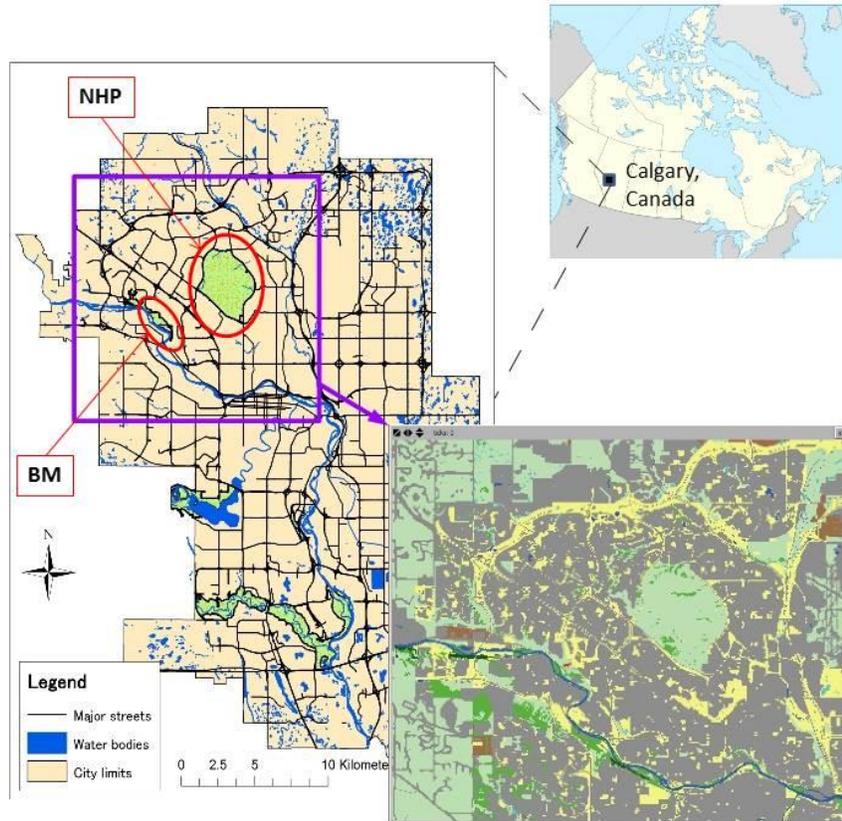


Figure 12: A map showing the area of the City of Calgary, Alberta, Canada, that was modelled in the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA (left) and its representation in the CEMCA (lower right). The CEmCA screen shows grassland areas in light green, forested areas in dark green, manicured grass in yellow, bare grounds in brown, water surface in blue, and urban areas in grey.

5.3.2.2 Entities

The primary agents in the CEmCA are individual coyotes. Each coyote is defined by a set of state variables defining their identity, location, behavior, and whether or not they are infected by *Em*. They also have state variable indicating their status as breeding (alpha) or non-breeding (beta) adult of a pack, or newly born pup/juveniles (Gese et al., 1996a). They are also given unique identifiers linking them to other agents. Their behavior was categorized by four **purposes** (*eat, rest, den, explore*) determined by the state variables of the coyotes and time of the day (day/night) and year (season), and three **activities** (*hunt, hide, travel*) among which they choose to fulfill their purpose.

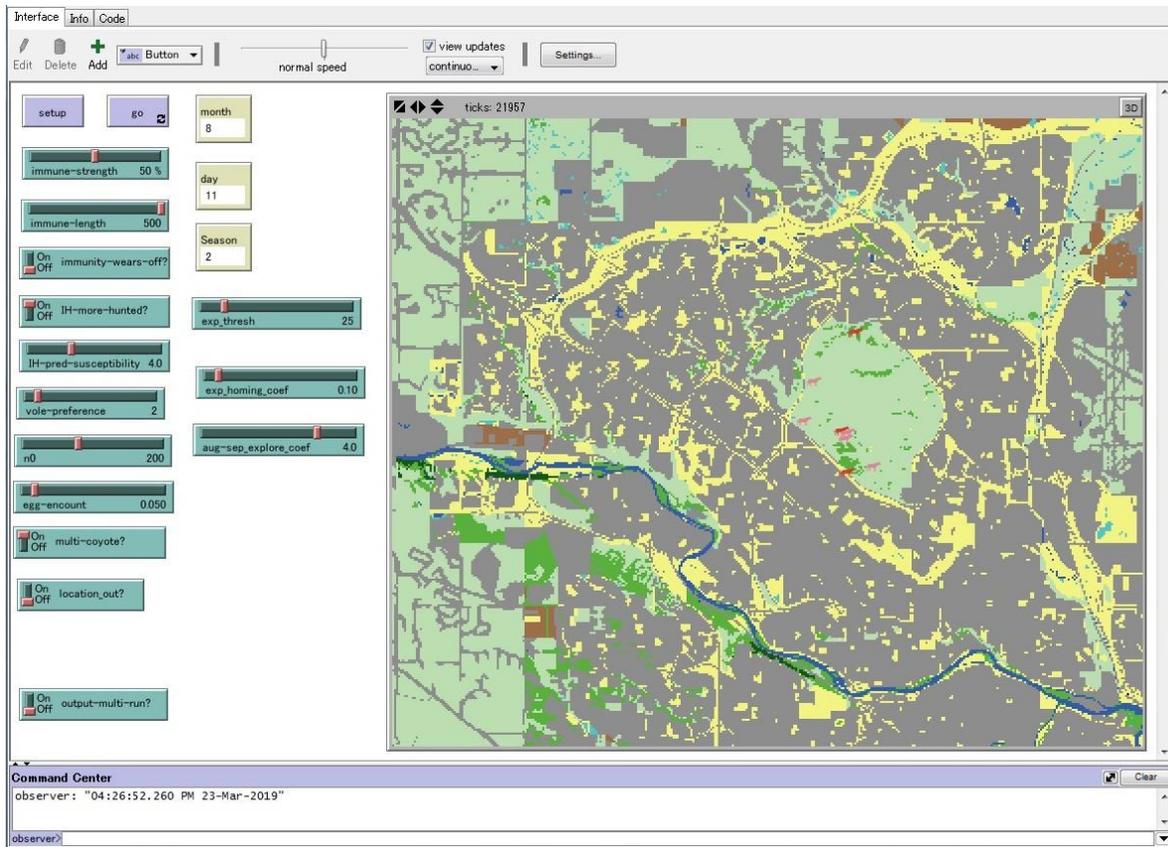


Figure 13: A screen shot of the *Calgary Echinococcus Multilocularis Coyote Agent-based model, CEmCA*, showing the landscape of north-western portion of the city of Calgary, Alberta, Canada. The screenshot also shows the locations of eight coyotes shown in red for adults and pink for newly born pups/juveniles. Several gauges and switches on the left of the screen allow users to manipulate some parameters easily.

Another entity in the CEmCA is the land. Lands are discretized into 50 x 50 meters square grids or cells. Each cell is identified by state variables indicating its location in XY coordinate, land cover type, permeability to coyote movement (Lamy, 2015), presence of trails, small mammal assemblage type, and identity of patch of habitat it is part of. Each cell also keeps track of the number of *Em* eggs, number of IHs, and the prevalence of *Em* infection among small mammals overall and among each species.

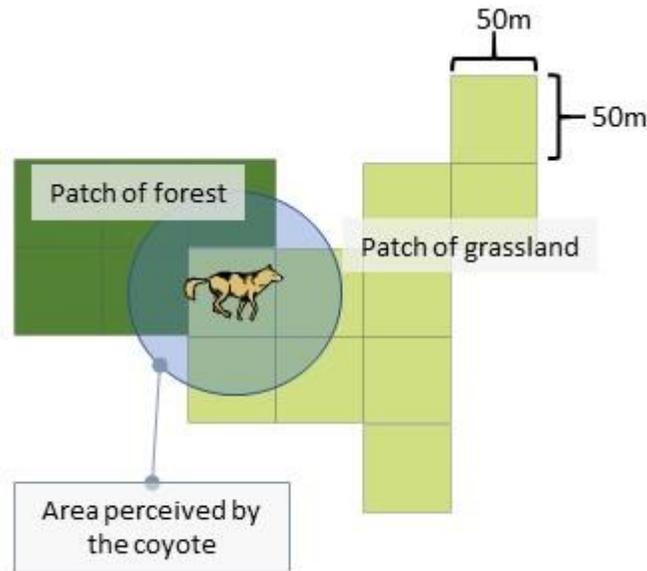


Figure 14: A diagram showing how the landscape is modelled in the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA. The landscape consists of square cells of 50m by 50m, and each of these cells has state variable designating its land cover. Group of connected cells with same land cover forms patches. Coyotes can perceive all the patches within one cell (i.e. 50m) of itself, so the coyote in the figure can perceive the patch of forest in addition to the patch of grassland it is in. The patch of forest and the patch of grassland are added to the memory of the coyote.

Another major entity in the CEmCA is *Em*. The parasites are represented as agents that can occur in three different states or stages (worms infecting individual coyotes, eggs inside feces, and larvae infecting small mammals). For simplicity, the *Em* worm agents were assumed to represent a “cohort” of worms that infected coyotes from a single IH. Worms have state variables identifying the host coyote, the number of worms in the cohort, and number of days since they infected the host. Similarly, the *Em* egg agents were not individual eggs but a “cohort” of eggs in one feces (they may also be described as agent feces). The eggs are immobile and bound to a cell of land. Their state variables identify the location and number of viable eggs in the feces, which is used for calculating the infection probability on potential IH. The larvae are individual small mammals that are assumed to have home ranges so small such that they are treated as immobile and bound to a cell of land. The IH agents have state variables indicating their location, species, the number of days since infection, and the number of *Em* protoscoleces which is determined by the days since infection.

The coyote packs are entities linking the coyote agents that belong to same family/packs and for keeping track of the epidemiological status of each pack separately. The packs have state variables recording the

prevalence of *Em* among coyotes in that pack, the total number of *Em* worms found within the pack, and the maximum intensity of worms found within the pack.

5.3.2.3 Design concepts

The CEmCA is designed based on an assumption that the patterns of *Em* transmissions emerge from DHs' behaviors such as where and what they hunt, and where they defecate. These behaviors in turn form from their perception and interaction with the landscape.

In the CEmCA, coyotes' behaviors emerge from compilation of simpler models. Coyotes' home range emerges from coyotes learning and memorizing the habitat patches they have visited or seen before, and choosing the preferred land cover. From these memories, they choose where to hunt or rest, based on the model described in Van Moorter et al. (2009), and where to travel through the landscape using biased and correlated random walk (Barton et al., 2009). Coyotes also take behaviors of exploration and attendance to den. In dispersal season, coyotes tend to explore farther and more often, while in pup-rearing season they tend to attend the den more often. A combination of these behaviors was designed to make coyotes' home range and use of lands for hunting and defecation realistic.

The model of coyote behaviors interacts with the model of *Em*. The model of *Em* considers three parasitic stages: (eggs, inside IH, inside DH). For each one of these stages there are simple models describing the number of viable eggs, the number of protoscoleces inside each IH, and number of eggs to be released in the fecal stool (i.e., next defecation event). The transmission between the DH to eggs, and IH to the DH, is a result of the coyotes' behavior.

5.3.2.4 Process overview and scheduling

The model moves by time steps of 30 minutes. At each time step, each coyote makes decision on its purpose, its activity based on its purpose, then take the action. While the coyotes take actions, they can become infected to *Em*, defecate, learn their surrounding landscape, and forget older memories of the landscape. Once all the coyotes in the simulation have made decisions and took action, the simulation moves to next time step.

The simulation runs with only set number of adult coyotes for one year, allowing the coyotes to learn the landscape. After one year, *Em* are introduced as adult worms to coyotes designated based on the simulation scenario. Afterwards, once a day, after all the coyotes have taken the above actions, each *Em* agents in the simulation will take action too. Each of the worm cohorts inside coyotes ages (and dies out at certain age) and produces eggs inside coyotes based on the number of worms and their age. Each of the egg cluster inside feces loses a certain number of viable eggs (and dies out if no more eggs are alive), based on the average temperature of the day, and the surviving eggs infect small mammals in the cell at a

probability determined by the number of eggs and by the density of small mammals inside the cell. Each of the infected small mammal (IH) ages (the number of days since infection), and the number of protoscoleces inside IH are calculated from its age (see appendix 2 for detail).

After the one year of simulation, each pack of coyotes reproduce litter of 3 to 8 pups once a year (Harrison & Gilbert, 1985). These pups are introduced at August 1st in simulation time when they start hunting small mammals on their own (Harrison & Harrison, 1984), and disperse in middle of November or February (Harrison, 1992) disappearing from the simulation (Figure 15).

The simulation ends after six years (five years of infection dynamics) on May 1st.

5.3.2.5 Submodels

Here we briefly describe main processes of the CEmCA. For more detail see appendix 2.

Coyote decision making

The coyote in CEmCA make decisions on its purpose and activities using heuristics rules. The decisions on its purpose are influenced by the season, the time of the day, the time since last hunt, the sex and class (adult or juvenile) of the coyote. Once the purpose is decided, then the coyote decides its activity based on the purpose and the current location of the coyote.

Coyote activities

In travelling, the coyotes can make 8 to 16 steps over the land cells within 30 minutes time step. The coyotes are assumed to travel through the landscape using biased and correlated random walk model (Barton et al., 2009). The coyote first decides its destination based on its purpose, such as hunting ground for the purpose to *eat*, den location for the purpose to *den*, etc. The coyotes are assumed to know the direction of their destination, and try to move toward that direction, try to stay in same course from its previous movement, and also try to choose a path that is easiest to travel through according to the permeability values. When the coyotes have purpose to *explore*, their movements are also influenced by the distance and the direction to their den, so that farther away from the den they are more likely to move toward the den.

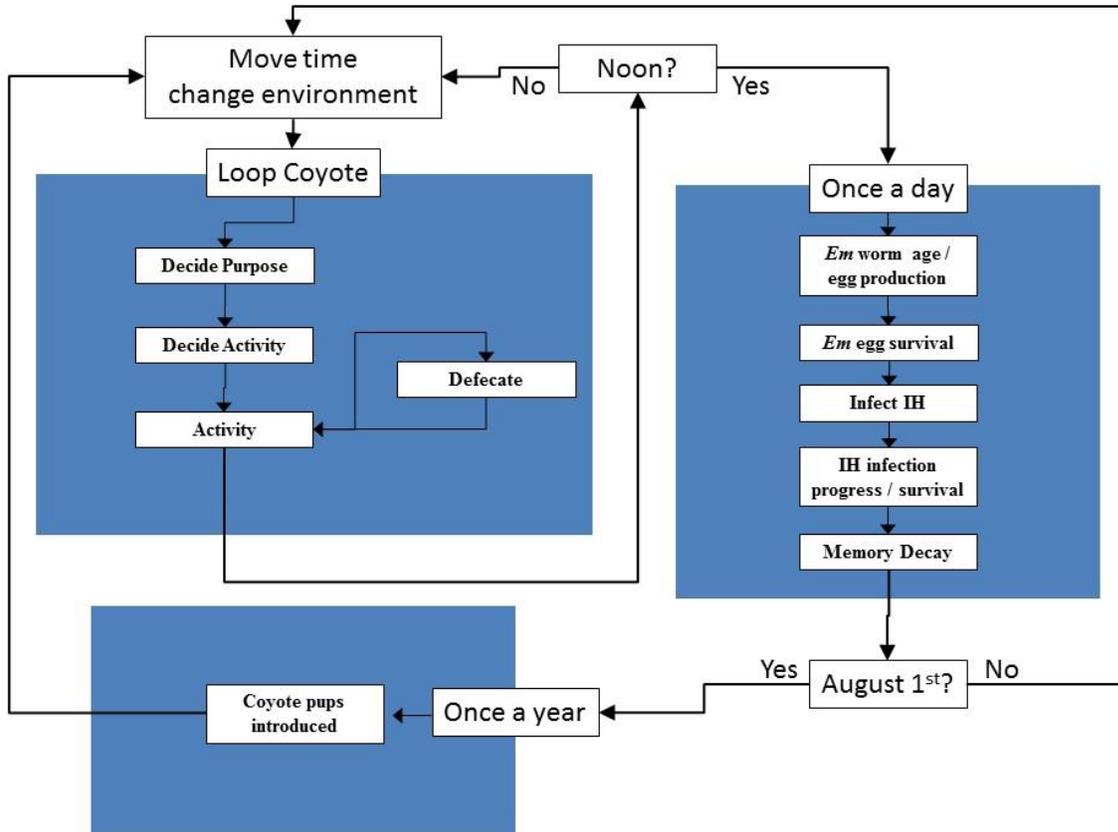


Figure 15: A flow chart showing the processes of the Calgary *Echinococcus multilocularis* (*Em*) Coyote Agent-based model, CEmCA. All the coyotes in the CEmCA takes decisions / actions at each time step. Once a day, submodels related to *Em* are processed. Once a year, coyote pups are introduced.

While hunting, the coyotes make random movement within lands that have natural land cover, search for a prey, attempt to catch a prey, and possibly become infected with *Em* six times within a time step. The success of prey search is dependent on the density of small mammals perceived by coyotes in the cell, which is in turn dependent on the assemblage type and season. In addition, some species of small mammals are perceived with higher density at some seasons, because they are assumed to be easier to detect or more actively searched by coyotes, and coyotes are assumed to seek small mammals as prey items more or less by season, influencing the perceived density of that species (Liccioli et al., 2015a). The success of prey capture following the detection is again dependent on the species and season.

While a coyote is resting, it simply stays immobile in a cell with natural land cover.

Coyotes become ready to defecate after predetermined time steps, calibrated to match the reported defecation rate (Monroy-Vilchis & Frieven, 2006). Coyotes can defecate in midst of hunting, travelling,

or resting if they are ready to defecate, is in a cell that has natural land cover type and has trails (Barja & List, 2014; also see chapter 4).

Coyote memory

Coyote agents have two types of memories, namely reference memory and working memory. Both memories simply consist of list of patch ID and associated memory strength of that patch. Coyotes constantly learn the patches of natural habitats and record or renew them in reference memory, while coyotes only record or renew the working memory of the patch of the cells they hunt in. The coyote chooses where to hunt or rest based on these memories, and stronger the reference memory the more likely the coyote is likely to choose that patch. Unlike the reference memory, for the working memory stronger the memory is the less likely the coyote is to choose that patch. The initial strength of the working memory is stronger than the reference memory, but the working memory degrades faster than the reference memory. This was intended to prevent coyotes from going back to same spot repeatedly (Van Moorter et al., 2009).

5.3.3 CALIBRATION

We conducted the following calibrations of the behaviors of the coyotes in the CEmCA (Grimm & Railsback, 2005). Unless otherwise described, calibrations were conducted with a single adult coyote in the system in order to accelerate the computation. In these simulations, the coyotes were placed in NHP, where a larger contiguous natural area is likely to make the coyote behave as in a natural environment similar to the environments of the studies used to calibrate. An averaged outcome of ten simulations were used for the calibration.

5.3.3.1 Time spent in each activity

We calibrated coyotes in the CEmCA to spend time on the three types of activities of hunt, travel, and rest, as it was described in (Gese et al., 1996a). Although this study was based on field observation in Yellowstone National Park in United States where coyotes' behaviors are expected to be different from that of Calgary urban areas, it described the coyotes' behavior in more detail than any other studies to the best of our knowledge. In order to calibrate the coyotes' behaviors, the parameters dictating the coyotes' decisions on purposes were adjusted in *ad hoc*. The simulation recorded the activity of coyotes at every time step, and the resulting percentage of time spent for each activity per season as compared with that in (Gese et al., 1996a).

5.3.3.2 Home range size

We calibrated coyote exploration behavior to match the patterns described in Gese et al. (2012). This study was chosen because it describes the differences in the sizes of home ranges by season and by the

degree of urbanization of the landscape. In order to calibrate the home range sizes of coyotes, the parameters used in the coyote's exploration behavior were adjusted in *ad hoc*. Parameters that determine the frequency and length of the explorations were adjusted, as well as the coefficient in the coyotes' correlated and biased random walk algorithms that makes coyote's likelihood to turn toward its den. We also looked into the difference in the home range sizes for coyotes placed in BM and NHP, as differences in the urbanization were known to change the size of home ranges (Gese et al., 2012). We also tested the difference in home range sizes by sex as male and female were observed with different home range sizes in some studies (Andelt & Gipson, 1979).

In order to obtain the home range size of the coyotes in the CEmCA, their locations were recorded at the end of every 30 minutes time step. These locations were converted to coordinates in meters (multiply by 50m/cell) and used to calculate home range sizes using the package *adehabitatHR* in R software (95% minimum convex polygon method; Calenge, 2006).

We calibrated the home ranges of coyote pups at the first three months of their introduction into the model according to the study by Harrison et al. (1991). For these calibrations, the simulation was run with multiple coyotes, and five pups that were introduced every year. After November the home ranges of pups are indistinguishable from those of adults according to Harrison et al. (1991), so their parameters were set equal to adults.

5.3.3.3 Den visit frequency

The parameters for coyotes' decisions in attending dens were calibrated to produce the pattern observed by Andelt et al. (1979). First, the total length of time the coyote spends with the activity of *hiding* at the den during the nighttime were recorded. Second, the frequency of days the coyote being found *hiding* at the den during the daytime were recorded. These were again looked into the differences between male and female.

5.3.3.4 Diet

Coyote diet was calibrated based on analysis of coyote feces collected in the City of Calgary (Liccioli et al., 2015a). In order to calibrate coyote diet, the number of each small mammal species consumed in each season in the simulation were recorded. The number of small mammals consumed per season (by total and by each species) were calibrated by changing the efficiency of prey search and capture, and on preference by season and prey species.

5.3.4 SENSITIVITY ANALYSIS

Simulations were conducted while changing the following parameters systematically, running 10 simulations at each parameter combination. The sensitivities were analyzed by comparing the mean infection prevalence of the last year the simulations.

The rate at which IHs contact *Em* eggs in the field was unknown (egg-contact rate). In order to understand its impact on the transmission of *Em*, simulations were conducted while systematically varying the rate at which small mammals encounter feces containing infective *Em* eggs per day, given that both the feces and small mammal were present in a cell. Another important but unknown aspect of the dynamics was how vulnerable an infective IH is to predation by coyotes compared to an uninfected small mammal (IH-predation; Vervaeke et al., 2006). A susceptibility parameter was introduced that multiplied the probability of an infective small mammal being detected and hunted by a coyote (see Appendix 2.7.3 for detail).

5.3.5. VALIDATION

For the validation of CEmCA's performance, the results from the sensitivity analysis were compared to the observations. We adopted pattern-oriented modelling approach in assessing our validation (Grimm et al., 1996). Three patterns of *Em* epidemiology in the City of Calgary were chosen for the validation purpose, namely spatial patterns in prevalence among DHs, seasonal patterns in the prevalence among DHs, and patterns of *Em* infection intensity among individual DHs. These patterns were quantified by overall mean and standard deviation. In addition, variance to mean ratio (VMR) was used as an index of the dispersion (Upton & Cook, 2014). In particular, the simulated mean and standard deviation of the infection intensity was expected to be different from observation by order of magnitude as all the involved models were tentative. Therefore, the characteristics of the dispersion was considered as an essential pattern. The notable pattern of dispersion of the infection intensity was the presence of few individuals with extremely high intensity compared to the population means (Guislain et al., 2008; Hofer et al., 2000; Yimam et al., 2002). To see if such individuals were successfully simulated, ratio of maximum-to-mean was used as a measurable index. These simulation results were compared against the observation in Calgary (see Catalano et al., 2012; and Liccioli et al., 2012 for methods and data on the individual intensity ; see Liccioli et al., 2014 for spatial and seasonal prevalences).

5.3.5. EXPERIMENTAL SIMULATION

Experiments were conducted with CEmCA to test the three hypotheses. First, small mammal assemblages of the area were 'manipulated' to test IH hypothesis. The experiments were conducted by assigning all the cells with natural land cover with one of the three assemblage types, to be compared against the simulations with modelled distribution of the small mammal assemblage (Mori et al., 2019). These manipulations were combined with the parameter settings of egg-contact rate of 0.5 % or 1 % per day and

IH-predation rate of 2 and 5 fold increase compared to the healthy small mammals, as the parameter combinations that were considered relatively realistic among the those used in above sensitivity analysis. The simulations were repeated 10 times for each parameter and assemblage combination. The results were analyzed by comparing the prevalence of the last year of the simulation, of overall prevalence and relative prevalence between BM and NHP. If the IH hypothesis is true, we would expect the simulations with different assemblage types to results in different prevalence, with assemblage type 1 expected to result in highest prevalence (Mori et al., 2019). In addition, if the IH hypothesis was the only hypothesis that explains the spatial heterogeneity (i.e. if the DH hypothesis is false), we would expect the similar prevalences in BM and NHP with the same assemblage types in both parks.

Second, the experiments were conducted with *Em* introduced only in one of the parks in simulation to test metapopulation hypothesis. This experiment was combined with the above experiment of changing the assemblage. Simulations of each combination was repeated 10 times. The results were analyzed by comparing the overall prevalence and relative prevalence of BM and NHP. If the meta-population hypothesis can explain the spatial heterogeneity of *Em* prevalence, then we would expect the difference in the prevalence to persist even after many years of simulation.

5.4 RESULTS

The model outputs in relation to the observed coyote behaviors are summarized in Tables 8-11. Overall, the coyote behaviors were successfully calibrated to simulate the patterns observed in the field study (Table 8,

Table 9, Table 10). The time coyote spent at each activity types were calibrated to be in very good match to the observation (Table 8). Home range sizes of simulated coyotes in NHP were noticeably larger than those of less developed areas as reported by Gese et al. (2012;

Table 9). However, the general pattern of seasonal increase or decrease in the home range sizes were matched. Simulated coyotes of BM were larger than those of NHP, which was expected because the coyotes in developed areas were observed to have larger home ranges than those in less developed areas (Gese et al., 2012). The differences in home-ranges between simulated male and female coyotes, in terms of which is larger, mostly matched with the observation by Andelt and Gipson (1979). For the den visit behaviors, in some seasons we could not make the simulated coyotes conform to the pattern observed by Andelt et al. (1979; Table 10). The time spent in the den was more frequent during daytime in season 1 and 2 for both sexes, season 4 and 6 for the male, , and longer during nighttime in season 4 for the female in simulations than the observed in some seasons (Table 10). The total number of small mammals in coyote's diet were generally successful in calibrating to the observed data by season, but not as successful by species (Table 11). Overall, we deemed the calibration mostly successful in capturing the overall pattern.

The results of the sensitivity analysis using multiple coyote simulations are shown in

Table 12. Both the egg-contact rate and the IH-predation had strong effects on the number of coyotes being infected. At the low values of egg-contact rate and IH-predation, *Em* transmit rarely and tend to die off early in the simulation.

The detailed results of validation are provided in Appendix 3. The average prevalence among DH between the BM and NHP (Table A3 - 1), and their average heterogeneity as calculated in standard deviations (Table A3 - 2), show a close match to the observation in several parameter combinations. However, while the observation consistently indicated BM to be higher in prevalence to NHP (Liccioli et al., 2014), the simulation resulted in NHP to be higher in prevalence than BM.

The mean prevalence among DH averaged by the seasons were close to the observed prevalence averaged by seasons in some parameter combinations (Table A3 - 3). However, the heterogeneity as expressed in VMR in simulation was much lower than that of observation (Table A3 - 4). While the simulation resulted in Spring being the season with highest prevalence as observed, the Winter prevalence was higher than summer or fall, and summer slightly higher than fall, which is not the order observed (Table A3-5 to 8; Liccioli et al., 2014).

Mean intensity of infection among individual DH were completely off from that of the observation, far greater by order of magnitudes (Table A3 - 9). The mean of the standard deviation (Table A3 - 10) and VMR (Table A3 - 11) were also much greater in simulation than observed, by one order of magnitude. However, means of the max-to-mean ratio were smaller than observed (Table A3 - 12).

In an experiment manipulating the small mammal assemblages, simulations with only assemblage type 1 or 3 resulted in extinction of *Em*, even at very high transmission parameters. The simulations with only assemblage type 2, on the other hand, resulted in much higher prevalence than the simulations with the modelled assemblage distribution (Table 13). The prevalences of simulation with only assemblage 2 was significantly higher than the prevalences of simulations with modelled assemblage in every parameter combination ($p = 0.05$).

Table 8: The simulated time a coyote spent on each activity type in each season of the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA, in the northwest area around Nosehill park of the city of Calgary compared to the observational study of Gese et al. (1996a). The classification of coyote seasons are based on Andelt and Gipson (1979). The values from the simulation shown here are the daily averages over a 5-year simulation (and standard deviation). Although Gese et al. (1996a) did not describe August and September, we assumed those months to have same pattern as July. Coyote seasons are defined as 1: Breeding (Feb.), 2: Gestation (Mar-Apr.), 3: Nursing (May – Jun.), 4: Pup training (Jul. – mid.Sep.), 5: Adolescence (mid.Sep. – mid.Nov.) and 6: pre-breeding (mid.Nov. – Jan)

Coyote Season

Coyote Activity (%)		1	2	3	4	5	6
Hunting	Sim.	8.1 (2.3)	6.6 (2.9)	9.2 (3.7)	7.8 (2.5)	14.4 (5.9)	8.0 (3.0)
	Obs.	5	5	5 ~ 10	5 ~ 10	10 ~ 15	5
Resting	Sim.	72.2 (10.4)	75.4 (15.0)	51.6 (18.5)	59.9 (11.5)	14.6 (11.9)	66.7 (19.4)
	Obs.	70	70	50 ~ 60	50 ~ 60	15 ~ 20	70
Traveling	Sim.	17.3 (10.6)	15 (15.6)	36.8 (20)	30.2 (11.1)	68.9 (14.9)	23.2 (21.0)
	Obs.	20	20	30 ~ 40	30 ~ 40	60	20

Table 9: Mean home range sizes (and standard deviation, in km²) of simulated coyote season of the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA. In the northwest area around Nosehill park of the city of Calgary in Bowmont (BM) and Nosehill park (NHP) at each season compared to the observation described in Andelt and Gipson (1979) and Gese et al. (2012). The values from the simulation shown here are the averages from a 5-year simulation. Note the coyote in BM has consistently larger home range than the coyote in NHP, which is consistent with the observed pattern of larger home ranges for coyotes in more urban areas (Gese et al., 2012). Coyote seasons are defined as 1: Breeding (Feb.), 2: Gestation (Mar-Apr.), 3: Nursing (May – Jun.), 4: Pup training (Jul. – mid.Sep.), 5: Adolescence (mid.Sep. – mid.Nov.) and 6: pre-breeding (mid.Nov. – Jan)

		Coyote Season					
		1	2	3	4	5	6
Sim	BM	18.67 (2.04)	22.01 (1.80)	24.36 (2.55)	13.74 (2.70)	35.06 (1.33)	25.30 (4.85)
	NHP	13.41 (1.25)	14.85 (0.76)	17.12 (1.38)	11.96 (1.69)	28.72 (0.66)	17.23 (1.39)
	Male (NHP)	12.43 (0.68)	15.00 (0.87)	19.25 (1.14)	15.12 (0.40)	28.82 (0.70)	15.28 (0.52)
	Female (NHP)	14.39 (1.47)	14.71 (0.66)	14.99 (0.43)	8.80 (0.66)	28.63 (0.66)	19.18 (1.31)
	developed	14.7	14.7	13.2	13.2	16.5	14.7
	mixed	17.7	17.7	8.6	8.6	14.2	17.7
Gese et al. 2012*	less developed	7	7	7.3	7.3	8.2	7
Andelt et al. 1979	male	6.9	8.4	10.4	14.6	21.1	17.9
	female	13.7	8.2	9.6	7.2	4.2	35.4

Table 10: The mean frequency (and standard deviation) of coyotes found at the den in of the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA, in the northwest area around Nosehill park of the city of Calgary (Sim.) compared to the observation (Obs.) of Andelt et al. (1979), for male (M.) and female (F.). The values from the simulation of the den visit in nighttime shown here are the averages hours coyote spent during the night time, while the den visit in daytime are in percentage of days the coyotes spent any time in the den location during the day time. Both values are average over 5-year simulation. The frequency was generally higher in simulation compared to the observation. Coyote seasons are defined as 1: Breeding (Feb.), 2: Gestation (Mar-Apr.), 3: Nursing (May – Jun.), 4: Pup training (Jul. – mid.Sep.), 5: Adolescence (mid.Sep. – mid.Nov.) and 6: pre-breeding (mid.Nov. – Jan)

		Coyote Season							
		1	2	3	4	5	6		
<u>Den visit in nighttime (h)</u>	M.	Sim.	0.54 (0.17)	0.22 (0.11)	0.92 (0.14)	1.16 (0.14)	0.02 (0.03)	0.68 (0.14)	
		Obs.	1.0	0	0.5	1.1	0	0	
	F.	Sim.	0.06 (0.06)	0.31 (0.11)	1.45 (0.22)	2.68 (0.27)	0.03 (0.03)	0	
		Obs.	0	0.3	1.4	1.5	0	0	
	<u>Den visit in daytime (%)</u>	M.	Sim.	90 (4.74)	53 (11.07)	19 (6.32)	99 (0.01)	1.6 (0.00)	92 (3.16)
			Obs.	44	12	0	67	0	56
F.		Sim.	11 (7.91)	71 (4.74)	86 (4.74)	100 (0.01)	1.6 (0)	0	
		Obs.	3	20	31	100	0	0	

Table 11: The number of small mammals consumed by a coyote in simulation of the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA, divided by species and season. The table shows the mean (standard deviation) of the ten simulations. The observations (Obs.) of Liccioli et al. (2015a) are also listed. The simulated coyotes' consumptions were calibrated to the total number of small mammals in all seasons, but the number of each species consumed were still notably different.

		Species					total
		Meadow vole	Deer mouse	Southern red-backed vole	Western jumping mouse	Shrew	
Spring	Sim.	4.9 (± 1.09)	79.325 (± 13.34)	4 (± 1.93)	2.03 (± 1.14)	0.4 (± 6.07)	198.7 (± 23.08)
	Obs.	120	5	30	< 5	< 5	180
Summer	Sim.	4.98 (± 2.32)	98.28 (± 29.75)	4.625 (± 1.66)	5.9 (± 1.11)	0.08 (± 2.63)	137.375 (± 33.64)
	Obs.	65	0	35	10	5	115
Fall	Sim.	24.73 (± 6.24)	51.1 (± 13.33)	24.63 (± 7.28)	0.5 (± 0.24)	0.3 (± 5.22)	115.1 (± 27.29)
	Obs.	25	40	10	5	0	90
Winter	Sim.	3.04 (± 1.14)	47.04 (± 15.52)	3.14 (± 1.50)	0.30 (± 0.33)	0.20 (± 4.24)	79.65 (± 15.22)
	Obs.	30	0	40	0	0	90

When the infective IH susceptibility to predation was set to twice the susceptibility of uninfected small mammals, and the egg-contact rate was set to 0.5%, BM on average had higher prevalence than NHP when all the assemblage was type 2. In every other parameter combination where the parasite remained in the system, NHP had higher prevalence than BM on average. However, the differences between the prevalences in two parks were not significant ($p = 0.05$).

Table 12: Table showing the prevalence (and standard deviation) of the last year of the simulation of the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA at each parameter combination. Parameters tested were the increase in IH susceptibility to predation as indicated by the coefficients to the detectability of infective IH to the hunting coyotes compared to uninfected small mammal, and the contact rate between small mammals and *Echinococcus multilocularis* eggs indicated in percentage. The shown prevalence are means of all the coyotes at all the days of the last year of all ten simulations.

		Egg-contact rate (%)		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH susceptibility to predation	<u>x1</u>	0	0.0947 (0.1474)	0.3072 (0.2666)
	<u>x2</u>	0	0.0967 (0.1992)	0.3432 (0.2827)
	<u>x5</u>	0.0938 (0.1576)	0.2170 (0.2726)	0.5206 (0.3089)
	<u>x10</u>	0.0238 (0.0553)	0.5057 (0.2899)	0.8181 (0.1873)

Table 13: Table showing the mean prevalence of the last year of the simulation using the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA, averaged over ten simulations, while varying parameters and the small mammal assemblages. The parameters tested were the contact rate between small mammals and *Em* eggs in percentage (0.5% & 1%), and the increase in IH susceptibility to predation as coefficient to the detectability of infective IH to the hunting coyotes compared to uninfected small mammal (x2 & x5). The assemblages “Model” indicate the modelled distribution of small mammals as described in Mori et al. (2019), while “1” “2” and “3” indicate simulations where all the small mammal assemblages in the simulations were of the assemblage type 1, 2, and 3 as classified in the same study, respectively.

		Egg-contact / IH predation susceptibility			
		<u>0.5% / x2</u>	<u>0.5% / x5</u>	<u>1% / x2</u>	<u>1% / x5</u>
Assemblage	Model	0.0221	0.0217	0.1027	0.3111
	1	0	0	0	0.1244
	2	0.3159	0.5590	0.7804	0.9843
	3	0	0	0	0

Table 14: Table showing the prevalence among coyotes in two areas (Bowmont, Nosehill park) of the last year of the simulation using the Calgary *Echinococcus multilocularis* Coyote Agent-based model, CEmCA. The simulation outputs were averaged over ten simulations. The treatments are the parameters of the contact rate between small mammals and *Em* eggs in percentage (0.5%, 1%), and the coefficients in IH susceptibility to predation to the detectability of infective IH to the hunting coyotes compared to uninfected small mammal (x_2 , x_5). The assemblages “Model” indicate the modelled distribution of small mammals as described in Mori et al. (2019), while “2” indicate simulations where all the small mammal assemblages in the simulations were of the assemblage type 2, as classified in the same study. The location where *Em* was initially introduced in the simulation. BM for *Em* introduced to Bowmont park, NHP for *Em* introduced to Nosehill Park.

		Egg-contact rate				<i>Em</i> start location
		0.5 %		1 %		
		x_2	x_5	x_2	x_5	
IH predation susceptibility	<u>x_2</u>	0,	0.3564,	0.0042,	0.7843,	<u>BM</u>
		0.0202	0.0289	0	0.5496	
	0, 0	0.0625,	0,	0.5944,		<u>NHP</u>
		0.4148	0.1340	0.5351		
	<u>x_5</u>	0, 0	0.2694,	0,	0.7731,	<u>BM</u>
			0.1699	0	0.6233	
	0,	0.3459,	0.0158,	0.8331.	<u>NHP</u>	
	0.1154	0.6538	0.4283	0.8894		
		<u>Model</u>	<u>2</u>	<u>Model</u>	<u>2</u>	
Assemblage						

The experiment introducing *Em* to only BM and NHP typically resulted in the higher prevalence in park where *Em* was introduced in most scenarios, even after 4 years of transmissions, though the differences were not significant ($p = 0.05$, Table 14). In some cases, the parasite died out or prevalence became saturated on both parks, resulting in little to no differences between the parks. The parasites tended to result in lower prevalence in 5 years if it was introduced to BM. Simulations with only assemblage type 2 had greater prevalence.

5.5 DISCUSSION

Overall, the CEmCA was mostly calibrated successfully and reproduced several patterns of coyote behavior such as the home range sizes and the activities of coyotes. There still were deviations from observed data for which we could have calibrated the CEmCA further. However, many of the literature reports were highly variable (home range) or limited (e.g. den visit frequency), while many of the patterns of when and where the increase or decrease was observed were in match with the observation, and we

consider the CEmCA to be reasonably calibrated. One possible factor for future consideration is that field observations were often the limited sample, while the simulation outputs were very thorough records, of coyote behavior. Use of virtual ecologist approach (Zurell et al., 2010), sampling the “observation” of simulation results in a same manner as an ecologists observing the reality, may improve our calibration. (For more thorough discussion on the calibration, please see Appendix 3.4.)

The results of sensitivity analysis suggested that the IH infection rate and susceptibility to predation have a strong influence on the transmission of *Em*. Because the transmission of *Em* easily died out when the IH had no increase in the susceptibility to predation, these results seemed to support the host manipulation hypothesis. Similar conclusions were drawn by Vervaeke et al. (2006) whose mathematical model suggest that such manipulation can explains the observed resilience of *Em*. These results suggest that future research on how the parasite manipulate IHs, and how likely it is for small mammal to ingest *Em* egg in the natural condition, are very important.

The results of the validations of the epidemiological patterns in the CEmCA indicate that the model performed rather poorly in the reproduction of the transmission of *Em*. One of the most notable diversion of the simulation results from the observation was that the spatial heterogeneity of the prevalence was reproduced, the pattern was reversed from the observation (Appendix 3-1). Because the primary purpose of this study was to understand the mechanisms and processes causing the spatial heterogeneity in the prevalence of *Em*, this result was of particular interest. The higher prevalence among simulated coyoted in NHP than in BM can be explained by the larger areas of assemblage type 2, which were better suited for *Em* transmission than other assemblages as shown in the results of experiments manipulating the small mammal assemblage types (Table 13). However, this is in contrast to Mori et al. (2019) where assemblage type 1 was associated with higher prevalence than assemblage type 2.

In Mori et al. (2019), it was speculated that assemblage type 1 is associated with higher prevalence of *Em* because of lower overall abundance of small mammals but higher proportion of susceptible species, increasing the chance of hunting coyotes to consume a susceptible small mammals. The assemblage type 2 was associated with lower prevalence because higher overall abundance of small mammals causes dilution effects (Civitello et al., 2015; Mori et al., 2019). While the dilution effects are considered likely to play a role in the transmission of *Em*, density-dependent prey preference, availability of other food source, and omnivorous and flexible diets can highly complicate the transmission (Baudrot et al., 2016; Raoul et al., 2015). Coyotes are highly omnivorous and mobile (Gese et al., 2012; Liccioli et al., 2015a) and it is conceivable that they would rely on other food sources if the small mammals are less abundant (Murray et al., 2015b). Coyotes can choose to hunt where the preys are abundant, rather than hunt at

places with lower prey abundance. Such behaviors were not incorporated in the CEmCA, but potentially have significant effect on the transmission. One possible scenario explaining the higher prevalence among observed coyotes in BM could be that it was not because there were more areas of assemblage type 1 in BM, but because there were less areas of assemblage type 2 that they prefer to hunt in, leading to concentration of coyote activities in smaller area. (For more thorough discussion on the validation, see Appendix 3.5.)

While the failures to reproduce observed patterns indicate that CEmCA was not successful in reproducing the patterns observed for the actual transmission of *Em* among coyotes in the City of Calgary, these results are the logical outcome of the assumptions and knowledge that went into building the CEmCA (Boschetti et al., 2011). Although the current model's outcomes are not reliable predictions of the real system, it can still be useful for exploring the systems and test hypotheses that are not possible with a real system. One approach is to run experiments with the model, to test alternate hypotheses that may produce the heterogeneities we observe in real system (Grimm & Railsback, 2005).

The first experiment changing the small mammal assemblage strongly supported the IH hypothesis. The small mammal assemblages seem to play very strong role in the transmission of *Em*. However, the results of the experiment is contrary to the assumption behind the IH hypothesis, the assumption of dilution effect where the higher proportion of the susceptible prey promotes the transmission of the parasite (Civitello et al., 2015; Mori et al., 2019). The dilution effect would be expected if the predation of the coyotes were based on the density of the prey (Baudrot et al., 2016). However, coyotes in Calgary are known to consume meadow voles more often than expected from their abundance in the field (Liccioli et al., 2015a). This is reflected (though insufficiently) in the behaviors of coyote in the CEmCA, countering the dilution effect. The higher density of small mammals in assemblage type 2 may also allow coyotes to consume more small mammals and increase the chance of infection. Further experimentation manipulating the prey preference of meadow voles may shed light on when the dilution effect becomes important.

The experiment also seemed to support the DH hypothesis as well. At one parameter combination BM had higher but non-significant prevalence than NHP, which never occurred with the modelled assemblage distribution. This result suggests a possibility that BM has features that are more favorable for *Em* transmission than NHP, predicted with DH hypothesis. Compared to NHP it is relatively confined park surrounded by residential areas (Figure 12), forcing coyotes to utilize smaller areas for hunting. It has higher density of trails than NHP, and coyotes are known to defecate along the trails more frequently (Barja et al., 2004; Barja & List, 2014; also see Chapter 4). These two factors would lead to coyotes

hunting and defecating in close proximity, in turn leading to more transmission of *Em* (Guislain et al., 2008; Raoul et al., 2015). However, the difference was not significant and observed in only one parameter combination. More work is required before we can extract any meaning to this result.

The results of second experiment strongly supported the meta-population hypothesis. Even after four years of transmission among coyotes, the prevalence among coyotes were usually higher in the park where *Em* was introduced (Table 14). Although longer simulations would likely eliminate the difference in prevalence between the two parks, it is also unrealistic for the simulation to run longer without the introduction of mortality and replacements of coyotes. Annual survival rate of coyotes in urban areas are reported in the range of 0.62 to 0.74 (Gehrt, 2007), though long time resident coyotes are likely to have higher survival rate (Murray & St. Clair, 2015). On the other hand, if realistic mortality and replacement of coyotes were added to the CEmCA, there is increased chance of local extinction of *Em* due to the temporary disappearance of hosts, leading to spatial heterogeneity in its prevalence. It is known that heterogeneous landscape and animal movements has significant influence on the epidemiology among wildlife and causes spatial heterogeneity (Lane-deGraaf et al., 2013; Real & Biek, 2007), and yet epidemiological model with heterogeneous landscape remains rare. This experiment perhaps highlights the importance of spatially-explicit ABM using realistic urban landscape most.

Although it was not conducted in this study, another possible experiment of interest is to test the effectiveness of the use of anthelmintic baits to deworm the coyotes, often used by policy makers to reduce the risks of Alveolar echinococcosis. A study by Nishina and Ishikawa (2008) using individual-based models of *Em* epidemiology among foxes in Hokkaido, Japan, indicate that the use of anthelmintic baits was most effective in early summer than in winter. However, their study did not include the factor of space in their analysis, or individuality among hosts. By using the CEmCA we can add spatial factors and address the complexities that occur. For example, while anthelmintic baits are known to be effective in reducing the local prevalence of the parasite, they can not eliminate the parasite or affect the neighboring areas (Hegglin & Deplazes, 2013; Takahashi et al., 2013). Study by White et al. (2018a) indicate that habitat fragmentation can promotes pathogen persistence. Experiments can be conducted where only one area is applied with the anthelmintic baits for its effectiveness, and to assess how long the application needs be continued, and how long before the parasite is reintroduced to the area after the application is stopped.

5.6 CONCLUSION

In modelling epidemiological systems, spatially-explicit ABMs hold great advantage over traditional models in that they can simulate behaviors and spatial factors that are considered important in the

transmission of parasites. While studies using agent-based models for *Em* transmissions are not new (e.g. Nishina & Ishikawa, 2008), only few studies exist that model the transmission of parasites in a spatially-explicit manner in a complex, heterogeneous landscape (e.g. Lane-deGraaf et al., 2013), and to the best of our knowledge no such study exists in trophically transmitted parasites with a complex life-cycle. White et al. (2018b) in their review state that the modelling of parasites that features complex life cycles, effects of urbanization, movement ecology, and individual heterogeneity of hosts are rare. However, in many epidemiological systems those features can be the key elements in understanding the transmission processes. In the CEmCA, we tried to incorporate most of these elements. Despite having shortcomings in reproducing the observed patterns, we believe that the CEmCA is promising for understanding the *Em* epidemiology, particularly in heterogeneous urban environments.

CH 6: CONCLUSIONS AND RECOMMENDATIONS

In this project, we tried to understand the transmission mechanisms of the *Echinococcus multilocularis* (*Em*) and their spatial and temporal patterns observed. We conducted 1) analysis of small mammal communities, 2) the analysis on the contamination of public parks by dog and coyote fecal matters, and these results were used in 3) developing a spatially-explicit Agent-based Model (ABM) the Calgary *Em* Coyote ABM (CEMCA) and analysis of the simulations results. Particularly, we used the CEMCA to conduct experiments testing three hypotheses explaining the spatial heterogeneity of the *Em* prevalence: 1) small mammals community (IH hypothesis), 2) how coyotes' behavior interact with the landscape (DH hypothesis), and 3) the separation of habitats (metapopulation hypothesis).

While the chapters 3 and 4 of this thesis are important for understanding the *Em* transmission and, can assess the effects of small mammal communities or the behaviors of coyotes on the transmission, they were also important in their contribution to the development of the CEMCA. Transmission of *Em* is a complex process with multiple mechanisms operating at various scales, and analyzing these processes separately potentially miss key interactions of these processes. The CEMCA allows the simulation of several mechanisms and their interactions simultaneously.

Using the CEMCA, the effects of small mammal assemblage, behaviors of coyotes, the landscape, and their interactions were tested. The sensitivity analysis and validation results indicated that there are still many unknown in the system. Despite these shortcomings, the experiments conducted still provided insights on the formation of spatial heterogeneity, and indicated that IH hypothesis and metapopulation hypothesis are true. Because of its spatially-explicit nature and use of complex landscape, the CEMCA was able to provide insights into the spatial aspect of epidemiology of *Em*.

We successfully developed an ABM that allowed us gain insights into the *Em* transmission processes and patterns. Although using an ABM to study *Em* epidemiology is not new, to the best of our knowledge this is the first ABM study that modelled *Em* transmission in spatially-explicit manner at such a fine scale, over a real and complex landscape. This study has broad implications to not just *Em* epidemiology around the world, but also to the broader epidemiology of trophically-transmitted parasites with complex life-cycle.

APPENDICES

APPENDIX 1

Appendix 1. SPSS output showing the parameter estimates and statistics of multinomial logistic regression model predicting the assemblage types. A1, A2, and A3 indicate assemblage type 1, 2, and 3 respectively. Negative coefficient of North_aspect for A1 indicate that A1 is more found in south-facing surfaces, while positive coefficient for A2 indicate they are found in north-facing surfaces. The significance values of each variable indicate the significance of that variable given rest of the model in place.

Parameter Estimates

assemblage ^a		B	Std. Error	Wald	df	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
								Lower Bound	Upper Bound
A1	Intercept	-9.405	11.281	.695	1	.404			
	North_aspect	-6.208	7.131	.758	1	.384	.002	1.715E-9	2364.437
	sd_slope	2.158	3.331	.420	1	.517	8.652	.013	5917.666
A2	Intercept	78.160	20678.413	.000	1	.997			
	North_aspect	614.594	.000	.	1	.	8.218E+266	8.218E+266	8.218E+266
	sd_slope	-66.459	6081.468	.000	1	.991	1.372E-29	.000	. ^b

a. The reference category is:A3.

b. Floating point overflow occurred while computing this statistic. Its value is therefore set to system missing.

APPENDIX 2. DESCRIPTION FOLLOWING ODD (OVERVIEW, DESIGN CONCEPTS, DETAILS) PROTOCOL (GRIMM ET AL., 2006; GRIMM ET AL., 2010).

A2.1 PURPOSE

Understand the epidemiology and the mechanism that results in the spatial heterogeneity of the *Echinococcus multilocularis* (*Em*) prevalence.

A2.2 ENTITIES, STATE VARIABLES, AND SCALE

<u>Entities</u>	<u>State Variables</u>	<u>Scale / units</u>
Coyote	Gender Location Home (den) location Pack ID Social status (class) Infection to EM <ul style="list-style-type: none"> • Number of worms • Number of eggs • Worm IDs Previous infection experience <ul style="list-style-type: none"> • Time since last infection Purpose Activity Destination <ul style="list-style-type: none"> • Patch-id • Patch-coordinate Time since last <ul style="list-style-type: none"> • Hunt • Den visit • defecation 	M/F X Y coordinate X Y coordinate 1 = alpha, 2 = beta, 3 = pups T/F T/F days 1 = eat, 2 = rest, 3 = attend den, 4 = explore 1 = hunt, 2 = hide, 3 = travel hours hours hours

	<p>Reference Memory</p> <ul style="list-style-type: none"> • Patch IDs • Time since last visit <p>Working memory</p> <ul style="list-style-type: none"> • Patch IDs • Time since last use 	<p>days</p> <p>days</p>
Pack	<p>Location (of the den)</p> <p>Number of coyotes</p> <p>Prevalence</p> <ul style="list-style-type: none"> • True prevalence • Observable prevalence <p>Intensity</p> <ul style="list-style-type: none"> • Total number of worms • Maximum intensity among pack members 	X Y coordinate
<p>Landscape</p> <p>Rectangular areas that contain 5 km buffer around Bowmont and Nose Hill parks in the North/Northeast Calgary, consisted of 50m x 50m cells</p>	<p>Land cover</p> <p>Patch ID</p> <p>Permeability to coyote movement</p> <p>Small mammal assemblages</p> <p><i>Infected Meadow vole</i></p> <ul style="list-style-type: none"> • <i>Number</i> • <i>Prevalence</i> • <i>infective</i> <p><i>Infected Deer Mouse</i></p> <ul style="list-style-type: none"> • <i>Number</i> • <i>Prevalence</i> • <i>infective</i> <p><i>Infected Southern red-backed vole</i></p> <ul style="list-style-type: none"> • <i>Number</i> • <i>Prevalence</i> • <i>infective</i> <p>Active EM egg density</p> <p>Infective IH prevalence</p>	Density of each species at each season.

	Trail	
Infected IH	Species Age (Time since infection) Location Number of protoscoleces	Days X Y coordinate
Coyote Feces	Age Location Number of eggs original number of eggs Infectivity	Days X Y coordinate T/F
EM worms	Age Number of worms Host ID Egg number	Days
Environment	Time <ul style="list-style-type: none"> • day • month • year Night/day Average temperature Snow on ground Season <ul style="list-style-type: none"> • small mammal • coyote 	Time step of 30 min (0 ~ 47) 1 = night, 0 = day Daily, degree Celsius cm 4 seasons 6 seasons of reproductive cycle

A2.3 PROCESS OVERVIEW AND SCHEDULING

At every time step (30 minutes), following processes are performed for individual coyotes. All the processes are carried out for each coyote before the next coyote is processed. These processes for coyotes are performed in set sequence and in the order of alpha male, alpha female, alpha beta, then pups.

1. *If new purpose is needed*, decide purpose
2. *If new activity is needed*, decide activity
3. Action: one of the following
 - a. Hunt

- b. Rest
- c. Travel
- 4. Defecate
- 5. Memorize
- 6. Memory decay

Once a day (at noon), following processes are performed after above processes. Each process are carried out for all relevant entities before next process is performed

- 7. Age worms
- 8. Produce eggs
- 9. Survival of eggs
- 10. Infection of small mammal
- 11. Infection progress of infected IH

Once a year at August 1st

- 12. Introduce coyote pups

At every time step, after above processes are completed.

- 13. Update time and environment

A2.4 DESIGN CONCEPTS

Basic principles

The model is designed based on the assumption that patterns of *Em* transmissions emerge from coyotes' behaviors such as home range, land use, hunting preference, defecation and territoriality, and their interaction with the landscape determine the transmission of *Em*.

Emergence

Home range and land use patterns of coyotes, and emergence of small mammal consumption patterns and defecation patterns.

Adaptation

Coyotes adapt to landscape by memorizing the land and choosing where to hunt or rest. Coyotes also adapt to change in season and time of the day by changing behaviors, but these adaptations are imposed rather than decided by coyotes.

Objectives

Coyotes aim to maximize survival and reproduction, but these objectives are implicit in the model.

Learning

Coyotes learn the surrounding landscape where they can successfully hunt and safely rest

Sensing

Coyotes can perceive the permeability and land cover types within one cell distance from itself. Coyotes are also assumed to be able to sense the distance and direction to their den and the habitats they memorized.

Interaction

There are no direct interactions between coyotes in the model. The interactions such as mating, breeding, feeding the pups, and defending the territories are implicit. Only interactions explicit in the model are indirect transmission of *Em* or removal of infected IHs.

Stochasticity

Coyote's decisions, movements, and hunting are all stochastic and influenced by random numbers. Small mammal infection and survival are also stochastic and uses probability functions.

Collectives

There is a collective of coyotes or packs in the model, indicating a social grouping of coyotes. However, the pack itself has little influence in the model, as it only indicates shared focal point in their home range i.e. den and all coyotes in the model belong to a same pack.

Observation

The model records the location of coyotes at the end of each 30 min time step, as well as its activity at the time and the land cover type of the cell it is occupying. The model also records time spent on each of the activities in each day, as well as the time coyote spent at den during the night and whether the coyote visited den during daytime or not.

At each day, the model records the numbers of the consumption of small mammals by species.

Each day, the model records the number of *Em* worms and eggs carried by each coyotes.

Each day, the model records the numbers of infected to infective intermediate hosts by species.

Each day, the model records the infection statuses of each individual coyotes. The output includes true prevalence and prevalence observable in the field (shedding eggs), total, mean, maximum, and variance of the number of worms among coyotes.

A2.5 INITIALIZATION

The simulation starts at the noon of March 1st 2010. For each of the coyote packs, three coyotes, two breeding pair (alpha male and female), and another adult coyote with random sex (beta), are placed at

their den. The simulation is allowed to run for one year with these three coyotes to let them learn the landscape as a spin-up. In the spin-up, coyotes do not reproduce, and *Em* is not present in the system. Once the spin-up is complete, *Em* is introduced to the simulation. Adult worms are introduced inside predesignated alpha male coyotes. The worms are given age of 0 and number of 10000.

A2.6 INPUT DATA

Several spatial data are used as inputs to the simulation at the start of a simulation. Map of permeability for coyote movement developed by Lamy (2015), small mammal assemblage map developed by Mori et al. (2019), land cover map and trail map developed by the city of Calgary.

Average daily temperature and snow height on the ground from environment and natural resources Canada, and time of sunrise-sunset from national research council Canada, are input to the simulation to model the change in environment.

A2.7 SUBMODELS

A2.7.1 Decide purpose

Coyote assesses its own situation and decides what it needs using series of simple heuristic rules. The purposes available are to *eat*, *rest*, *attend den*, and *explore*.

First, the coyote assesses whether it is day or night.

If it is nighttime, the coyote assesses whether the time since last *hunt* activity is more than a parameter *freq-hunt*. If so, the purpose is set to *eat*. If it has recently hunted, it assesses whether to *attend den* based on a probability parameter *night_den_visit*. If it decided not to attend den, then it decides whether to *explore* or *rest* based on probability parameter *rest-or-explore*.

If it is daytime, the coyote assesses whether to *attend den* or not based on a probability parameter *day_den_visit*. If it decides not to attend den, it will assess whether to *rest* or not based on a probability parameter *prob-day-rest*. If it decided not to attend den or rest, then it assesses whether the time since last *hunt* activity has been more than the parameter *freq-hunt* or not, and if so then it decides to *eat*. If it is still undecided on its purpose, then it chooses either to *rest* or to *explore* based on a probability parameter *rest-or-explore*.

Once the purpose is set, it sets the state variable *change-p* to 1 for next submodel *Decide activity* to be carried out, while the state variable *change-a* for submodel *Decide purpose* is set to 0.

When the coyote's purpose is decided, the model also determines how many time steps the coyote will spend pursuing that purpose. These time steps are calibrated to reproduce the time the coyote is observed

to spend on the three activities of *travel*, *hunt*, and *rest (hide)* in each season as observed by Gese et al. (1996a).

A2.7.2 Decide activity

Once the purpose is set, the coyote decides its action that is needed to fulfill its purpose based on another series of simple heuristic rules. The coyote chooses among activities of *travel*, *hunt*, and *hide*.

If the purpose is to *eat*, the coyote assesses whether it needs to *travel* to *hunt*. Each coyote has a state variable *goal-reached* that indicates whether the coyote needs to travel or not. If the *goal-reached* is 0, then the activity is set to *travel*. If the *goal-reached* is 1, then the activity is set to *hunt*.

If the purpose is to *rest*, again the coyote assesses whether it needs to *travel* or not by checking the state variable *goal-reached*. If the *goal-reached* is 0, but if the current location is suitable for resting i.e. natural land cover of grassland, deciduous forest, or coniferous forest, then the activity is to *hide*. If the *goal-reached* is 0 and the current location has non-natural land cover types, then the activity is to *travel*.

If the purpose is to *attend den*, then the coyote will assess whether it is already at den or need to travel. If the *goal-reached* is 0, then the activity is to *travel*. If the *goal-reached* is 1 (i.e. it is at the den), then the activity is to *hide*.

If the purpose is to *explore*, then the activity is to *travel*. The coyote also assesses whether to continue exploring or change purpose in next time step by checking the state variable *e-steps*, which counts down at every time step while exploring.

Once the activity is decided, the state variable *Decide activity* is set to 0.

A2.7.3 Hunt

In hunt submodel, coyote takes six sub-steps within the 30 minute time step. In each of the sub-steps, the coyote move, search and capture prey. The number of sub-steps is chosen to represent slow movement speed of coyotes (300 to 600 meters per hour; Grubbs & Krausman, 2009; Lamy, 2015). The hunting is repeated for the length of hunting determined in *Decide purpose* submodel. When the coyote finishes hunting, the flag *change-p* is raised indicating the need to decide new purpose in the next time step.

Movement

When the coyote is hunting, it moves in almost pure random walk manner. It assesses current cell and eight neighboring cells for its value as a hunting ground. The coyote then moves to the cell with the highest value, or stays where it is if the current cell has the highest value. The value of the cells are

assigned a random value in the range of 1 to 4 if the land cover type of the cell is either deciduous forest or coniferous forest, and 3 to 6 if the land cover type is grassland, and 0 for every other land cover types.

Search prey

After movement phase, the coyote searches for a prey within the cell it is in. The model first determines whether the coyote finds a small mammal prey or not, based on the total density of small mammals in the cell. Spatial distribution of the small mammal assemblages were based on field study (Liccioli et al., 2014; Mori et al., 2019). The densities of small mammals were estimated by assuming that the annual average of meadow voles in the assemblage type 2 is equal to 30 animals per hectare (Getz et al., 2001). We then assumed that the average trap capture rates in each assemblage types were linearly correlated with the density of the small mammals for each species and at each season.

We suspected that the coyote perceive density of small mammals differently from actual density, because some animals are more detectable than others. Coyotes are known to preferentially hunt meadow voles more than deer mouse (Liccioli et al., 2015a), and some parasites are known to manipulate their host to take more risky behaviors thus making them more detectable to predators (Lafferty, 1999). Therefore the “perceived” density of small mammals is calculated with coefficients by species and infectiveness, which is described later.

The probability of a hunting coyote detecting a small mammal is calculated using a logistic function and the perceived total small mammal density $dens$ in the cell as a predictor variable.

$$d = \frac{L}{1 + e^{(-1 * K * (dens - dens_0))}}$$

where L is the asymptotic value of $2/3$, K is a slope with a value of 0.07 , and $dens_0$ is a middle point of the curve with a value of 65 . These parameters were derived on an assumption that the detection rate at the average density in assemblage type 2 (69.5 animals per ha) is equal to the average detection rate in grassland observed in observational study in Yellowstone (4.5 times per hour, (Gese et al., 1996b)). Further, the asymptote is assumed to be reached around 110 animals per ha, the highest density of small mammals estimated for the ABM.

Once the coyote detects a prey, then the model decides which species it is based on the relative perceived density of each species.

Catch prey

When the coyote detects small mammal prey, it is assumed the coyote automatically attempt to catch the prey. Although Gese et al. (1996b) describes detection rate and attempt rate separately, these two rates were generally correlated and followed same pattern such that we assumed the attempt rate can be implicit in the detection rate to simplify the model.

The probability of successful capture of small mammal is assumed constant (0.35), roughly approximating the ratio between detection rate per hour and catch rate per hour observed in Gese et al. (1996b) study.

If an infected IH is present in the cell the coyote was hunting, then there is a chance that IH is killed and *Em* is transmitted to the coyote. If the capture of small mammal is successful, and if no parasite manipulation is assumed, the probability that caught animal is an infected IH is simply equal to the prevalence of *Em* among that species. If the parasite manipulation is in effect, the “prevalence” of the species *i* as perceived by coyote $P_{i,p}$ is re-calculated by increasing the infective IH using the *susceptibility_predation* parameter

$$P_{i,p} = \frac{N_{i,infective} * susceptibility_predation}{N_{i,non_infected} + N_{i,infected} + N_{i,infective} * susceptibility_predation}$$

where $N_{i,non_infected}$, $N_{i,infected}$, and $N_{i,infective}$ are number of healthy animals, number of *Em* infected but yet infective animals, and number of *Em* infective animals of species *i* respectively.

Calibration

Using the model described above as a base model, several changes have been introduced to calibrate the model. The mode was calibrated so that it will result in coyote consuming small mammals in approximately same number as those estimated for coyotes in the Calgary area (Liccioli et al., 2015a), including the annual average consumption, relative number (or the preference) of prey species consumed, and the seasonal patterns. The calibration was carried out simulating coyotes in Nosehill park, a most contiguous natural area in the simulation space and therefore likely to produce most natural behavior.

The seasonal pattern was calibrated first. The numbers of small mammals estimated to be consumed by coyotes were higher in winter/spring and lower in fall than simulation results because of the estimated density of small mammals. The reasons for the difference between the estimate and simulation can be many. For example, the other food source for coyotes may be available in fall, leading to reduced effort to capture small mammals. The time coyote spend hunting was also variable by season (Gese et al., 1996a). However, this variation mostly increased the difference in the small mammal consumed, as coyotes are observed to hunt longer in summer and fall rather than in spring and winter.

To calibrate these seasonal patterns, we assumed that during winter/spring coyotes are spending more efforts in searching small mammal prey than other food items. The seasonal coefficients were introduced to the detection rate of small mammals, increasing the detection rate in winter/spring while reducing the detection rate in fall. In addition, coefficients were introduced to the hunt success rate by season, allowing easier capture of small mammals in spring than in summer, assuming the increase in newborn small mammals in spring allow for increased catch success.

The patterns in the species consumed, or the prey preference by coyotes, were calibrated next. Coyotes in Calgary area were consuming meadow voles preferentially relative to their abundance in the field, while deer mouse and shrews were consumed less than their relative abundance (Liccioli et al., 2015a).

Meadow voles are known to prefer meadows and grassland (Iverson & Turner, 1972; Snyder & Best, 1988), while deer mice are known to prefer shrub cover and coarse woody debris (Lee, 2004; Stapp & Van Horne, 1997). The habitat preference toward grassland in the hunting behavior of coyotes should lead to more meadow voles being consumed than deer mouse. However, the land cover preference of simulated coyote did not reproduce the species consumption pattern estimated by Liccioli et al. (2015a). The grassland preference for hunting by coyote were experimentally increased but had little impact on the consumption pattern of the coyote.

To reproduce the pattern of coyote consumption of small mammal prey species, another parameter was introduced to the coyote prey search behavior. The detection rate for meadow voles and southern red-backed voles were increased, while the detection rate for shrew was reduced.

Parasite host manipulation

It is suspected that infection to *Em* will manipulate infected IH to be more vulnerable to predation, thus increasing the probability of successful transmission to a definitive host (reference here). In order to simulate such a process, we assumed that only small mammals that are infective (i.e. at least some protoscoleces are present) have increased vulnerability to the predation. We introduced another parameter that will increase the chance of infective small mammals to be detected.

A2.7.4 Hide

A coyote will simply remain in a cell and do nothing until the set time step *rest-for* is spent.

A2.7.5 Travel

The *travel* submodel first asks the coyote if it has decided its destination. If the coyote is yet to decide its destination, another submodel *decide-goal* is called.

While the coyote is travelling, it takes number of sub-steps, randomly decided between 8 to 16, to represent movement speed of 700 to 1600 meters per hour when a coyote is at fast pace (Lamy, 2015). At each sub-step, coyote makes a simplified correlated and biased random walk toward its destination (Barton et al., 2009).

In the correlated and biased random walk, the coyote first evaluates each of the eight neighboring cells based on its coyote permeability value, its angle relative to the destination, and its angle relative to the coyote's previous movement. The value U_t of the cell is calculated as

$$U_t = permeability + \beta_c \times cor + \beta_b \times bias + r$$

where *permeability* is a predicted permeability of coyote movement (Lamy, 2015), *cor* is the angle between the coyote to the cell and coyote's previous movement direction, *bias* is the angle between the coyote to the cell and the direction toward coyote's destination, *r* is the random value of normal distribution with mean of 0 and standard deviation of 30, β_c and β_b are coefficients calibrated visually using netlogo view panel for a reasonable movement. Once the coyote assigns U_t value to all eight neighboring cells, it will move to a cell with the highest U_t value.

When the coyote's purpose is to *explore*, the calculation of U_t value is modified to

$$U_t = permeability + \beta_c \times cor + 0.5 \times \beta_b \times bias + \beta_h \times homing + r$$

where the term *homing* is an angle between the coyote to the cell and the direction toward den, *r* is now a random value with normal distribution with mean of 0 and standard deviation of 45. The coefficient β_h increase as the distance from the den increases and calculated as

$$\beta_h = e_coef \times (dist_den - e_threshold)^2$$

where *dist_den* is the distance between the coyote and its den, *e_threshold* is a threshold distance from which this homing factor starts, and *e_coef* is a coefficient. The values for *e_threshold* and *e_coef* were calibrated to reproduce the home range sizes reported in literature (Andelt & Gipson, 1979; Gehrt, 2007; Gese et al., 2012; Grinder & Krausman, 2001; Grubbs & Krausman, 2009; Harrison & Gilbert, 1985; Murray et al., 2015b; Wilson & Shivik, 2011).

A2.7.6 Decide-goal

The destination is decided based on the coyote's purpose. If the purpose of the coyote is to *eat* or to *rest*, the coyote searches through the memory for a patch of natural habitat appropriate for its purpose. There

are two types of memories, namely “reference memory” and “working memory” (Van Moorter et al., 2009).

If the purpose is to *eat*, all the patches in the memory are assessed of its value U_e calculated as

$$U_e = \frac{(1 - v_{work}) * v_{ref} * u_{landcover} + r}{dist}$$

where $u_{landcover}$ is a value assigned based on the land cover type, v_{ref} is a strength of reference memory associated with that patch, v_{work} is a strength of working memory associated with that patch, r is a random value between 0 and 1, and $dist$ is the distance to the center of that patch from coyote’s present location. The coyote will choose the patch with greatest U_e value as its destination. If the purpose is to *rest*, the coyote will simply choose a patch in the reference memory with least distance from its present location. Once the destination patch is decided, the coyote then finds a cell in that patch that is closest to itself as a destination to go to.

If the coyote’s purpose is to *attend den*, the destination is den. If the purpose is to *explore*, the coyote will pick a direction (random integer between 0 and 359) as a “destination” and travel toward that direction.

A2.7.8 Defecate

Because defecation does not take whole time step of 30 minutes to carry out, it is carried out while the coyote is carrying out other activities. Each coyote has a state variable keeping track of the time that has passed since last defecation, and if this variable is above parameter *interval-feces*, the coyote becomes ready to defecate and will defecates at next opportunity.

We assumed that coyote will perceive any trail as possible landmark for marking a territory (Barja & List, 2014; Gese & Ruff, 1997). When the coyote is ready to defecate, for every sub-step of hunting or travelling, or while it is resting, it assesses the cell it is present in to see if there are trails running through the cell or not. If there are any trails, the coyote will defecate in that cell.

When the coyote defecates, all the *Em* eggs that were inside the coyote is transferred to the feces and an entity **feces** are created on that cell, with the age of 0 and the number of eggs equal to the number of eggs that were inside the coyote. If there is snow on the ground, we assumed the feces will be frozen or above the snow cover and cannot infect small mammals, and therefore the infectivity of the egg is set to 0. Otherwise the infectivity of the egg is set to 1.

A2.7.9 Memorize

The memories are simple tables of the habitat patch IDs and a value attached to that patch indicating how fresh the memory of that patch is to the coyote. It is assumed coyotes will perceive landscape by patches of habitat, and they can perceive the patches that are one cell (50 meter) away from itself.

Patches are added or renewed to the reference memory while a coyote is travelling or hunting. When the coyote travels or hunts, it adds to its reference memory the patch ids of the cell it is present in and the eight neighboring cells at every sub-step of its activity. If the perceived patch is already in the memory, the memory value of the patch is renewed. A newly memorized patch of habitat is assigned a constant value *ref-fresh*.

Working memories are added or renewed while a coyote is hunting. Working memory keeps track of only the patches the coyote hunted in, and therefore does not memorize the patches in the eight neighboring cells. Again, if the patch the coyote hunted in is already in the working memory the memory value is renewed. A newly memorized patch is assigned a value of *work-fresh*.

The parameters *ref-fresh* and *work-fresh*, along with the memory decay rate $r_{reference}$ and $r_{working}$ in the submodel *Memory decay*, were calibrated so that it would take at least a month before the working memory becomes less than reference memory.

A2.7.10 Memory decay

Once a day at noon, both reference memory and working memory of each coyote decays or becomes weaker. Both types of memories use a same formula for its decay, and the strength of memory M_t at time t is calculated as

$$M_t = M_{t-1} - r \times (1 - M_{t-1}) \times M_{t-1}$$

where M_{t-1} is the value of memory at time $t-1$, r here is a rate of memory decay (Van Moorter et al., 2009). The memory decay rates are assigned separately for reference memory and working memory, thus the two types of memory decay at different rate.

A2.7.11 Age worms

Once a day at noon, *Em* worms inside coyote ages. Because the model of *Em* egg production used by Ishikawa et al. (2003) predicts no eggs produced after day 60, when the age of the worms reaches 60 days, they die and are removed from the simulation.

A2.7.12 Produce eggs

Once a day at noon, the each *Em* worms with age above 30 days produce eggs. The number of eggs $N_{egg/worm}$ produced in a day by a worm is calculated based on a model by Ishikawa et al. (2003)

$$N_{egg/worm} = \frac{a_{egg} \times \exp\left(a_{egg} \times (b_{egg} - (age_{worm} - 30))\right)}{(1 + \exp(a_{egg} * (b_{egg} - (age_{worm} - 30))))^2}$$

where age_{worm} is the age of the worms in days and a_{egg} and b_{egg} are parameters. The actual number of eggs produced is the $N_{egg/worm}$ multiplied by the number of worms. The produced eggs are added to the state variable N_{eggs} of the host coyote.

A2.7.13 Egg survival

The eggs in the feces in the environment are exposed to the environment and gradually die from heat and desiccation. Once a day at noon, the number of eggs in the each feces $N_{egg,t}$ at time t is calculated as

$$N_{egg,t} = N_{egg,t-1} - \frac{N_0}{d}$$

where N_0 is the number of eggs when the age of the feces was 0, d is a number of days the eggs are expected to survive at the average temperature of that day (Ishikawa et al. 2003), calculated as

$$d = \exp(-0.135 * (temp - 43.49)) [N_i]$$

where $temp$ is the average temperature of the day.

Also in this submodel, if the infectivity of the feces was 0 and if there was no snow on the ground that day, the infectivity of the feces is set to 1.

A2.7.14 Infect small mammal

Once a day at noon, each of the feces with infectivity of 1 has chance to infect small mammals in the cell it is in. It is assumed the probability of small mammals coming in contact with the feces, or the contaminated area around the feces, is constant for all the species of the small mammals ($P_{contact}$).

The numbers of animals of species i that come in contact with the eggs ($N_{contact,i}$) are estimated by generating random number $[N_i]$ times, where $[N_i]$ is an integer less than or equal to the average density of the small mammal of species i estimated to be in that cell (N_i). One additional contact may occur with probability of $(N_i - [N_i]) * P_{contact}$. Only meadow voles, deer mouse, and southern red-backed voles are known to be susceptible to *Em* infection, and the $N_{contact,i}$ for other species are simply ignored in the model.

For those animals that contact the *Em* eggs, there is a probability of infection P_{infect} that is calculated as a logistic function based on the number of eggs in the feces N_{eggs} ,

$$P_{infect} = \frac{L}{1 + \exp(-1 * k * (N_{egg} - n0))}$$

where asymptotic parameter L was assumed to be 0.8 and the values for parameters k and $n0$ were systematically varied and tested over reasonable range for its effect.

It was assumed the removal of *Em* eggs from the ingestion by small mammals is insignificant compared to the N_{egg} in the feces and is ignored.

A successful infection of small mammal will create an entity **IH** in the cell. The new IH will be given a state variable indicating its species (1 for meadow vole, 2 for deer mouse, 3 for southern red-backed vole), age in days (0), infectivity (0), and number of protoscoleces (0).

A2.7.15 Infection progress IH

Once a day at noon, each of the IH will gain age, possibly die from causes other than coyote predation or *Em* infection, and progress in its infection. The probability of mortality of each small mammal is assumed to be constant for all species and at all stage of infection, and is assumed to be 1.15%, or ~50% mortality in 60 days (Getz et al. 1960).

The number of protoscoleces in IH $N_{ps,t}$ at IH age t above 40 days is calculated as

$$N_{ps,t} = N_{ps,t-1} + 0.3 * N_{ps,t-1} * \frac{1 - N_{ps,t-1}}{3700000}$$

using the model used in Ishikawa et al. (2003). It is assumed the *Em* infection will cause certain death of the small mammal host at 150 days after getting infected.

A2.7.16 Introduce pups

Once a year at August 1st, three to ten newborn coyotes are introduced to the simulation at the dens.

Coyotes are known to give birth in early April, they do not to hunt on their own until August (Harrison et al., 1991). Observational study of pup rearing and their feces content in Maine suggested before August, small mammals are rarely included in their diet (Harrison & Harrison, 1984). Given our primary interest in the transmission of *Em*, we assumed that the pups can be safely ignored from the model in April-July.

The pups are given sex randomly, empty memory, purpose to *explore*, and activity of *travel*. The pups are given $e_threshold$ and $e_coefficient$ different from adults, and calibrated to produce the home range sizes reported in Harrison et al. (1991) for August, September, and October. After November their home range sizes become practically indistinguishable from adult coyotes (Harrison et al., 1991), and are given the same parameters as adult coyotes.

A2.7.17 Update time and environment

At the end of every time step, the model updates the global state variables time, day, month, and the year of the simulation time. Seasons for the coyote behaviors are updated as defined in Andelt and Gipson (1979), and the behavioral parameters of the coyotes that change by season are also updated. State variable indicating the four seasons are also updated, which in turn updates the density of small mammals. Nighttime/daytime is also updated.

Date-specific events such as introducing *Em* worms and calling submodels such as *introduce-pups* are called from this submodel at pre-defined date.

<u>Parameter</u>	<u>Value (unit)</u>	<u>Source</u>
<i>freq-hunt</i>	5 (hours)	Calibration to Gese et al. 1996
<i>rest-or-explore</i>	Coyote season 1, 2, & 6: 0.7 Coyote season 3, 4, & 5: 0.2	
<i>prob-day-rest</i>		
<i>night_den_visit</i>		Andelt et al. 1967
<i>day_den_visit</i>		
<i>Vole-preference</i>	2	Calibration to Liccioli et al. 2015
<i>Shrew-preference</i>	0.5	
<i>Spring-detection-coefficient</i>	3	
<i>Fall-detection-coefficient</i>	0.5	
<i>Winter-detection-coefficient</i>	2	
<i>Spring-capture-coefficient</i>	2	
β_c	10	
β_b	300	
<i>e_threshold</i>	1250 (m)	
<i>e_coef</i>	0.1	
<i>interval-feces</i>	28 (hours)	Calibration to Monroy-Vilchis and Frieven 2006
<i>ref-fresh</i>	0.75	
<i>work-fresh</i>	0.999	
<i>r_reference</i>	0.01	
<i>r_working</i>	0.15	
Worms life span	60 (days)	Based on model of egg production by Ishikawa et al. 2003
<i>a_{egg}</i>	0.423	Ishikawa et al. 2003
<i>b_{egg}</i>	5	
α	0.3	
<i>P_{max}</i>	3700000	

APPENDIX 3.

A3.1 SPATIAL HETEROGENEITY

Table A3 - 1: Table showing the mean of the prevalences (and standard deviation) in Bowmont park (BM), North Hill Park (NHP), and their average. These were calculated from results of 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, conducted at each parameter combinations. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. Observed prevalence in BM, NHP, and their average was 63.07, 17.28, and 40.175 respectively.

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility		0	0.37 (1.19)	1.44 (3.79)
	<u>x1</u>	0	15.86 (23.69)	50.74 (43.91)
		0	8.12 (18.15)	26.09 (39.50)
		0	0.52 (1.11)	2.55 (4.90)
	<u>x2</u>	0	16.29 (34.36)	55.66 (46.31)
		0	8.41 (25.00)	29.10 (42.06)
		0	0.79 (1.63)	29.95 (32.11)
	<u>x5</u>	14.00 (26.94)	35.15 (45.41)	66.90 (46.22)
		7.00 (9.95)	17.97 (35.89)	48.43 (43.13)
		3.49 (11.05)	19.85 (23.23)	70.25 (23.32)
<u>x10</u>	1.88 (5.93)	70.93 (38.45)	89.29 (25.82)	
	2.69 (4.33)	45.39 (40.52)	79.77 (26.17)	

Table A3 - 2: Table showing the difference in prevalence between Bowmont Park and North Hill Park expressed as mean (and standard deviation) of standard deviations between the two parks, averaged over 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, conducted at each parameter combinations. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. Observed standard deviation between BM and NHP prevalence was 32.38.

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0	11.48 (16.57)	34.87 (30.13)
	<u>x2</u>	0	11.15 (23.52)	37.55 (31.31)
	<u>x5</u>	9.90 (19.05)	24.30 (31.39)	37.89 (26.77)
	<u>x10</u>	3.80 (8.45)	36.12 (26.10)	23.03 (18.79)

A3.2 SEASONAL HETEROGENEITY

Table A3 - 3: Table showing prevalences calculated as a mean of prevalences in four seasons. Shown values are the mean (and standard deviation) calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 23.80, calculated from the data over the entire city of Calgary.

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	9.47 (14.20)	30.72 (26.85)
	<u>x2</u>	0 (0)	9.67 (20.42)	34.33 (28.65)
	<u>x5</u>	8.38 (16.03)	21.71 (28.03)	52.07 (30.85)
	<u>x10</u>	2.38 (5.06)	50.58 (27.97)	81.82 (16.45)

Table A3 - 4: Table showing seasonal heterogeneity of prevalences in the Variance to Mean Ratio (VMR) of prevalences in four seasons. Shown values are the mean (and standard deviation) of the VMR calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed VMR was 0.08217

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	NA	0.0217 (0.0055)	0.0121 (0.0031)
	<u>x2</u>	NA	0.0150 (0.0048)	0.0084 (0.0042)
	<u>x5</u>	0.0123 (0.0081)	0.0092 (0.0046)	0.0110 (0.0086)
	<u>x10</u>	0.0190 (0.0040)	0.0166 (0.0128)	0.0096 (0.0135)

Table A3 - 5: Table showing mean (and standard deviation) prevalences in the simulated Spring calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 43.47

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	11.58 (17.67)	35.13 (30.63)
	<u>x2</u>	0 (0)	11.60 (24.46)	37.68 (31.14)
	<u>x5</u>	10.07 (18.83)	24.18 (31.27)	57.56 (34.50)
	<u>x10</u>	2.47 (6.00)	58.02 (32.07)	90.15 (13.62)

Table A3 - 6: Table showing mean (and standard deviation) prevalences in the simulated Summer calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 10.52

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	8.91 (14.20)	28.67 (24.91)
	<u>x2</u>	0 (0)	9.20 (19.47)	31.94 (26.51)
	<u>x5</u>	8.91 (16.49)	19.89 (25.71)	48.59 (28.48)
	<u>x10</u>	2.38 (5.27)	48.53 (27.67)	77.68 (19.34)

Table A3 - 7: Table showing mean (and standard deviation) prevalences in the fall calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 21.80

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	6.51 (10.18)	25.64 (22.72)
	<u>x2</u>	0 (0)	7.72 (16.31)	29.99 (25.39)
	<u>x5</u>	6.44 (13.23)	18.97 (24.53)	45.90 (27.45)
	<u>x10</u>	1.91 (4.06)	42.44 (24.32)	75.29 (18.33)

Table A3 - 8: Table showing mean (and standard deviation) prevalences in the winter calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 19.40

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	10.89 (15.35)	33.45 (29.46)
	<u>x2</u>	0 (0)	10.14 (21.51)	37.71 (31.84)
	<u>x5</u>	8.08 (15.79)	23.78 (30.73)	56.22 (33.85)
	<u>x10</u>	2.78 (6.03)	53.33 (29.50)	84.16 (15.52)

A3.3 INDIVIDUAL HETEROGENEITY

Table A3 - 9: Table showing mean (and standard deviation) infection intensity among infected coyotes calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 23,726.6

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	570,201 (624,584)	1,622,392 (1,422,044)
	<u>x2</u>	0 (0)	418,822.8 (883,259.6)	2,307,568 (2,041,489)
	<u>x5</u>	237,667 (461,645)	1055,763 (1386,894)	3,606,991 (2,353,399)
	<u>x10</u>	188,019 (397,258)	2244,909 (1,436,852)	5,177,787 (1,490,451)

Table A3 - 10: Table showing mean (and standard deviation) standard deviations of infection intensity among infected coyotes calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 53,547.47

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	0 (0)	483,654.7 (668,902.3)	1,774,900 (1,573,792)
	<u>x2</u>	0 (0)	516,041.1 (1,094,331)	2,037,028 (1,783,142)
	<u>x5</u>	336,677 (657,076)	1,117,231 (1,456,396)	3,367,451 (2,066,602)
	<u>x10</u>	209,543 (441,763)	2,343,740 (1,379,281)	4,933,613 (1,160,328)

Table A3 - 11: Table showing mean (and standard deviation) Variance to Mean Ratio (VMR) of infection intensity among infected coyotes calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, CEmCA, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 120,848.92

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation susceptibility	<u>x1</u>	NA	2,119,760 (231,062)	3,657,302 (965,236.8)
	<u>x2</u>	NA	3,639,933 (808,845.5)	2,807,710 (1,286,210)
	<u>x5</u>	1,774,729 (1,290,703)	3,270,971 (347,066.4)	4,350,479 (1,245,342)
	<u>x10</u>	1,627,739 (132,463)	3,360,288 (584,598.5)	4,946,058 (1,013,643)

Table A3 - 12: Table showing mean (and 95% confidence interval of the mean) maximum-to-mean ratio of infection intensity among infected coyotes calculated from 10 simulations using the Calgary *Echinococcus Multilocularis* Coyote Agent-based model, at each parameter combination. One of the parameters tested were IH predation susceptibility, which indicate the multiplication to the detection rate of infective intermediate hosts (IH) compared to a healthy small mammal. Another parameter tested were “Egg-contact rate” indicate the percentage of a small mammal to encounter *Echinococcus* egg laden feces if it is in the same 50m x 50m cell. The observed mean was 10.91

		Egg-contact rate		
		<u>0.5 %</u>	<u>1 %</u>	<u>2 %</u>
IH predation	<u>x1</u>	NA	5.08 (2.04)	7.36 (1.77)
	<u>x2</u>	NA	8.53 (3.46)	4.95 (1.76)
susceptibility	<u>x5</u>	10.02 (3.92)	6.08 (0.60)	6.89 (2.09)
	<u>x10</u>	3.75 (0.32)	6.58 (1.49)	6.83 (1.41)

A3.4 DISCUSSION ON CALIBRATION

Overall, the CEmCA was mostly calibrated successfully and reproduced several patterns of coyote behavior such as the home range sizes and the activities of coyotes. However, there still were deviations from observed data for which we could have calibrated the CEmCA further. Home range sizes, for example, tended to be larger than the less developed or mixed habitats as classified in Gese et al. (2012). While these larger home ranges of simulated coyotes suggest needs for better calibration, the coyote home ranges reported in the literature were highly variable. Besides the season, the home range sizes vary from study to study, and by the urbanization of the coyote’s habitats (Gehrt, 2007; Gese et al., 2012), coyote’s sex (Andelt & Gipson, 1979), whether the coyote is resident or transient (Gehrt et al., 2009; Grinder & Krausman, 2001), and coyote’s health (Murray et al., 2015b). Although our simulated coyotes’ home range sizes did not conform to the sizes described in the study by Gese et al. (2012) or Andelt and Gipson (1979), our simulation produced general patterns of 1) seasonal increase/decrease, 2) larger home range sizes in BM where urbanization is greater, and 3) the relative home range sizes between male and female. The home ranges of simulation were all within the range of reported home range sizes as well. All these results suggest that the coyote’s home ranges sizes in CEmCA are reasonable reproduction of the observation.

The diet of the simulated coyotes was the most difficult behavior to calibrate and resulted in much deviation from the observed in the species composition. Part of the deviation probably arose from the fact that the observed data was obtained from the entire city of Calgary, while the simulation was restricted to northwestern areas of Calgary. The distribution and abundances of small mammal species are expected to be different at different parts of the city (Liccioli et al., 2014; Mori et al., 2019). Coyotes are also highly

omnivorous and are known to consume variety of foods besides small mammals, including larger mammals such as deer and hare, invertebrates, plants and fruits, and anthropogenic foods (Liccioli et al., 2015a; Lukasik & Alexander, 2011b). On the other hand, only the small mammals were simulated explicitly in CEmCA to keep the complexity of the model manageable, and the consumption rate of the small mammals were primarily driven by their abundances. It is possibly that other factors are driving coyote's small mammal consumption in reality, such as the seasonal availability of other foods sources. For example, diseased coyotes are reported to rely on anthropogenic foods more than healthy coyotes (Murray et al., 2015b). Given so many factors that could have influenced the estimate by Liccioli et al. (2015a) that were not modelled in the CEmCA, we consider our calibration to be reasonably successful. And although deer mice were consumed at much higher rates than observed while meadow voles and southern red-backed voles were consumed at much lower rates, these three species were all known to be susceptible to *Em* infection (Liccioli et al., 2013). It is likely that they would compensate each other in the transmission of *Em* and cause little issue.

One issue that was common in all the calibration was that a simulation model can record and output every single act of the coyotes and provides outputs, while the observation data are estimates from limited observation samples. This is exemplified in the calibration of the coyotes' den visit frequency. The simulation records every visit by coyotes, while field observations were recorded only when the researchers were actually observing the den, something that requires a lot of time and labor. The complete records of the simulation also produce artifacts like that of the daytime den visit rate in season 5, where every simulation resulted in 1.6% rate. This is equivalent to one day in the season 5, suggesting that coyotes were at their den on the first day of the season 5 as a result of the behavior of the night before. One solution to the difference in observability between reality and simulation is the use of virtual ecologist approach (Zurell et al., 2010), sampling the "observation" of simulation results in a same manner as an ecologists observing the reality.

A3.5 DISCUSSION ON VALIDATION

The results of the validations of the epidemiological patterns in the CEmCA indicate that the model performed rather poorly in the reproduction of the transmission of *Em*. While the spatial heterogeneity of the prevalence was reproduced, the pattern was reversed from the observation (Appendix 3-1). Because the primary purpose of this study is to understand the mechanisms and processes causing the spatial heterogeneity in the prevalence of *Em*, this result was of particular interest. The higher prevalence among simulated coyoted in NHP than in BM can be explained by the larger areas of assemblage type 2, which were better suited for *Em* transmission than other assemblages as shown in the results of experiments

manipulating the small mammal assemblage types (Table 13). However, this is in contrast to Mori et al. (2019) where assemblage type 1 was associated with higher prevalence than assemblage type 2.

In Mori et al. (2019), it was speculated that assemblage type 1 is associated with higher prevalence of *Em* because of lower overall abundance of small mammals but higher proportion of susceptible species, increasing the chance of hunting coyotes to consume a susceptible small mammal. The assemblage type 2 was associated with lower prevalence because higher overall abundance of small mammals causes dilution effects (Civitello et al., 2015; Mori et al., 2019). While the dilution effects are considered likely to play a role in the transmission of *Em*, density-dependent prey preference, availability of other food source, and omnivorous and flexible diets can highly complicate the transmission (Baudrot et al., 2016; Raoul et al., 2015). Coyotes are highly omnivorous and mobile (Gese et al., 2012; Liccioli et al., 2015a) and it is conceivable that they would rely on other food sources if the small mammals are less abundant (Murray et al., 2015b). Coyotes can choose to hunt where the preys are abundant, rather than hunt at places with lower prey abundance. Such behaviors were not incorporated in the CEmCA, but potentially have significant effect on the transmission. One possible scenario explaining the higher prevalence among observed coyotes in BM could be that it was not because there were more areas of assemblage type 1 in BM, but because there were less areas of assemblage type 2 that they prefer to hunt in, leading to concentration of coyote activities in smaller area.

The seasonal pattern of prevalence among simulated coyotes were again at first appeared to be similar the observed, with mean prevalence in close match with observed mean (Appendix 3-3). However, the seasonal heterogeneity of the prevalence in the simulation results were far smaller than the observation (Appendix 3-4). Some of the mechanisms suspected to produce the seasonal heterogeneities in prevalences were the longer survival of *Em* eggs in colder temperature (Veit et al., 1995), population dynamics and reproductive cycle of small mammals (Burllet et al., 2011), and seasonal diet composition of the DHs (Burllet et al., 2011; Liccioli et al., 2015a). Of the three mechanisms, one likely issue with the CEmCA was the seasonal patterns of small mammal population dynamics and coyote's diet. The small mammal population density estimate was lowest in spring (Mori et al., 2019) but the estimated consumption of the small mammal by coyotes were highest in spring (Table 11; Liccioli et al., 2015a).

Small mammals are generally observed to be at the lowest population density in early spring, to gradually increase toward fall, and decline during winter (Getz et al., 1987; Madison & McShea, 1987; Rodd & Boonstra, 1984). Therefore, the seasonal population dynamics of the small mammals estimated for the CEmCA is reasonably realistic. The model determining the coyote's diet in the CEmCA may not be as reasonable. The consumption rate of small mammals by the coyotes were assumed to vary by the density

of the small mammals. However, given the higher consumption rate of small mammals observed among coyotes in Calgary (Liccioli et al., 2015a), and similar pattern described for foxes in Switzerland (Burlet et al., 2011), this assumption needs re-assessment.

However, we caution in emphasizing too much on the seasonal heterogeneity of the *Em* prevalence. The CEmCA results were assessed in comparison to the seasonal pattern in *Em* prevalence observed in the city of Calgary (Liccioli et al., 2014). However, in Hokkaido Japan, the seasonal pattern of prevalence among foxes were opposite, with high prevalence observed in winter and summer, low prevalence observed in spring and fall (Morishima et al., 1999). In Switzerland, the highest prevalence among small mammals were observed in spring (Burlet et al., 2011), while no *Em* positive small mammal was found in spring in Calgary area (Liccioli et al., 2014). Although the ecosystems of Hokkaido Japan and Switzerland are distinctly different from Calgary, and behaviors of foxes are different from coyotes, it is possible that different seasonal patterns would emerge in Calgary if studies are continued, especially as the population dynamics of small mammals are known to be highly variable from year to year (Getz et al., 1987; Getz et al., 2001).

Of the three patterns used in validation, individual infection intensities were most different from observations (appendix 3-9). Although we generally assume qualitatively that the infection intensity has a strong influence on the transmission rate of *Em* (Hofer et al., 2000), there is very little quantitative understanding of the relationship between infection intensity and transmission. Only few epidemiological models of *Em* explicitly take into consideration the individuality of the hosts (Atkinson et al., 2013a). The quantitative effects were modelled only tentatively in Nishina and Ishikawa (2008), whose models we have adopted for the CEmCA.

While the range of infection intensities found in the CEmCA were rather expected, the differences in the heterogeneity indices among individual infection intensities between simulation and observation were more concerning (Appendix 3-10 to 12). The much larger VMR (Appendix 3-11) and somewhat smaller max-to-mean ratio (Appendix 3-12) indicate that the simulated coyotes had infection intensity distribution have heavier tail than the coyotes in reality. Part of this could be due to the smaller population in the simulation ($n = 15\sim 55$) compared to larger sample sizes of coyote studies in Calgary area ($n = 146$). Smaller population in the simulation allows single super-spreader to influence the mean and creates heavier tale than a larger population. There are also potential bias with the sampling of coyotes in real life. Observation data of individual infection intensities were mostly derived from road-killed or hunted coyotes (Catalano et al., 2012; Liccioli et al., 2012). Coyotes are known to be more frequently road-killed in spring or fall (Murray & St. Clair, 2015). Because coyotes are known to have seasonal patterns in

prevalence (Liccioli et al., 2014), this seasonal pattern in road-kill can skew the data. Murray and St. Clair (2015) also indicate that there is tendency for road-killed coyotes to be more active during the day, compared to coyotes avoids the car accidents. It is possible that active time of the coyotes can influence the consumption of small mammals that are mostly nocturnal (for example of Meadow vole, see Hamilton, 1937) and therefore bias the infection intensity of the samples. Coyotes that have conflicts with human, and probably are likely to be hunted, are known to be less healthy and rely more on anthropogenic foods (Murray et al., 2015a; Murray et al., 2015b), which leads to two counteracting tendency for reduced immunity that can increase the infection intensity, and reduced diet on small mammals that can reduce the intensity.

It is also conceivable that there are mechanisms in the transmission cycle that produce super-spreaders that were not included in the CEmCA. For example, coyote might defecates and hunts at the proximity to each other more so than in the CEmCA, because coyotes might mark their preferred hunting ground with feces as part of their territories (Gese & Ruff, 1997). If this is the case an infected coyote can become re-infected more frequently by hunting the small mammals that it infected, resulting in multiple infection and high intensities. Alternatively, this could come about simply through memory of where they have had more success in hunting. Although the strength of reference and working memory of coyotes in the CEmCA simply relies on the freshness of the memory for the sake of simplicity (Van Moorter et al., 2009), in reality the strength of the reference memory is likely to be strengthened or weakened by the perceived prey density and/or hunting success (Hirvonen et al., 1999). If the host manipulation of IH by *Em* does occur, making the IH to be easier prey (Vervaeke et al., 2006), coyotes might be incentivized to return to the site where they became infected for hunting and defecation.

Some studies found found younger DHs tended to have higher intensities (Hofer et al., 2000; Torgerson, 2006). This suggest that older individuals have immunities acquired from past infection to *Em* that lowers the infection intensity. Currently the CEmCA has simple immune response with constant strength that toggles on or off for each individual coyote based on their past infection experience, which makes young individual with single infection experience just as immune as old individuals. In addition, the CEmCA's model of coyote reproduction is a simple model of juvenile coyotes that remain in the system for several months before they disperse and disappear from the model. Perhaps more dynamic immune response to *Em* with a more realistic model of coyote's population dynamics, where older individuals die and are replaced with younger individual, may produce greater heterogeneities in individual infection intensities. However, some studies found the age to be unrelated to the infection intensities (Guislain et al., 2008; Yimam et al., 2002), while other studies found infection to sarcoptic mange in association to higher intensities (Massolo, unpublished data), and more research is needed.

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