Évaluation de la validité des modèles de risque pour prédire l'incidence des gastroentérites d'origine hydrique au Québec

Mémoire

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Résumé

Les analyses de risque microbiologique, dont l'ÉQRM (évaluation quantitative du risque microbien) proposent de nouvelles techniques pour évaluer les conséquences sanitaires liées à la contamination microbiologique de l'eau potable. Ces modèles intègrent les données physico-chimiques et microbiologiques des usines de traitement d'eau pour quantifier un risque à la santé. Le projet visait à évaluer le lien entre le risque estimé selon un modèle ÉQRM et l'incidence de giardiase observée. Les banques de données des maladies à déclaration obligatoire et d'INFO-SANTÉ ont été utilisées pour comparer le résultat de l'analyse de risque à celui des analyses épidémiologiques. Les municipalités considérées les plus à risque par l'ÉQRM ont une incidence de gastroentérite et de parasitoses plus élevée. Cependant, l'ampleur du risque prédit ne correspond pas à celui observé. Il est souhaitable que les modèles d'ÉQRM incorporent des données populationnelles pour prédire avec une plus grande exactitude le risque épidémiologique.

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ADC: Acute digestive condition
AIC: Akaike information criterion
ARIMA: Autoregressive integrated moving average
CCDR: Canada include the Canadian Communicable Disease Report
CDW: Committee on drinking water
CI: Confidence interval
CT: Contact time
DALY: Daily adjusted life years
DNA: Deoxyribonucleic acid
ÉQRM: Évaluation quantitative du risque microbiologique
FSA: Forward Sortation Area
GE: Gastroenteritis
IESWTRE: Interim Enhanced Surface Water Treatment Rule
IR: Incidence rate
LPR: Longitudinal prevalence ratio
LT1ESWTR: Long Term 1 Enhanced Surface Water Treatment Rule
LT2ESWTR: Long Term 2 Enhanced Surface Water Treatment Rule
MADO: Maladies à déclaration obligatoire
MED-ECHO: Maintenance et exploitation des données pour l'étude de la clientèle hospitalière
NESP: National Enteric Surveillance Program
NTU: Nephelometric Turbidity Units
OR: Odd ratio
P_i: Probability of infection
P_{ill}: Probability of illness
ppl-yr: people-year
pppy: Per person per year
QMRA: Quantitative microbial risk analysis
RCT: Randomized control trial
RNA: Ribonucleic acid
RR: Relative risk
SD: Standard deviation
SWTR: Surface water treatment rule
USEPA: United States Environmental Protection Agency
UV: Ultra violet
WBD: Water borne disease
WTP: Water treatment plant

Dedication

To those with never ending patience and kindness

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Foreword

This thesis contains an article submitted to the «Journal of Water and Health». I contributed to the study's conceptualisation, was entirely responsible for the analysis and drafting the manuscript, as well as the critical revisions. Drs Pierre Payment, Benoît Barbeau, Annie Locas, Réjéan Dion, and Patrick Levallois actively participated in study conceptualisation and critical revision to improve contents.

The article has been modified to better reflect tables and figures order. The included document will be different from the one published as reviewers will request document modification.

Introduction

Potable drinking water is a precious commodity and its availability is essential to the development and health of a nation. Access to potable drinking water is a basic human right and effective regulations and policies should be enforced in order to ensure the fair distribution of clean water (Majowicz et al., 2008; World Health Organization, 2008). This is made more complex as raw water quality is forever fluctuating. Indeed, both natural and anthropomorphic events lead to an unstable source water makeup, necessitating treatment (Greer et al., 2008; LeChevallier et al., 1991a, 1991b; Levin et al., 2002; Ongerth, 1989; Rose et al., 1991a). Consequently, water treatment technologies have been implemented to reduce the risk of disease associated with consuming water. This includes control measures applied at the source water, the treatment plant, the distribution system and at the point-of-use (Reynolds et al., 2008). Despite this, water-borne diseases (WBD) still occur in countries with state-of-the-art water treatment systems (Bruce-Grey-Owen-Sound Health Unit, 2000).

WBD have multiple morbidities, among which diarrhoea is the most frequent and the most observable (Payment, 2003). It has been estimated that, on average, every person living in Canada has one episode a year (Payment, 2003). In Canada, from 1975-2004, over 200 WBD outbreaks have been reported (Health Canada, 2009). From 1940 to 1994 there were 578 waterborne diseases outbreaks in the United States alone, affecting 600 000 individuals (Craun et al., 2006a). Generally, the outbreak microorganism source is unknown, however, the most commonly identified causal pathogens are protozoan parasites (21%), and more precisely, *Giardia* (Reynolds et al., 2008). Quebec reported 940 individual cases of giardiasis in 2010 (12.2 per 100 000 per year) (Ministère de la Santé et Services sociaux, 2011). In Calgary, between 1999 and 2002, *Giardia* infections occurred at a rate of 19.6 per 100 000 per year (Calgary Health Region, population1 million) (Laupland et al., 2005); the Ontarian province reported, in 2011, an infection rate of 9.48 per 100 000 per year (Public Health Ontario, 2012).

Protozoan outbreaks were most frequently linked with source water location, water plant design, treatment barrier failure, rain and climate change introducing surface runoff, and

presence of livestock (Curriero et al., 2001; Hrudey et al., 2004; Risebro et al., 2007a; Risebro et al., 2007b; Rizak et al., 2008). Other outbreak risk factors, highlighted in Rizak et al.'s review are the maintenance, repair, and upgrading of water system plants as well as changes in the water treatment process (Rizak et al., 2008).

The parasites present in industrialized countries' raw water are of particular concern to system operators because parasite cysts are highly resistant to disinfection, unlike their bacterial and viral counterparts. Parasites require more than simple chemical disinfection to eliminate them from potable water (LeChevallier et al., 1991a). The cysts are also problematic as microbiological lab tests to verify their presence are costly, have a high probability of recovery loss, and are infrequently performed (United States Environmental Protection Agency, 2005).

Current regulations have been established for many years, and it has become necessary to revise our existing water norms (Theron et al., 2002). While the guidelines delimitates what is defines safe drinking water, no clear definition is presented, leaving ambiguity to those designing and planning treatment plants. Among other criteria, the propose revisions suggest that emphasis should shift from relying on pathogen concentration alone to understanding the pathogen's effect on human populations (Hellard et al., 1997). Quantitative microbial risk analysis (QMRA) models have the possibility to quantify pathogen effect within a population and bring new methods of assessing the risks associated with drinking water (van Lieverloo et al., 2007; World Health Organization, 2008). These models, in a drinking-water context, quantify a risk characteristic and generate the potential consequences following the consumption of the water. Albeit, the measurement error of these models is generally unknown and acceptability of their use is still being defined (Macgill et al., 2001). QMRA risk results have rarely been contrasted with epidemiological data, hence the apparent validity of these models remains undefined. Work is being done to encourage pairing QMRA with material flow analysis (use and transformation of a resource modified as it move through a system or region) to develop a comprehensive risk prevention plan (Nguyen-Viet et al., 2009), but the validation is not complete.

This presented project aims to compare the probability of illness estimated by using Health-Canada's QMRA model with the illness recorded in health surveillance records. This comparison will be done using three sites within the province of Québec, including an urban, a rural site and a metropolitan site. We will use passive surveillance to retrospectively evaluate the prevalence of gastrointestinal illness, and when possible, giardiasis. This will provide insight as to the use of QMRA for health officials in order to reduce the risk of microbiological burden associated with drinking water.

Chapter 1: Literature Review

Literature concerning the characteristics and monitoring of diseases is impressive. In this following review, gastroenteritis and giardiasis will be characterized, including *Giardia's* pathology and pathogenicity, including a description of the susceptible population. We will focus on the waterborne aspect of this disease, although other mode of transmission do exists, notably secondary transmission through person to person contact and fomites (Einsenberg et al., 2007). The review will then discuss the occurrence of *Giardia* in surface waters as well as notable outbreaks associated with the presence of *Giardia* in drinking water. Then, surveillance, notably passive surveillance (traditional and syndromic), will be presented in the context of detecting gastroenteritis. Canadian water treatment process will be explained in general terms in order to facilitate the understanding of its importance for QMRA. QMRA models, their applications and current epidemiological knowledge regarding these models will be explored in order to highlight the relevance of testing QMRA in a practical environment. Lastly, the methods by which guidelines are established will be explained.

1.1 Gastroenteritis

1.1.1 Characterization of gastroenteritis

Waterborne outbreaks are generally characterized by a sudden increase of "highly credible" acute gastroenteritis. Gastroenteritis is defined by an inflame gut leading to nausea, vomiting, abdominal cramps, and various degrees of diarrhoea for approximately 4.2 to 4.8 days on average in Canada (Majowicz et al., 2008). The severity of the disease can range from asymptomatic to mild discomfort to chronic diarrhoea or death (dehydration) (Adam, 1991; Cliver et al., 2002; Health Canada, 2009; Public Health Agency of Canada, 2001). Waterborne outbreaks rarely lead to chronic diarrhoea, that is repeated episodes of diarrhoea lasting for at least four weeks; the general population will mostly ail from a self-limiting and acute (sudden and intense) onset of gastroenteritis. Case definitions of gastroenteritis tend to vary, and may be tailored to a particular study's need (Majowicz et al., 2008). A proposed definition by Majowicz et al (2008) consisted of 3 or more loose stools or

vomiting, within 24 hours (assuming no existing gastrointestinal disease, drug or alcohol ingestion, or pregnancy) (Majowicz et al., 2008).

1.1.2 Transmission

Typically, waterborne gastroenteritis will occur following the infection of a microorganism. These pathogens are generally subdivided into three families: bacteria, viruses or parasites (Table 1). Illness is generally precipitated through fecal oral contamination, accomplished either by fecal matter entering the water distribution system, inter-human transmission, or through other vectors. Parasites such as *Giardia and Cryptosporidium*, two common water parasites, tend to be found in the environment in their cystic or oocystic form. Once ingested, *Giardia, Cryptosporidium* complete or undergo a portion of their life cycle including reproduction within the human host. They are then shed through the passing of feces as either trophozoites or (oo)cysts. Only the cyst can infect a host and induce a pathogenic response (not the trophozoites) and are therefore the more important health concern (Adam, 1991). Protozoan parasites are not screened on a regular basis and hence represent an interesting venue for studying their potential use in routine surveillance. Of the two main waterborne parasites, *Giardia* will be the focus of this study.

1.1.3 Occurence

Globally, diarrhoeal diseases are quite common; average disease incidence is 0.7 per person per year (pppy) (Mara et al., 2007). This risk is substantially higher in individuals less than 5 years old, (3.7 pppy); notably in areas with poor sanitation (Mara et al., 2007). Diarrhoeal diseases differ from GE due to their exclusion of cases reporting solely fever, cramping or vomiting. In industrialized countries, the risk is generally around 0.2 diarrhoeal disease pppy (Mara et al., 2007). Globally, the main source of diarrhoeal illness is contaminated water. Of the 1.8 million deaths due to diarrhoeal illness, it is estimated that 88% is due to drinking water (World Health Organization, 2014). In Canada, as mentioned earlier, the burden is on average one episode per person a year. In Québec, 11 to 40% of the annual gastroenteritis can be attributed to ingestion of safe drinking water (Colford et al., 2005; Payment et al., 1997). With regards to parasites, in Québec (2006), *Giardia* was reported 28

times more frequently than *Cryptosporidium* (Public Health Agency of Canada, 2014b) making it of primary concern for drinking water treatment plants management within the province.

Table 1. Common water pathogens

	Bacteria	**Virus**	**Parasite**
Micro organism	*Escherichia coli, Salmonella spp,* *Shigella spp., Campylobacter spp., Legionella spp.,* *Vibrio spp.*	Rotavirus, Astrovirus, Adenovirus, Norovirus	*Cryptosporidium spp., Giardia spp., Cyclospora spp.*
Morphological Characteristic	Single cell organism (Prokaryote) No nucleus Two type: gram, positive, gram negative; Fast reproductive rate Divers shapes and size (spiral, spherical, ball, rods) Motility through flagella or pili	Smallest and simplest forms of infectious agents Able to replicate within another living cell 20-100 nm, RNA or DNA based viruses	Eukaryotic organism, Single-celled protozoa to multicellular helminth worms, Contains distinct organelles, Complex life cycle
Pathogenic Mechanism	Increase electrolytes secretion or water secretion through toxin interaction with the lumen Decreased intestinal absorption May cause ulceration	Increased water secretion or electrolytes secretion	Mucosal adherence Malabsorption Villi erosion
2012 Canadian notifiable disease burden, all cause,. Rate per 10 000*	*Campylobacter spp:* 29.3 *Vibrio spp.:* 0.003 *Escherichia coli*:1.94 *Legionella spp.:*1.39 *Salmonella spp,:* 19.67 *Shigella spp.:* 3.08	Norovirus: 2.2	*Cryptosporidium spp.:* 1.56 *Giardia spp.:* 11.12 *Cyclospora spp.* 0.32

*(Public Health Agency of Canada, 2014b)

1.1.4 Vulnerable population

Disease morbidity varies greatly with respect to an individual's health status. Generally, the vulnerable population compriseds immunocompromised or immunovulnerable individuals, as well as those without prior exposure or those living in rural areas (Ljungstrom et al., 1992; Reynolds et al., 2008; United States Environmental Protection Agency, 1998). Children less than five years of age are particularly susceptible due to their under-developed immune system and susceptibility to fecal-oral contamination in daycares (Groupe

scientifique sur l'eau, 2003b; ICAIR Life Systems Inc, 1984; Laupland et al., 2005; Thompson, 2004; United States Environmental Protection Agency, 1998). In 2009, the hospitalization rate for children under five for cause of gastroenteritis and norovirus (all cause confounded) was 50 per 10 000 (Desai et al., 2012). The elderly (over 60 years of age) also have a susceptible immune system, although they are less vulnerable than children to GE illness, including illness caused by giardiasis. Individuals with genetic illnesses or conditions which weaken their immune system, such as diabetes, AIDS, cancer, malnutrition and pregnancy are equally susceptible and cannot mount a sufficient response to prevent infection or re-occurring episodes (Lengerich et al., 1994). Individuals practicing anal intercourse or oral-anal sex are also at a higher risk of gastrointestinal illness (Heymann, 2008).

1.2 Giardia

1.2.1Characteristics

1.2.1.1 Identification

Giardia is a parasitic protozoan (a single celled, flagellated parasite), most recognizable for its two visible nucleates. The ovular cysts measure 13 µm and the trophozoites are 9-21 µm long, 5-15 µm wide and 2-4 µm thick. They are monoxenous; with a complex lifecycle with a portion needing to be completed within a single host (Adam, 1991; Karanis et al., 2007).

1.2.1.2 Environment

Giardia cysts are resistant to extreme weather events. This reduces the likelihood of cyst reduction during the winter, a period wherein many pathogens cannot proliferate or survive. They can survive up to 2 months in an environment with temperatures as low as 8 ^{o}C, whereas at 21 °C they survive around 26 days. At -20 °C and 54 °C, the cysts are denatured (ICAIR Life Systems Inc, 1984; Schaefer et al., 1984; United States Environmental Protection Agency, 1998).

1.2.1.3 Host, infection dose

Giardia can be found within many host species including, humans, farm animals, domestic animals, and wild animals (Feng et al., 2011). *Giardia lamblia,* assemblage A and B are the most commonly type of *Giardia* to infect humans (Table 2) (Feng et al., 2011; Frost et al., 2000; Monis et al., 2009). Of these assemblages, only two are believed to be truly zoonotic, although research is not yet conclusive for all species (Feng et al., 2011; McDowall et al., 2011). Within a host, *Giardia* proliferates in large numbers. Infected humans can shed up to $1.44x10^{10}$ infectious cysts (8μm x 12 μm) per day (Porter, 1916; Smith et al., 1995). The shedding of animals into the water source or agriculture run-off introduces a wide variety of *Giardia* cysts (Table 3), which can infect a human host (ICAIR Life Systems Inc, 1984; Krewski et al., 2004; Leclerc et al., 2002).

While there are numerous *Giardia* species, only one species has zoonotic potential: *Giardia lamblia*. *Giardia lamblia*, is also known as *Giardia duodenalis* or *Giardia intestinalis*. *Giardia lamblia* is the term used in clinical paper whereas *Giardia duodenalis* is the term used in other scientific literature and approved by the International Code of Zoological nomenclature (Monis et al., 2009).

Table 2. *Giardia duodenalis* assemblages

Assemblage	**Zoonotic potential**	**Host**
Assemblage A (subassemblage :AI, AII, AIII) (proposed : *G. duodenalis*)	Yes	Humans, non-human primates, domestic and wild ruminants, alpacas, pigs, horses, domestic and wild canines, cats, ferrets, rodents, marsupials and other mammals
Assemblage B (subassemblages : BIII BIV) (proposed : *G. enterica*)	Yes	Human, non-human primates, cattle, dogs, horses, rabbits, beavers, muskrats
Assemblage C (proposed: *G. canis*)	No	Domestic and wild canines
Assemblage D (proposed: *G. canis*)	No	Domestic and wild canines
Assemble E (proposed: *G. bovis*)	No	Livestocks, cattle, pigs, sheeps, goats
Assemblage F (proposed: *G. cati*)	No	Cats
Assemblage G (proposed: *G. simondi*)	No	Mice, rats
Assemblage H	No	Seals, gulls

(Feng et al., 2011; Monis et al., 2009)

Table 3. Approved *Giardia* species

Species	Zoonotic potential	Major Host
G. agilis	No	Amphibians
G. ardeae	No	Birds
G. microti	No	Muskrats and voles
G. muris	No	Rodents
G. psittaci	No	Birds
G. varani	No	Lizards
G. duodenalis (lamblia, intestinalis)	Yes	Mammals

(Feng et al., 2011; Monis et al., 2009)

1.2.1.4 Incubation

Incubation periods have been reported to last between 3 and 25 days with a median of 7 to 10 days (or 14 days) (Benenson, 1995; ICAIR Life Systems Inc, 1984; Public Health Agency of Canada, 2014a; United States Environmental Protection Agency, 1998). Other reported incubation times include 9 to 22 days with a mean of 13.1 (Rendtorff, 1954; Rendtorff et al., 1954), 12 to 19 days (Jokipii et al., 1985), or 7.25 days (Nash et al., 1987).

1.2.1.5 Transmission and infectiousness

The typical mode of transmission is through person-to-person contact or faecal-oral ingestion of cysts (Health Canada, 2012; Thompson, 2004). Other methods include the ingestion of contaminated food or water, and unsafe anal intercourse (Public Health Agency of Canada, 2001).

1.2.1.6 Infection

Infectious dose in humans can be as low as 1 cyst but, usually, between 10-100 cysts are needed to induce a symptomatic infection (Karanis et al., 2007; Rendtorff, 1954). Infection will lead to clinical illness in 50-67% of cases (Gerba et al., 1996). In Canada, it is assumed that 5-10% of the adult population has symptomatically suffered from giardiasis (Health Canada, 2012). Generally, there is a greater percentage (11-35%) of potentially giardiasis seropositive individuals (Isaac-Renton et al., 1999; Ljungstrom et al., 1992). However, antibodies found within the serum may only be sign of past and not current infection (United States Environmental Protection Agency, 1998).

The dose-response relation of *Giardia*, as measured by Rendtorff et al (1954), was verified using clinical data by Zmirou-Navier et al (2006) (Rendtorff, 1954; Rendtorff et al., 1954; Zmirou-Navier et al., 2006). Assuming a 2L water intake containing 10 cysts/ 100L, the Rendtorff response model yielded a 12% excess risk, when taking into account an abatement factor for germ viability, infectivity and virulence in a natural setting, and an 11% excess risk when taking into account acute digestive conditions (Zmirou-Navier et al., 2006). Consequently, according to the model, only 20% of the cysts are assumed to be infectious (Zmirou-Navier et al., 2006).

1.2.1.7 Pathogenicity (virulence)

The pathogenicity of a giardiasis infection is very similar to that of other GE illnesses: the predominant clinical symptom is acute diarrhoea (malabsorptive). The main differences lie in the stool consistency, which is described to be greasy, frothy, grey or yellowish, and very malodorous (Adam, 1991). Other symptoms include fever, malaise, nausea and cramps, dehydration, loss of volume, lactose intolerance (Adam, 1991). Rare chronic symptoms can include nutrient malabsorption, anorexia, constipation, upper gastro-intestinal tract discomfort, and other immunodeficiencies such as hypogammaglobulinemia (Farthing, 1996; ICAIR Life Systems Inc, 1984; United States Environmental Protection Agency, 1999).

Mortality rate of giardiasis in developed countries is less than 0.01% (Gerba et al., 1996; United States Environmental Protection Agency, 1998). Typically the infection is asymptomatic (25% to 75% of the cases) (Janoff et al., 1990; United States Environmental Protection Agency, 1998). In untreated patients, symptoms may last less than one week; however the median illness duration is six weeks (Adam, 1991). However, for some individuals symptoms can last for many months and be classified as chronic diarrhoea (United States Environmental Protection Agency, 1998).

1.2.2 *Giardia* distribution

1.2.2.1 Giardia occurence

In Canada, *Giardia* is the most frequently reported intestinal protozoan parasite (Adam, 1991; Farthing, 1996), although the incidence is declining (from about 35 to 13 cases per 100 000 persons from 1990 to 2004) (Public Health Agency of Canada, 2006). A study revealed that 18% of the reported diseases in the National Enteric Surveillance program (infectious gastroenteritis) between April 2001 and 2004 were parasites, primarily occurring in late spring or early fall in Ontario (Edge et al., 2006).

1.2.2.2 Giardia presence in surface water

Surface waters are frequently contaminated with pathogens, among which are *Giardia* parasites. Canada is not exempt of this contamination. Sources of water contamination include animal feces (cattle, dog, cat), urban discharge and sewage discharge (Reynolds et al., 2008). This contamination can be exacerbated by rainfall, which introduces contaminants into the water (Wallis et al., 1996; Wallis et al., 2001). Contamination frequently occur during water treatment plant failure, and more precisely when the filtration process is not optimal (Reynolds et al., 2008; Westrell et al., 2004). Within American surface water, *Giardia* cysts contamination load may range from 4 cysts/L to 14 000 cysts/L in certain areas, according to a survey across the United States (Donovan et al., 2008; United States Environmental Protection Agency, 1998).

In the sanitary waste waters of the St-Lawrence River (Québec), *Giardia* cysts are often present in high concentration. The maximum concentration of *Giardia* identified was 3 800 cysts/100L (Barbeau et al., 2000), although significant variations exist (geometric mean varying from 2 000 cysts/100L to 7 cysts/L) (Payment et al., 2000). Alberta has an annual geometric mean of 8 to 98 cysts/100L, British Columbia 60 cysts/100L, and Ottawa 1 to 52 cysts/100L (Chauret et al., 1995; Health Canada, 2012). It is critical to remember that treated water in Canada is rarely tested for *Giardia* and hence the occurrence of this protozoan in drinking water is relatively unknown.

In the United States surface water *Giardia* cysts concentration average varies from 0.23 to 22 cysts/100L, notably smaller than the aforementioned range (United States Environmental Protection Agency, 1998). Surface water sampling of 14 states relayed that 81.2% of those water sources tested positive for *Giardia*, ranging from 0.04 to 66 cysts/L (LeChevallier et al., 1991b), with concentrations of 87 000 cysts/100L reported during the spring (Gammie et al., 1998; Health Canada, 2012). This supports the notion that *Giardia* has the potential to be a frequent source of infection (Payment et al., 2011). The caveat in evaluating surface water for the presence of cysts is that the pathogen's viability is often unknown (LeChevallier et al., 1991b). Consequently, the ability to identify and enumerate cysts varies depending on the laboratory assessment technique used (United States Environmental Protection Agency, 1998). Other limits to cyst enumeration concerns the total sample volume: a relatively small sample (described as less than 100L) may yield an inflated pathogen concentration (Wallis et al., 2001).

1.3 Epidemic and endemic cases of waterborne giardiasis and gastroenteritis

1.3.1 Source allocation

During the 20th century, treatment and prevention of diseases have greatly improved. Despite these improvements, gastrointestinal outbreaks (defined by a minimum of two individual cases caused by a similar source) regularly occur throughout the year. These outbreaks are either defined as an increase in endemic cases, a sporadic cases or an epidemic outbreak. Sporadic cases refer to a sudden increase that occurs irregularly, infrequently, and randomly. Endemic cases are usually present in the population within a given geographical area at a steady state (constant prevalence) with an expected increase. Sporadic cases cannot be associated to another case or source according to the available information albeit it may be possible to identify the source of a sporadic outbreak (Groupe scientifique sur l'eau, 2003a). A certain number of sporadic outbreaks are expected within a given timeframe. In contrast, epidemic outbreaks represent a higher incidence of cases in a community during a given time period.

Epidemic cases and sporadic cases can be distinguished through their epidemic curve; an epidemic point source curve will have a more traditional gaussian shape (Figure 1); an epidemic continuous exposure curve will have an abrupt incline and a larger upper boundary (Figure 2), whereas a sporadic cases will be indicated through a sudden increase in cases for a short period of time (Figure 3) (World Health, 2008). These two types of outbreaks may be considered jointly when tallying epidemics. However, transmission pathways causing these outbreaks can be difficult to determine as they may be of foodborne, waterborne or airborne origin (Einsenberg et al., 2007).

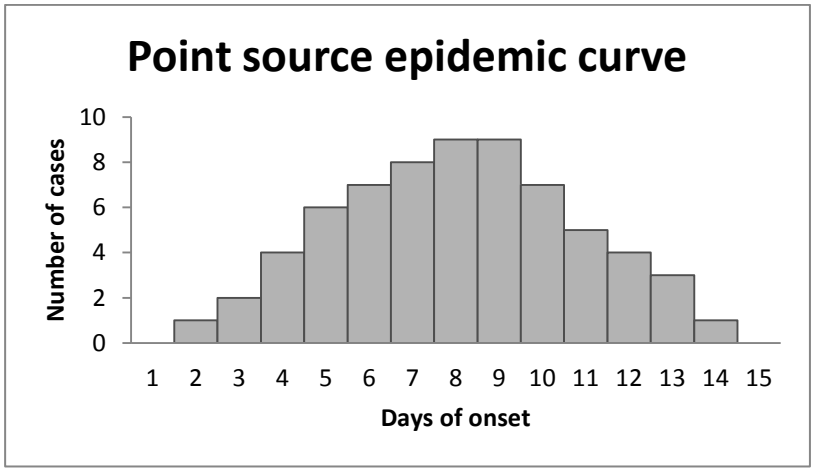

Figure 1. Distribution of a point source epidemic curve

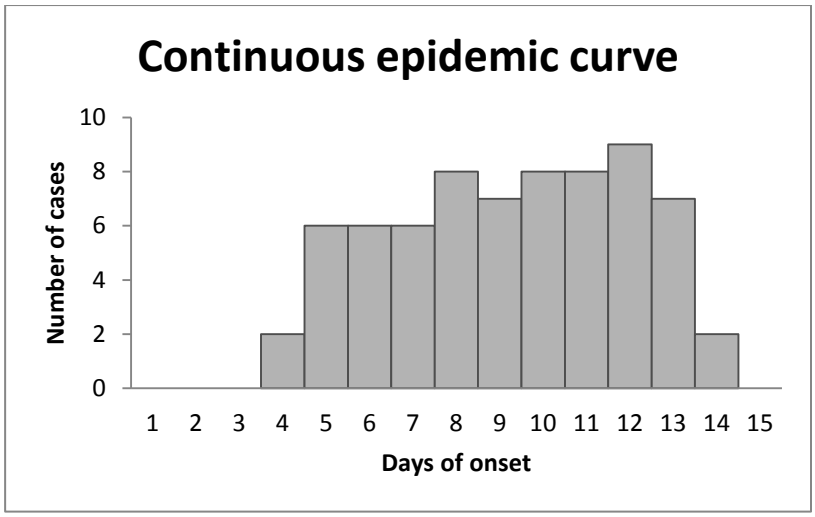

Figure 2. Distribution of a continuous epidemic curve

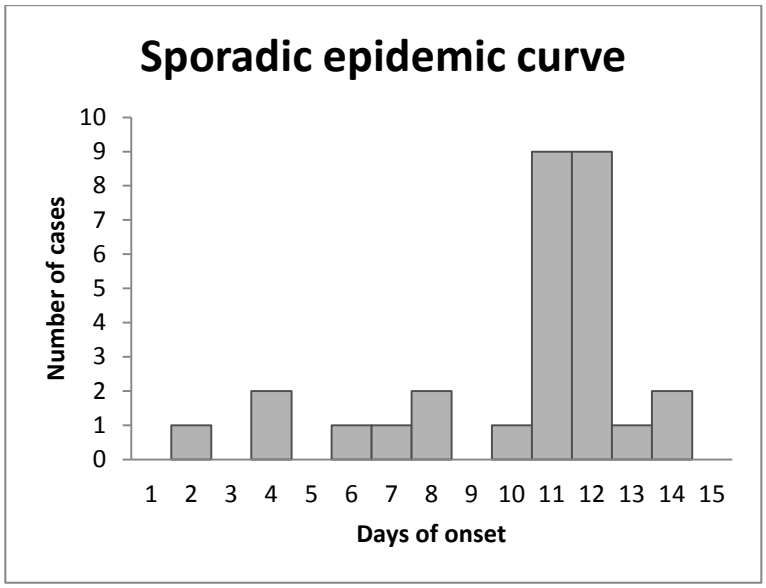

Figure 3. Distribution of a sporadic epidemic curve

Ideally, to determine the cause of an outbreak, the infected individuals must have a common exposure and an epidemiological connection. Possible outbreaks are detected through various surveillance databases and can be associated to an exposure identified according to time, place, common contact, symptoms and clinical signs, etiological agents, or pre-established drinking or bathing water issues. The strength of the association will vary greatly in accordance to the causality criteria (temporal sequence, strength of statistical association, dose-response, specificity of association, consistency of the association, biological plausibility, and coherency with existing theories). These associations will enable the exposure (Groupe scientifique sur l'eau, 2003a). The United Kingdom and the CDC proposed qualifying the source of the association according to water quality results and strength of epidemiological statistics (Table 4 and Table 5).

Waterborne outbreaks are classified by their alleged causes: deficiency in water treatment system, disturbance in the distribution system, untreated ground or surface water, or unknown treatment deficiency (Messner et al., 2006). Other causes, given the fecal-oral route of most waterborne pathogens, may be due to secondary or person-to person transmission (Craun et al., 2006a; Einsenberg et al., 2007). To illustrate the difficulty of identifying the source, of the 20 000 cases of GE reported each year in the United States,

only 1-2% of cases are associated with an outbreak, limiting the possibility of attributing a cause to the epidemic (Daly et al., 2010; Yoder et al., 2007). It is difficult to attribute cases of gastrointestinal disease solely to water consumption, as there are very few pathogens whose transmission route is uniquely through water, there are delays in epidemiological investigations, there is minimal information regarding water consumptions, and there are many dispersed and rare cases (Craun et al., 2006a; Groupe scientifique sur l'eau, 2003a).

Table 4. CDC classification of strength of evidence (adapted)

Level of evidence	Epidemiologic and clinical laboratory data	Environmental data
Strong	**Provided and adequate**	**Provided and adequate**
	Epidemiologic data provided about exposed and unexposed individuals, with relative risk or odds ratio ≥2 or p-value ≤0.05 OR Molecular characterization of pathogens linked to multiple persons who had a single identical exposure	Laboratory data or historic information concerning water treatment plants OR Molecular characteristics of pathogens isolated from water and at least one clinical specimen were identical
Moderate	**Provided and adequate**	**Not provided or inadequate**
	Epidemiologic data provided about exposed and unexposed individuals, with relative risk or odds ratio ≥2 or p-value ≤0.05 OR Molecular characterization of pathogens linked to multiple persons who had a single identical exposure	No data was available for laboratory test of the water and no historic information
Fair	**Provided but limited**	**Provided and adequate**
	Epidemiologic data provided that did not meet the criteria for Strong or Moderate or claim made that ill persons had no common exposures, beside water, but no data was provided	Laboratory data or historic information concerning water treatment plants OR Molecular characteristics of pathogens isolated from water and at least one clinical specimen were identical
Poor	**Provided but limited**	**Not provided or inadequate**
	Epidemiologic data provided that did not meet the criteria for Strong or Moderate or claim made that ill persons had no common exposures, beside water, but no data was provided	No data was available for laboratory test of the water and no historic information

(Blackburn et al., 2004)

Table 5. UK Communicable Disease Surveillance Centre, categories of evidence (adapted)

Level of Association	Evidence
Strongly associated	Pathogen identified in clinical cases is also found in water AND evidence from an analytical (case-control or cohort study) demonstrates association between water and illness OR Pathogen identified in clinical cases is also found in water AND descriptive epidemiology suggest that the outbreak is water related and excludes obvious alternative explanations OR Water quality failure and/or water treatment problem of relevance but outbreak pathogen is not detected in water AND evidence from an analytical (case-control or cohort) study demonstrates association between water and illness.
Probably associated	Water quality failure and/or water treatment problem of relevance but outbreak pathogen is not detected in water AND descriptive epidemiology suggest that the outbreak is water related and excludes explanations OR Pathogen identified in clinical cases is also found in water OR Evidence from an analytical (case-control or cohort) study demonstrates association between water and illness
Possible associated	Water quality failure and/or water treatment problem of relevance but outbreak pathogen is not detected in water OR Descriptive epidemiology suggests that the outbreak is water related and excludes obvious alternative explanations

(Tillett et al., 1998)

1.3.2 Attributed waterborne disease outbreaks

Despite the difficulty in identifying an epidemic's sources there are several outbreaks and cases for which water was recognized as the principal vector (Craun et al., 2006a; Issac-Renton et al., 1992; Jephcott et al., 1986; Stuart et al., 2003; United States Environmental Protection Agency, 1998). According to a world-wide review on water-associated outbreaks, compiling information from national statistic registers, a total of 325 parasitic protozoan outbreaks (40.6% *Giardia)* were identified between 1954 and 2003, of which the majority occurred in North America (Karanis et al., 2007). More specifically, the outbreaks were mainly reported in the United States (7.5 times more outbreaks recorded in the United States than in Canada) (Karanis et al., 2007). In Canada, one of the largest outbreaks occurred in Edmonton, with over 800 cases identified (United States Environmental Protection Agency, 1998; Wilson et al., 1982). In the United-States from 1920 to 2002 nearly 1 870 outbreaks were associated with drinking water (10 648 identified cases per year) (Craun et al., 2006b). The period dating from 1991 to 2002 found 207 outbreaks of which the aetiological agent was unknown (Craun et al., 2006a; Craun et al., 2006b). There is presumed to be an estimated 38 318 732 total cases per year in the United States, of which 2 000 000 are giardiasis (Craun et al., 2006a). These variations suggest that documentation sources, outbreak, and case definition will greatly modify the number of cases.

Table 6 presents a subset of articles, identifying key outbreaks in developed countries, selected for their reporting of recent waterborne outbreaks (starting from 2000), focusing on parasitical outbreaks, and their effect on the population at risk. The extent of the population affected by the water contamination varies greatly and the observed associations, while elevated, lack precision. Existing water treatment risk management programs, ability to respond quickly to the crisis, pathogen type, population immunity, and exposure all have a significant impact on the likelihood of developing an illness and will have a role in limiting the precision of an investigation. We observed that, in recent years, the most frequent cause of a waterborne outbreak is sewage effluent contamination caused by malfunctioning valves as opposed to lack of filtration (Beaudeau et al., 2008; Daly et al., 2010; Jameson et al., 2008; MacKenzie et al., 1994; Neira-Munoz et al., 2007; Nygard et al., 2006; Rimhanen-

Finne et al., 2010; Stirling et al., 2001; Stuart et al., 2003; Tuncay et al., 2008; Werber et al., 2009). This highlights the need for effective risk management programs and regular evaluation of water treatment plants infrastructure.

Table 6. Waterborne parasitical outbreaks reported in recent period (2000-2012) sorted by microorganism and number of cases

Author	Location	Microorganism	Cases	Measure	Method	Cause
Neira-Munoz 2007	Portsmouth, United-Kingdom	*Cryptosporidium*	- 35 cases (November-December)	-odds ratio (for tap water, all ages): 2.0 95% CI: 1.3 -3.1	-case-control -faecal sample - review of water companies 24h *Cryptosporidium* monitoring program results -interviews	-contamination in drinking water -no observed problems in drinking water system
Jameson 2001 and Stirling 2001	North Battleford, Canada	*Cryptosporidium*	-5 800 – 7 100 cases (March-April); -1,907 reported in the Battleford Health Service Area	-38% unadjusted attack rate	-descriptive and cross-sectional study -review of the health service centre records -convenience sampling of pharmacy sales -telephone surveys	-filter breakthrough -communication issues
Daly 2010	New-Hampshire, United - States	*Giardia intestinalis*	-17 confirmed cases -14 probable cases (August-September)	-risk-ratio 4.7 95% CI: 1.5-14.4	-cohort study -questionnaire on water consumption habits -local hospital co-operation for *Giardia* specimen -sanitary survey of water facilities -water filter testing -water distribution and surface water sampling	-contaminated well water that failed to meet regulations - under contaminated surface water influence and faecal contamination
Rimhanen-Finne 2010	Nokia, Finland	*Giardia duodenalis*	-37 laboratory confirmed cases (December-March)	-prevalence rate 5.7 95% CI: 0.8 - 40.7 p=0.043 -incidence rate 5.3 per 10,000 inhabitants	-cross-sectional study -interviewed cases reported in national registry -sampled from the 11 drinking water distributions sites -soft deposit sampling from the pipelines	-sewage water effluent entered drinking water system (ground water)
Nygard 2006	Bergen, Norway	*Giardia*	-1 300 laboratory confirmed cases -2 500 syndromic surveillance (Pharmacy sales) (September – February)	-Relative risk 18 (95% CI 15-22) -Odds ratio 5.9 (95% CI: 1.7-21)	-prospective/retrospective study -at time of outbreak, identified all cases; 2 controls for one case -laboratory confirmed cases and metronidazole prescription -case control study using individuals living in the central supply zone, and non-affected controls living in the same regions	-sewage overflow caused by excessive rainfalls -significant linked with the consumption of 5 or more glasses of tap water

CI: Confidence interval

Beyond outbreak scenarios, prospective studies help verify the causality and the incidence of illness by studying endemic cases. To this effect, the water sources have either been directly manipulated or a global change has been applied to the municipal water treatment (such as adding filtration) allowing researchers to observe the effect on the incidence of gastrointestinal disease in the population. In the context of this project, we are interested in the association between drinking water and the occurrence of endemic gastro-enteritis in the population provided by local municipal drinking water. During our study's sample period no outbreak had occurred. According to existing regulations, the risk posed by the consumption of tap water should be infinitesimal.

Table 7 presents a selection of renown experimental studies, using a randomized control trial (RCT) design, situated in developed countries, having evaluated whether water was an important vector for pathogen distribution and the incidence of gastroenteritis (Casman et al., 2001; Colford et al., 2009; Colford et al., 2002; Colford et al., 2005; Hellard et al., 2001; Payment et al., 1991a; Payment et al., 1991b; Payment et al., 1997). There has been multiple studies evaluating the water as a vector yet not all presented strong evidence and certain provided no evidence (Tillett et al., 1998). A systematic review evaluating all waterborne intervention trials for improving water quality generally found an improvement suggesting that water was a cause of endemic gastroenteritis albeit most studies were not conducted in developed countries (Clasen et al., 2006).

The experimental studies included in this review differ from observational studies in that the consumers water consumption habits were modified in order to find the true impact of drinking water on gastroenteritis incidence as oppose to only recording its incidence. However, in these experimental (mostly blinded studies), the effect of a treatment device did not modify the incidence of gastroenteritis events, suggesting the water is not the principal cause of illness. This conclusion was not observed in the Payment studies (Payment et al., 1991a; Payment et al., 1991b; Payment et al., 1997). The relatively pristine water quality of all other RCTs may explain this difference.

Table 7. Experimental waterborne disease studies

Author, year, country	Objective	Intervention	Water treatment	Method	Results
Payment et al, 1991 a et b, Canada	-determine the rate of gastroenteritis linked to the consumption of municipal drinking water	-randomized control trial -unblinded -treatment group received reverse osmosis filtration unit with an additional charcoal filter -control group used usual treatment	-surface water -respected North American water standards, notably in terms of chlorine and coliforms -uses conventional treatment (flocculation, coagulation, filtration, disinfection (ozone and chlorine) -raw water contaminated with human sewage discharge	-606 participating households -regular tap water consumers; children between 2 and 18 must be present in household -1 year and a quarter duration -self-administered questionnaire, reported, completed every two-weeks; included water consumption habits -a nurse collected the information by telephone -microbiological water analysis -case definition: 2 or more liquid stools or more than one vomiting episodes, one liquid stool with abdominal cramps/nausea/ vomiting, vomiting with abdominal cramps/nausea	-annual incident rate of 0.76 episodes per person-year in control group, 0.5 in treatment group. -35% of the gastrointestinal illness cases are related to drinking water -treated water was absent of indicator bacteria and human enteric viruses, bacterial growth was noted on filters -caution used with filtration unit as they experienced bacterial growth
Payment et al, 1997, Canada	-to determine if drinking water respecting existing water quality norms can be associated with gastrointestinal illness	-randomized control trial with 4 treatment arms: -unblinded - tap water -tap water with purge valve -bottled plant water -purified bottled water	-Surface water -Followed North American water standards, notably in terms of chlorine and coliforms -uses conventional treatment (flocculation, coagulation, filtration, disinfection) -300km watershed subject to urban and rural contamination -has a relatively pristine lake acting as a buffer before entering the system	-selection of 350 families -1 year study -excluded: immuncompromised and immunosurpressed participants -biweekly telephone surveys -daily diary-questionnaires forms, reported every 2 weeks -water consumptions survey -case definition for high credible gastrointestinal illness: vomiting or liquid diarrhoea, soft stool or nausea paired with abdominal cramps.	-14% more gastrointestinal illness in tap water consumers than purified bottle water (rate ration 1.15) -19% more gastrointestinal illness in tap water consumers with purging valve than purified bottle water (rate ratio 1.24) -children 2-5 years old were most affected -14-40% of gastrointestinal illness attributable to drinking water -highest period of illness was autumn and winter - no pathogens or indicator detected in treated water

Hellard et al 2001, Australia	-estimate the rate of gastrointestinal illness after consuming minimally treated forest catchment water.	-randomized control trial, double blind -treatment group received active UV filtration device -control group received sham filtration device	-pristine water source devoid of farming activities, human habitation and recreational activities -forest catchment water drawn from reservoir in which it is kept for 12 month prior to uses -water is chlorinated but not filtered	-600 families of 4 healthy individual which must have two children between 1 and 15) -68 month period -weekly diary reports, returned every 4 weeks, potential illness cause specified -fecal sample collection during episodes of gastroenteritis. -information collected by assigned study staff -water quality monitoring -event defined in 24hrs, the passing of two loose stools, 2 or more bouts of vomiting, 1 loose stool and abdominal cramps or nausea, vomiting with abdominal cramps or nausea, and 6 days between episodes	-2 669 cases of HCGI during the study. 1,317 with active filters and 1,352 with inactive filters -0.80 cases per person-year -rate ratio 0.99 (95% CI: 0.85-1.15) -15% attributable to drinking water
Colford et al, 2002, United-States	-estimate the risk of HCGI related to drinking well water -determining if group can be successfully blinded to assignment for a four month period	-pilot trial -randomized control trial, triple blind -treatment group received active UV filtration device -control group received sham filtration device	-compliant with the United-States federal and state standards -contaminated with industrial and agricultural waste -conventional treatment (coagulation, flocculation, sedimentation, filtration and chlorination and, part way through the study, ozonation)	-77 households -healthy families recruited - health outcome recorded daily in health diaries -water outcome measured by self-reporting -event defined as: high credible gastroenteritis: vomiting, liquid diarrhoea, soft stool or nausea paired with abdominal cramps, six days between events	-Relative Rate ratio 1.32 (95% CI: 0.75-2.33) -82 episodes and 2.63 episodes per person year in active group; 103 episodes, and a 3.48 episodes per person year in inactive group -24% attributable to drinking water
Colford et al, 2005, United-States	Estimate the risk of HCGI related to drinking well water	-randomized control trial, triple blind -treatment group received active UV filtration device -control group received sham filtration device	-single pathogen challenged water source -compliant with United-States federal and state standards -conventional treatment (coagulation, flocculation, sedimentation, filtration and chlorination)	-456 households (227 active device household, 229 sham device households) -two, six months cycles in which participants switched from active to sham or vice versa; health outcome recorded daily in health diaries -water consumption measured by self-reporting and flow meter- -event defined as: high credible gastroenteritis: vomiting, liquid diarrhoea, soft stool or nausea paired with abdominal cramps, six days between events	-relative rate 0.98 (95% CI: 0.86-1.10) -707 HCGI events in active group, 672 in inactive group -less than 11% attributable to drinking water -no reduction in HCGI illness observed -2% reduction with use of filter
Colford et al, 2009, United-States	Estimate the rate of highly credible gastrointestinal illness (HCGI)	-randomized control trial, triple blinded -treatment group received active filtration device -control group received sham filter	-combination of surface and ground water -respects United States water treatment standards -uses sand filtration for ground water, diverts surface water to filtration ponds -water is then chlorinated and pH adjusted	-714 households -older adult population - two 6 months period -daily health diaries collected every month -event defined as high credible gastroenteritis: vomiting, liquid diarrhoea, soft stool or nausea paired with abdominal cramps, six days between events	- incident rate ratio of 0.88 (CI 95%: 0.77-1.00) for episodes of HCGI (GEE model) (sham vs filter) -during the first cycle :2.83 episodes/year for active group, 2.76 episodes/year for inactive groups -12 % reduction with use of filter

1.4 Public Health Surveillance

Surveillance is a method of collecting and evaluating trends of morbidity and mortality in a continuous and systematic manner (German et al., 2001). Its primary goal is to gather and diffuse pertinent information to public health authorities. In turn, these authorities should use the knowledge to create and implement programs to improve the population's health. Generally, traditional surveillance is divided in two major approaches: passive and active. Active surveillance consists of actively searching for cases in the community, medical offices, hospitals and pathology departments. This will generally occur during field investigations, where health information is obtained and analyzed purposefully by an organization. An active surveillance system will have a network which actively communicates with the aforementioned sectors to obtain information. This requires a considerable amount of resources and time. Passive surveillance refers to the sharing of health information, in form of reports, between health related organizations.

Passive surveillance tools used to detect gastroenteritis outbreaks can include hospital records, analytical laboratory results, over the counter sales record, and absenteeism (school or work). They have been utilized by a number of researchers to identify outbreaks and their timeline, especially when paired with water sample results (Febriani et al., 2009; Harter et al., 1985; Hopkins et al., 1985; Jephcott et al., 1986; Laupland et al., 2005; Semenza et al., 2007; Wallis et al., 2001). Generally, surveillance studies are done in a defined geographical region to determine the frequency and potential sources of disease for a pre-determined time span (>1 year) (Harter et al., 1985; Hopkins et al., 1985; Moore et al., 2008). For example, in Colorado, a 3-year program identified 18 WBD outbreaks for which *G. lamblia* was the most frequent cause of disease (50%). The element precipitating the outbreak generally was inadequate chemical pre-treatment and a lack of filtration (Harter et al., 1985; Hopkins et al., 1985).

1.4.1 Traditional systematic surveillance

In Québec, there are two principal registries that health authorities use to assess provincial health: Data Maintenance and Exploitation to Study Hospital Clientele (*Maintenance et exploitation des données pour l'étude de la clientèle hospitalière – MED-ECHO)* and Notifiable Diseases (*Maladies à déclaration obligatoire –MADO)*. MED-ECHO is an information system that encompasses all information regarding reasons for patients receiving hospital care including emergency room visits, hospitalisation and the dispensed medical care (Febriani et al., 2009; Gilbert et al., 2006). The MADO is a registry which archives all laboratory confirmed government regulated notifiable intoxications and illnesses (Direction générale de santé publique, 2004).

Existing efforts in Canada to create a national integrated enteric pathogen active surveillance program catered to waterborne diseases includes the C-EnterNet program (Public Health Agency of Canada, 2006). Its purpose is to support activities that will help reduce the burden of disease, notably gastrointestinal ones, by implementing a sentinel site surveillance program in local health units. C-EnterNet goals include detecting changes in human enteric disease, in pathogen exposures, to conduct source attribution, and to improve the analysis, interpretation and dissemination of laboratory and epidemiological data. It uses sentinel site surveillance system implemented within local health units which actively sample retail foods, agricultural operation and water sources for pathogens. According to the C-EnterNet pilot system, the three most frequently reported enteric infectious diseases in Canada are: salmonellosis, campylobacter and giardiasis (Public Health Agency of Canada, 2006). For *Giardia*, most cases identified were endemic cases and not outbreak cases despite the 100% *Giardia* positive sample from the pilot site.

Current passive surveillance systems in Canada include the Canadian Communicable Disease Report (CCDR) and the National Enteric Surveillance Program (NESP) (Public Health Agency of Canada, 2012a, 2012b). The CCDR reports weekly information concerning infectious disease, flu occurrence, influenza reports, preliminary outbreak reports and other pertinent health

announcements, case reports, epidemiological reports, international notes, notifiable diseases summary list, and recommendation from consensus conferences. (Public Health Agency of Canada, 2012a).

The NESP focuses on foodborne pathogens, including bacteria, viruses, and parasites (Public Health Agency of Canada, 2012b). It reports and analyses laboratory confirmed human enteric disease cases in Canada to determine whether cases are significantly higher than expected according to a 5 year moving average. This information is provided weekly by each provincial public health laboratory and is combined with the National Microbiology Laboratory and the Centre for Food-borne, Environmental and Zoonotic infections (Public Health Agency of Canada, 2012b). Once the data are analyzed, results are disseminated to the participating laboratory, the Canadian Food Inspection Agency, Health Canada, the Public Health Agency of Canada, and key stakeholders. Afterwards, these groups collaborate with international programs to facilitate multijurisdictional epidemiological investigations, in order to monitor and prevent outbreaks.

1.4.2 Syndromic surveillance

An alternative mean to survey the population's health can be accomplished through syndromic surveillance. Unlike traditional surveillance, syndromic surveillance monitors symptoms and related anomalies related to a specific disease or illness indicators of a group of diseases. Items such as over-the-counter medicine (OTC) sales, emergency room visits, 911 calls, ambulance dispatches, patient transfer between hospitals, absenteeism (work and school), health care telephone lines and insurance records are studied (Berger et al., 2006; Caudle et al., 2009; Heffernan et al., 2004; Rolland et al., 2006). An important advantage of incorporating syndromic surveillance information is the real time feedback; health-care telephone help lines are designed to integrate information as soon as it is received (Caudle et al., 2009; Doroshenko et al., 2005; Moore et al., 1993; Moore et al., 2008; Proctor et al., 1998; VuHenry et al., 2004; Wallstrom et al., 2005).

Gastroenteritis is particularly well adapted for syndromic surveillance given their non-specific clinical outcome, their self-limiting nature and their exclusion from routine diagnostic tests (Berger et al., 2006; Risebro et al., 2007b). This translates into an important underreporting and an increase in gastroenteritis cases may not be detected using laboratory surveillance (Flint et al., 2004; MacDougall et al., 2008; Majowicz et al., 2005).

In British Columbia, it was estimated that only 1 case is reported at the provincial level for every 347 cases in the community, (MacDougall et al., 2008) similar to Ontario's 1 in every 312 (Majowicz et al., 2005). This suggests that laboratory results are uncommon and non-representative of the actual burden of gastroenteric diseases, albeit essential for confirming its presence. Confirmed diseased events among stool samples submitted are also rare, notably for viruses and parasites. In a Québec study, of the 388 submitted stool samples to hospital laboratories, only 4 cases were confirmed for *Giardia* (Levallois et al., 1999). Even when testing positive, around 10% of stool tested for *Giardia* in Canada are not reported to the provincial health authorities (Flint et al., 2004).

Additional contributing factors to under-reporting are: laboratory cost, delays in reporting findings (upwards of 24 hours), excessive time delays in transportation, damaged containers, insufficient stool, inappropriate or absence of transport media, unconfirmed diagnosis, case non-recorded cases, missing data, non conformity to case definitions, and non-standardized analytical methods (Flint et al., 2004; Risebro et al., 2007b).

To determining the effectiveness of syndromic surveillance, a few studies have compared the number of syndromic cases to those identified through laboratory analysis or a previous established surveillance system (Doroshenko et al., 2005; Proctor et al., 1998). Generally, telephone healthlines receive an important volume of calls concerning respiratory and gastrointestinal symptoms (VuHenry et al., 2004) and hence are pertinent to understanding the relation between gastrointestinal illness and water consumption (Levallois et al., 1999). A study found that the calls for gastrointestinal syndromes, in relation to emergency room visits, have a positive predictive value of 37.1%, a sensitivity of 72.0% and a specificity of 95.9% (VuHenry et

al., 2004). This sensitivity value may reflect the lack of usage of these health lines, which may be limited to certain individuals. The high specificity is with regard for the healthlines to identify gastrointestinal syndromes and not a specific disease. Thus, hotlines are efficient in identifying potentially ill individuals (high sensitivity) and less effective in identifying actually ill patients (low specificity). Sensitivity values are therefore subject to professional judgment reflecting on the capacity of the surveillance system (Blackburn et al., 2004; Doroshenko et al., 2005).

Generally, syndromic surveillance has been reported in the literature in order to understand its relevance in detecting outbreak (Balter et al., 2005; Heffernan et al., 2004; MacKenzie et al., 1994; Marx et al., 2006; Moore et al., 2008; Wallstrom et al., 2005). Regular surveillance reports as mean of understanding the baseline level of a region, are generally only internal reports (Vrbova et al., 2010). A study to assess the spatial-temporal diffusion of influenza and norovirus using telehealth data confirmed that such surveillance methods were able to asses rises in the number of cases, suggesting that surveillance was indeed able to confirm baseline level, notice peaks and differentiate sporadic cases from epidemic outbreaks (Cooper et al., 2008). This was also identified in the New York City sentinel surveillance program and the Ontario real-time surveillance program for emergency department visits, allowing recognition of instances when a health intervention is needed (Balter et al., 2005; Heffernan et al., 2004; Moore et al., 2008).

In Canada, several studies have been done on both the Telehealth line (Ontario) and Info-Santé (Québec) (Edge et al., 2004; Edge et al., 2006; Gilbert et al., 2006). A feasibility study conducted to determine the use of Info-Santé CLSC to predict waterborne disease occurrence concluded that it was feasible to use the Quebec Telehealth line as a surveillance system (Info-Health Local Community Health Centre) (Gilbert, 2004). It also highlighted that a significant portion of the population uses the system: over 6 500 calls per day, and the study reported an incident rate of 19.12 calls per 1 000 people years (Gilbert et al., 2006). In Ontario, it was found that 10% of the calls were for gastrointestinal illness, as oppose to 0.2% emergency department visits (Caudle et al., 2009). Hence, phone surveillance is an efficient source for understanding the population's general health status and can alert health officials of potential outbreaks.

1.5 Water treatment process

The Canadian water treatment process is a multi-barrier system, which aims to reduce the risk associated to raw water and to provide water which respects existing regulations and norms (Table 8). The first barrier involves the protection and assessment of the source water by determining its vulnerability, inventorying land usage, delineating the water shed, and identifying intake zones. The other barriers are components of the water treatment plant sanitization infrastructure. In Canada, regulations on source water protection (as well as all drinking water regulations) are done at the provincial level, with regional specification (Flinch et al., 2001). Source water assessment may be done by means of a sanitary survey of the watershed or, less commonly, by studying the prevalence of waterborne illness found in the community (Federal-Provincial-Territorial Committee on Drinking Water, 2012).

Water treatment plants traditionally included most recommended components, which are: pre-treating the water (typically with chlorine), coagulation, flocculation, sedimentation, filtration, disinfection and, occasionally, post-chlorination. These are to reduce and eliminate bacteria, viruses and protozoan, as well as to ensure physical water quality parameters are met. These water quality parameters include: turbidity, colour, taste, odour, temperature, and pH.

Table 8. Guidelines for microbiological parameters for public water systems

	Canada	**Quebec**
Escherichia coli and Fecal coliforms	-the maximum acceptable concentration for *Escherichia coli* or fecal coliforms is 0/100ml	-all water samples must be exempt of fecal coliforms, *E. coli*, enterococus bacteria, and F-specific viral coliphage -raw water samples must be collected for three years to determine if additional treatment is necessary
Total coliforms	-the maximum acceptable concentration of total coliforms is 0/100ml if less than 10 water samples were taken. -if more than 10 samples were taken no more than 10% should detect total coliforms	- water samples must not detect more than 10/100 ml total coliforms and for every 30 day sampling period
Cysts/Oocysts	-99.9% reduction or inactivation of cysts and oocysts, unless source water quality requires greater reduction	-minimum 99.9% reduction or inactivation of cysts and a minimum 99.9% reduction or inactivation of oocysts
Viruses	- 4-log reduction or inactivation, where treatment is required	- minimum of 4-log virus elimination
Turbidity	- ≤0.1 NTU is the ideal filtration system threshold -chemically assisted filtrations: ≤0.3 NTU for 95% of the samples -slow sand or diatomaceous earth filtration, ≤ 1.0NTU for 95% of the samples -membrane filtration: ≤ 0.1 NTU for 99% of the samples	-water samples must never exceed 1.0 NTU -chemically assisted filtrations: ≤0.3 NTU for 95% of the samples for a 30 day time frame -90% of the water samples must not exceed 1.0 NTU -slow sand or diatomaceous earth filtration, ≤ 1.0NTU for 95% of the samples -Membrane filtration: ≤ 0.1 NTU for 99% of the samples

(Federal-Provincial-Territorial Committee on Drinking Water, 2012; Ministère du développement durable l'environement et les parcs, 2012)

NTU: Nephelometric Turbidity Units

1.5.1 Chlorination, coagulation, flocculation, sedimentation

The initial chlorination is used to reduce the biological and mineral burden of the water in order to facilitate coagulation and reduce the formation of secondary compounds. However, pre-chlorination has been abandoned in most plants due to issues related to trihalomethanes (THM) formation. Particles are agglomerated together by means of coagulation and flocculation. This occurs following the addition of a coagulating compound (aluminum sulfate or ferric chloride) which neutralize the charges (Betancourt et al., 2004; Flinch et al., 2001; Gilbert, 2004). Hence, the concentration of coagulation used is highly important for the initial removal of cysts and for the reduction of turbidity, which facilitates the final disinfection (LeChevallier et al., 2004; United States Environmental Protection Agency, 1998). Coagulation and flocculation aims for at least 1 to 3-log removal of bacteria, viruses and protozoa (LeChevallier et al., 2004). Flocculation and coagulation is accomplished through gentle water agitation. The precipitates adhere to microbial, biological or chemical compounds found within the water (Federal-Provincial-Territorial Committee on Drinking Water, 2012; LeChevallier et al., 2004). In turn, sedimentation, which leads to clarification, deposits particulate matters. These are removed through filtration. These steps account for a 1.5-log removal of *Giardia* (Health Canada, 2012).

1.5.2 Filtration

The remaining suspended compounds are filtrated through porous material and are strained, adsorbed, sedimented, or coagulated by the porous granular filter media (Betancourt et al., 2004). The remaining particles are retained in the filter's lattice preventing them from entering the disinfectant process. This filtering step is crucial to the elimination of *Giardia* and *Cryptosporidium,* as neither pathogen is sensitive to usual disinfection; without this step, a greater frequency of outbreaks is observed (Goh et al., 2005; United States Environmental Protection Agency, 1998; Wallis et al., 1996). Filtration will result in a greater log removal of the protozoans than disinfection alone (Goh et al., 2005; Wallis et al., 1996). While filtration is an effective prophylactic to preventing cysts from contaminating drinking water, certain filtration types perform more efficiently than others. For example, granular activated carbon is more

efficient than dual or mixed media filters (LeChevallier et al., 1991a). Online treatment plant monitoring becomes crucial to insure proper filtration (Health Canada, 2012).

1.5.3 Recommended log removals

The USEPA recommends a 2.5-log reduction of *Giardia* during the coagulation, flocculation, sedimentation, and filtration process (Flinch et al., 2001). In turn, disinfection is responsible for 0.5-log reduction (Flinch et al., 2001). An effective system subject to low turbidity (0.1-0.2 Nephelometric Turbidity Units - NTU) has the potential to remove over 4-log units and, in particularly polluted water, up to 4.7-log (see Table 8 for Québec's norms) (Flinch et al., 2001; Health Canada, 2012; Payment et al., 1993). These combined treatment and log removal have for purpose of achieving an incidence of 10^{-4} infections per year of *Giardia*, deemed to be an acceptable risk (Federal Register Reference, 1989). This threshold was established following Rose et al (1988) evaluation of surface water and characterisation of pristine water (Rose et al., 1988).

1.5.4 Disinfection

Disinfection introduces chemical compounds that inactivate the structural components of the remaining pathogens and neutralizes the chemical structures by mean oxidation, hydrolysis, de-amination, or photochemical reactions. Each pathogen and corresponding water temperature has an ideal chemical compound contact time (CT) (see Table 9 for recommended concentrations). *Giardia* cysts are particularly susceptible to ozone, which requires a lower CT than chlorine, has fewer by-products, is a powerful oxidant, and has no residual effect for large contact time (Flinch et al., 2001). The inactivation of *Giardia* increases 2- to 3- fold for every 10°C rise in temperature, and is hence less efficient in colder temperatures. At a higher pH for chlorine, the efficiency is also reduced. A 1 to 10 NTU increase can result in an 8-fold decrease in free chlorine efficiency (Health Canada, 2012; Hoff, 1986). Consequently, those elements, and disinfection by-products, dictate the required chemical concentration.

Table 9. Maximum residual disinfectant concentrations and regulated disinfection by-products (DBP) according to the Canadian Guideline for drinking water treatment

Compound	Chlorine	Chloramines	Chlorine dioxide	Bromate (DBP)	Chlorate (DBP)	THM	HAA
Concentration	4mg/L	4mg/L	(0.8mg/L)	10µg/L	1mg/L	100µg/L	80µg/L

THM: trihalomethanes; HAA: haloacetic acids

(Federal-Provincial-Territorial Committee on Drinking Water, 2012)

1.5.5 Ultra-violet radiation

An alternative to, or in addition to, disinfection, ultra-violet light may be used (UV). UV light at low doses (1 mj/cm^2) is effective at inactivating *Giardia* cysts, regardless of temperature (4-log) (Betancourt et al., 2004; Li et al., 2009a; Linden et al., 2002). When exposed to the UV light, the DNA and RNA form dimmers and inhibit the transcription and replication of nucleic acid (LeChevallier et al., 2004). Advantages include a shorter contact time and no identified secondary by-product – in part due to its non-reliance on chemical additives (Sakamoto et al., 2001). However, performances vary in accordance to the source lamp, causing an uncertainty in the dose and efficiency during high turbidity (Betancourt et al., 2004; Linden et al., 2002).

1.5.6 Distribution system

Although most efforts concentrate on drinking water treatment plant control measures, the distribution system may potentially be an indirect cause of microbiological contamination if breaks or fissures are present. This is why post-chlorination occurs at several areas along the distribution system. Between 2001 and 2005, 20% of the outbreaks in the United States were linked to deficiencies in the distribution system, a figure which has increased from 1990 to 2002 (Blackburn et al., 2004; Reynolds et al., 2008). Reports indicate that poor or outdated water distribution equipment (pumping, pipe, storage) are at fault (Reynolds et al., 2008), in part due to the hydraulics' integrity, leading to insufficient pressure within the pipes which, in turn, results in

the introduction of non-potable water into the system due to back-siphonage (Reynolds et al., 2008).

1.5.7 Turbidity

Turbidity values are used to assess both water quality and the subsequent drinking water treatment. It is an effective and inexpensive parameter used to define source water quality variations (Allen et al., 2008). It is assessed by evaluating light's refraction in water, which is measured by turbidimeters in NTU. A higher concentration of suspended particulate matter will result in a higher turbidity reading. According to the Canadian Water Guidelines, the acceptable turbidity limit, for surface waters and ground water under the influence of surface waters, is currently set at between 1 and 0.1 NTU (Federal-Provincial-Territorial Committee on Drinking Water, 2012). Anything above 3.0 NTU is unacceptable[1] (Federal-Provincial-Territorial Committee on Drinking Water, 2012). Nonetheless, the guidelines' foremost goal is to encourage the avoidance of erratic spikes in turbidity and to maintain an average low rather than consistently achieve 0.1 NTU. This is assumed to be feasible through the use of the multiple barrier system, and, more notably, the filtration component of the water treatment system (Allen et al., 2008; Hrudey et al., 2004).

Generally consumers will notice an excess in turbidity when the NTU exceeds 5, at which point water is markedly cloudy. The opacity is used as a proxy for water quality for 3 main reasons. Firstly, suspended matters may contain toxins and metals which have a potential negative impact on the effectiveness of coagulation, flocculation and sedimentation (Bellamy et al., 1985; Health Canada, 2009). Secondly, particles can harbour and provide nutrients to micro-organisms encouraging their proliferation and shielding them from disinfection (LeChevallier et al., 1991a; Seidler et al., 1982; Wu et al., 2005). Lastly, turbidity interferes with bacterial enumeration, provoking difficulties in determining adequate CT and increases the risk of having harmful

[1] Chemical-assisted filtration requires less than or equal to 0.3 NTU and cannot exceed 1NTU. Slow sand or diatomaceaous earth filtration lower threshold is 1.0 NTU (95% of the time) and upper threshold is 3.0NTU. Membrane filtration must comply to 0.1 NTU 99% of the time and shall not exceed 0.3 NTU.

chemical by-products such as trihalomethanes (Allen et al., 2008; LeChevallier et al., 1991a; Liu et al., 2006).

Excess in turbidity has been linked with both agricultural and urban run-off during adverse weather events such as rainfall and snow run off, although not always to superior pathogenic concentration (Beaudeau et al., 2010; Dechesne et al., 2007; Health Canada, 2003; Lim et al., 2002). Water turbidity can be either associated with the summertime, coinciding with fecal coliforms multiplication, or fall periods -in which systems are at a greater risk due to colder temperatures (Charron et al., 2004; Edge et al., 2006; Laupland et al., 2005; Mounts et al., 2000; Payment et al., 1997; Semenza et al., 2007).

Nonetheless, there is currently some controversy over the use of turbidity as a water quality parameter. While several outbreaks (notably Milwaukee's *Cryptosporidium* outbreak in 1993) have been associated with an increase in turbidity, recent reviews of the scientific literature by Mann et al. (2007) and by Allen et al. (2008) have highlighted that turbidity is generally an unreliable risk estimator (Allen et al., 2008; Dechesne et al., 2007; Mann et al., 2007; Morris et al., 1996). In part, this is due to the lack of information concerning the presence of pathogens within the water. When pathogens are inconsistently present in the source, it is unlikely that a higher concentration of particulate matter corresponds to an increase in water contamination, unless it is within a rural area, or a sector prone to industrial or sewage run-off (Allen et al., 2008; Febriani et al., 2009; Proctor et al., 1998). Regardless, some quality studies have found a positive association between an increase in turbidity and GI incidence while other found no statistically significant association, or had inappropriate design (no a priori framework, multiple lag testing) (Allen et al., 2008; Aramini et al., 2000; Beaudeau et al., 2010; Gilbert et al., 2006; Mann et al., 2007; Schwartz et al., 1997; Tinker et al., 2010).

Interestingly, Gilbert et al.'s (2006) study found a significant correlation (33% and 76%) between turbidity and Tele-health reported gastro-intestinal illness but also suggests that only a fraction of the cases are related to drinking water (Gilbert et al., 2006). The role of turbidity in causing GI outbreaks was also documented in Vancouver from 1993 to 2004 (Aramini et al., 2000). It

showed an association of 2.1%, 0.8% and 0.9% of emergency-associated gastroenteritis related physician visits from individuals residing within the three water distribution areas, of which 1.3%, 0.2% and 0.3% was explained by turbidity variation. Association between hospital visits and turbidity has been studied by Tinker (2010) and Schwartz (1997) (Schwartz et al., 1997; Tinker et al., 2010). While Schwartz found a positive association, through multiple lag time testing, Tinker's study highlighted a lack of effect of turbidity on GI health outcomes with a rate ratio of 0.98 for every 0.1 NTU increase (Schwartz et al., 1997; Tinker et al., 2010). Finally, a study conducted in the Havre in France noted that an interruption of chlorine and an increase of turbidity in raw water led to an increase of OTC sales a week and a half (lag 6 and 10 days) after the event (relative risk 1.10-1.25) (Beaudeau et al., 2010). The authors do however caution that seasonal effects are possible and that the increase in OTC sales is not assuredly correlated with water exposure.

Given the uncertainty in associating turbidity with gastroenteritis outbreaks, it has been proposed that the value of turbidity as an efficient parameter for water quality depends on site-specific water characteristics (Allen et al., 2008; Febriani et al., 2009; LeChevallier et al., 1991a; Lim et al., 2002; Tinker et al., 2010). An analysis of the components of turbid water has shown that not all turbid water yields an important concentration of pathogens, and instead may only be composed of matter such as silt, lime, plankton, and non-pathogenic micro-organisms (Health Canada, 2003). The dynamics of the source water can vary greatly, both geographically and through time.

1.6 Quantitative microbial risk analysis models

Quantitative microbial risk analysis (QMRA) of drinking water is a relatively recent concept. Its principal goal is to incorporate water treatment plant specific information and microbiological pathogen information in order to quantify risk to humans. The following will elaborate the concepts involved in risk assessment, the use of QMRA, the creations and variations of QMRA models, and the use of QMRA in epidemiology.

1.6.1 QMRA development and risk management

To begin, it is essential to understand how QMRA models are created. Risk itself is, according to Hunter et al (2003) «the possibility of loss, harm or injury» and evaluating the likelihood of such an event occurring. Risk assessment, briefly, consists of four steps, namely identification, exposure assessment, defining a dose-response, and characterizing the risk.

The initial component of risk assessment consists of identifying and formalising a hazard. The risk, for the purpose of QMRA, is a microbiological hazard, such as the presence of *Giardia* in drinking water. Its presence will be evaluated through assessment of the water catchment, reservoir, treatment and reticulation. Once the organism is identified, the illness effects, transmission pattern, susceptible population, severity, and contagiousness are considered (Einsenberg et al., 2007; Hunter et al., 2003; Medema et al., 2006).

The second component pertains to evaluation of risk exposure, wherein microbiological hazard is assessed (Health Canada, 2009). Evaluation of the exposure requires knowledge on the concentration and distribution of the pathogen in both source and tap water. The degree to which the cysts are removed or inactivated, stored and distributed through the water treatment provides data concerning the final concentration of pathogens and this concentration pronounces itself on system effectiveness in eliminating cysts (Medema et al., 2006; Rose et al., 1991b). Exposure is also assessed by quantifying the quantity of unboiled municipal water consumed per person on a daily basis (Health Canada, 2012; Hunter et al., 2011; Jones et al., 2007). The identified consumed litres vary from 2 - 1.4 L/day, although the consumption may be as low as 0.10 L/day. Given this variation, it is more representative to use country-specific data as the overall amount of water consumed varies across different countries (Caron et al., 2004; Hunter et al., 2003; Jones et al., 2007; Mons et al., 2007; Rose et al., 1991b).

The third component comprises of defining a dose-response relationship establishing an association between the exposure (*Giardia*) and the risk of infection (Health Canada, 2012). Typically, the dose is presented in units of organisms ingested (Soller, 2006). The relationship is

commonly configured, for microbiological data, using an exponential or Beta-Poisson model (Haas et al., 1999; Haas et al., 2001; Hunter et al., 2003) (
Table 10). Other models used include deterministic models and Bayesian hierarchical models (Greiner et al., 2013; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Schmidt et al., 2013a).

For the common method (exponential or Beta-Poisson) this is assessed through volunteer feeding studies or by monitoring individual's water consumption dosed with a known concentration of pathogens (Rendtorff, 1954; Zmirou-Navier et al., 2006). For samples that have no detectable pathogens or very low non-zero values, they are either treated as zero or are set at the detection limit (Haas et al., 2001; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). Afterwards, the parameters are computed by mean of maximum likelihood techniques, however, confidence intervals are wide and there is uncertainty concerning the actual response, notably at low pathogen concentrations (Haas et al., 1999; Haas et al., 2001; Teunis et al., 2000).

The final component characterises the intrinsic risk associated with drinking water, taking into consideration both the exposure and the dose-response parameters (Haas et al., 2001; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). The risk can be presented as both point estimates or as a distribution of estimates (Haas et al., 2001; Karavarsamis et al., 2010). This is accomplished through stochastic imputation of the data's distribution. One method used is the Monte-Carlo analysis, which takes into account uncertainty and variability, a critical component of QMRA as the biological and chemical components of the model are subject to both (Haas et al., 2001; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). The final risk can be reported by probability of infection, probability of illness and by Disability Adjusted Life Years (DALY) along with their distribution, tabular risk or graphical representation of risk (Dufour et al., 2003; Health Canada, 2012; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Locas, 2009; Schoen et al., 2010). DALY is a measurement to quantify the impact of disease burden on an individual's lifespan; the reduced years are subtracted from an ideal lifespan free of disease or disability (Gold et al., 2002).

These components allow professionals to manage risk by weighting the consequences of the risk assessment against regulatory measures. When according an importance to the estimated risk, it is crucial to remember that low concentrations of parasites can lead to over- or under- estimation recommended treatment effectiveness (Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Smeets et al., 2010). Finally, in order to control risk, communication must be done. This involves the information dissemination to the appropriate parties (World Health Organization, 2003). This will allow health officials and the public to determine if the perceive risk is acceptable (Gerrard et al., 1999; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Krewski et al., 2004).

Table 10. Typical dose-response model

Model Name	Assumption	Formula	Variables
Exponential	-microorganisms are distributed randomly and follows an exponential distribution -one organism must survive inside host for infection to occur	$P_{inf} = 1 - e^{-rd}$	r= probability of the organism to survive and reach host. d= ingested dose
Beta-Poisson	-microorganisms are distributed randomly; follows a Poisson distribution -one organism must survive inside host for infection to occur -ingested quantity of organisms is not constant	$P_{inf} = 1 - \left(\frac{N}{\beta}\right)^{-\alpha}$ Alternatively presented as $P_{inf} = 1 - \left[1 + \frac{d}{N_{50}}(2^{1/\alpha} - 1)\right]^{-\alpha}$	β and α describe the model distribution, α describes the slope parameter, β or N_{50} = median infectious dose; increase as the model becomes steeper *d*= ingested dose

P_{inf}, d = 1 – exp (-0.01999 P_{ex} ^{d}) (Rose et al., 1991b)

P_{ex} d = daily probability density function of an inhabitant of the contaminated area being exposed to a pathogen or , when the probability is higher than 1, the expected number of pathogens consumed per person

Model created by Teunis et al. 1996, original data: Rendtorff 1954. (Rendtorff, 1954; Rendtorff et al., 1954; Teunis et al., 2000; van Lieverloo et al., 2007)

r for giardia has a CI of (0.007 -0.3) (Rose et al., 1991b)or (0.0097-0.036)(Federal Register Reference, 2006)

The yearly probability of infection

$P_{infection/year}$= 1(1- $P_{infection}$)^{365} (probability obtained from the Beta Poisson model)

assumes not everyone has a critical illness

Risk of illness= $P_{infection}$/year*S*I

S= proportion of individual susceptible to infection

I= the proportion of individuals who develop symptomatic illness after infection
I=0.24 for giardia
S=1

1.6.2 QMRA application

QMRA models have been innovated following a paucity of evidence pertaining to the distribution or pathogens in the water, notably that of parasitic agents (Einsenberg et al., 2007; Smeets et al., 2010). These models allow the simultaneous assessment of diverse risks factors and generate the potential harm following the consumption of water from source to tap (Ryu et al., 2008). They are useful for generating predicted consequences as the models themselves integrate source water quality information, in addition to treatment barrier information and pathogen-specific characteristics. Hence, they are useful in understanding how a change in the source water would impact the quality of the drinking water (Schijven et al., 2011). The models can also defend and optimize existing treatment procedures and establish a system's critical limits, such as a storm events, contamination events and barrier failure (Health Canada, 2012). The prescribed use of QMRA models is to help manage water sanitation programs (Health Canada, 2012). However, QMRA usefulness in an epidemiological context has not been fully explored.

QMRA predictions are the preferred methods of estimating risk rather than relying uniquely on coliforms indicators (Schmidt et al., 2011). Risk evaluation can be reported in probability of infection, probability of illness, and disability adjusted life-years (DALY) (Dufour et al., 2003; Health Canada, 2012; Locas, 2009; Schoen et al., 2010). Of these outcomes, probability of infection is the most commonly adopted measure of risk. However, it is very difficult to evaluate infection within a population without taking serological samples, as many individual infections are subclinical (Frost et al., 2000). Hence, despite public health official preference towards the interpretation of QMRA models by means of infections, it is not an easily interpretable measure.

Currently, QMRA models are very useful at establishing risk for a given water quality, using this information to determine optimal management strategies, and developing plans to

improve the quality of drinking water. This risk can be estimated for different pathogens and is especially useful for illnesses that are poorly detected by current surveillance systems (Health Canada, 2012). Many risk assessment models, with a few exceptions, are static and do not consider susceptibility, secondary or person-to-person transmission, or other similar dynamic relations including water temperature variability (Einsenberg et al., 2007; Haas et al., 2001; Soller, 2006). Temperature variation is especially important for Canadian drinking water systems, as disinfection is less effective at colder temperatures and is included in many northern-based models (Barbeau et al., 2000).

QMRA models are also applied toward verifying that drinking water respects established tolerable risk level (current standards 10^{-6} DALY, less than 10^{-4} infections per year) (World Health Organization, 2008). Thus, they are used to evaluate consumers' potential risk following the ingestion of municipal water, to qualify the burden of waterborne disease in a given community, to develop water quality norms, and to implement optimal and cost-effective treatments (Dufour et al., 2003; Medema et al., 2006; Rose et al., 1991a; Rose et al., 1991b; Ryu et al., 2008; Smeets et al., 2010; Soller, 2006). Through this, priority can be assigned to the most hazardous components of a water treatment plants allowing plant managers or risk managers to manage their budget (Astrom et al., 2007; Medema et al., 2006; Schoen et al., 2010).

Generally, once a dose-response model is defined in a site-specific manner, it is possible to determine the quantity of log-cysts to remove in order for the water be compliant with acceptable risk and to set critical limits (i.e., for daily risk of 10^{-4} if source water has 250 cyst/L, 3-log removal of *Giardia* cysts would need to be achieved) (Rose et al., 1991b; Smeets et al., 2010). However, most models overestimate endemic risk in the population, as the model is subject to both variability and uncertainty due to lack of information concerning a pathogen's viability and pathogenicity, the population's acquired and innate immunity and epidemics, the capability of water treatment plants to inactivate or remove pathogens (including uncertainty with CT calculation methods) and other individual

variability within the population (Haas et al., 1999; Jaidi et al., 2009; Rendtorff, 1954; Rose et al., 1991b). Models often rely on a point estimate of pathogen concentration or enumeration based counts, which, in itself, has uncertain concentration estimates and is subject to temporal variation, random sampling error and analytical errors (Schmidt et al., 2011; Schmidt et al., 2013a). Consequently, QMRA results should be considered as an aid for water treatment plant management or municipal water management (Pintar et al., 2012) rather than as an estimation of absolute risk (Jaidi et al., 2009; Medema et al., 2006; Smeets et al., 2010). There are missing some epidemiological studies to confirm this message.

Current regulation requires a minimum 3-log reduction of *Giardia* for water to be of permissible drinking quality — water that has, according to the USEPA, less than 1 infection per 10 000 people year. This comprises, in terms of a logarithmic fraction, both the physical removal by means of filtration and the inactivation by a disinfectant (Messner et al., 2006). This baseline was instated using *Giardia* as a reference, given that it is resistant to traditional disinfection methods (Hunter et al., 2003). If water is very contaminated or if turbidity is elevated (March-June), it is suggested the water treatment plant operators remove over 3-log of cysts (Assavasilavasukul et al., 2008; Rose et al., 1991b; Ryu et al., 2008). In the US the Long Term 2 Enhanced Surface Water Rule (LT2) integrates QMRA models to assess risk using Monte-Carlo Simulation (Federal Register Reference, 2006). For example, a study which evaluated the risk associated with the Saint-Lawrence river water showed that conventional water treatment plants using chlorine was associated with a risk of 1.09^{-04} (1.09 infections/10 000 individuals/year), slightly higher than the prescribed risk level established by the USEPA (Barbeau et al., 2000). The risk is greatly reduced with the addition of ozone: 2.81^{-07} (2.08 infections/ 10 000 000 individuals/year) (Barbeau et al., 2000). Consequently, WTP fed by the Saint-Lawrence River may consider the addition of ozone.

1.6.3 QMRA models

The models, despite their limits, do incorporate many important components that allow them to characterize the risk. Models can range from being simple, relying only on contamination values (Jaidi et al., 2009), to complex, including elements such as average ingested tap water (Payment et al., 1997), pathogen concentration and infectiousness, ozone or chlorine inactivation, physical abatement, pathogen recovery data (none, limited recovery, or paired recovery) and pathogen count data (between 10% and 96% recovery rate for *Giardia* cysts), and other water treatment plant operational data (pH, temperature, residual disinfectant, flow rate) to produce a series of risk distribution (Barbeau et al., 2000; Havelaar et al., 2001; Jaidi et al., 2009; Petterson et al., 2007; Ryu et al., 2008; Zmirou-Navier et al., 2006). This type of model is used in Health Canada's QMRA probabilistic risk model. Certain models incorporate other parameters such as treatment effect and cyst recovery (Barbeau et al., 2000; Jaidi et al., 2009; Petterson et al., 2007).

Models have evolved from their origins and have become more diverse. The initial use of threshold notion of infection has been criticized, and focus has now shifted towards dose-response models (Teunis et al., 2000). Current models differ with regards to distribution (varied, Poisson, beta-Poisson log, exponential, Monte-Carlo, Weibull), mean (arithmetic or geometric) and water sampling methods (continuous, transversal, filtration or grab-sampling) (Assavasilavasukul et al., 2008; Barbeau et al., 2000; Benke et al., 2008; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Jaidi et al., 2009; Rose et al., 1991b; Ryu et al., 2008; Schmidt et al., 2011; Smeets et al., 2010). Despite this wide range of values, models approximate certain parameters (Beta-Poisson dose-response model) albeit they must be justified (Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). Consequently, Monte-Carlo simulations are useful for generating a range of values instead of relying on a single or mean risk value (Jaidi et al., 2009).

Depending on the available evidence, certain models are more suitable to provide information concerning the water, facilitating the choice of model (Jaidi et al., 2009). The Beta-Poisson should not be used when little information is available; it is mainly effective when the pathogen concentrations are above detectable limits (or a log-normal distribution). Results are misleading at low pathogen doses, unlike the exponential model, which is more suitable for scenarios where cysts concentration is below detection limits (Jaidi et al., 2009; Teunis et al., 2000). Consequently, it is possible to develop well-adjusted models for a specific water source.

1.6.4 Epidemiology and QMRA

Epidemiological investigation provides vital information on risk. It characterizes an epidemic (an increase in the prevalence of disease above expected level) by identifying its determinants and its distribution (Last, 1995). Through investigation, especially in the context of outbreaks, the pathogens source can be identified. This allows researchers to determine the vector, such as water, provide information concerning events that provoked the outbreak and delimitate the risk (Hunter et al., 2003). In turn, this information is used to evaluate an outbreak's impact on public health (Soller, 2006). Few studies have established a link between epidemiological studies (notable for endemic cases) outcomes and QMRA models predictions. Research has often identified discordances or lack of consistency between the QMRA and epidemiological study results (endemic cases) (Mara et al., 2007; Rose et al., 1991b; Zmirou-Navier et al., 2006). However, as highlighted by Mara et al. (2007), QMRA models and epidemiological study are not devoid of flaws. Both have a margin of error that needs to be taken in account (Mara et al., 2007). Elements such as acquired immunity, cysts viability, repeated infection, actual water consumption, and secondary transmission are not taken into account by the QMRA models, frequently resulting in an overestimation of the risk and hence differ from epidemiological study results (Eisenberg et al., 2006; Mara et al., 2007; Pintar et al., 2012; Rose et al., 1991b). Unlike QMRA, which ideally tries to estimate the true burden of infection in a population, epidemiology can only assess apparent or reported illness in the population (Hunter et al.,

2003; Nguyen-Viet et al., 2009). This can be summarized by asserting that QMRA provides a measurement of potential risk and epidemiology measures actual risk (Medema et al., 2006).

Another barrier, for *Giardia* models, is related to the dose-response model. These models were developed in an adult population and hence is not an appropriate approximation for the actual at-risk population (Zmirou-Navier et al., 2006). Despite the notion that different age groups or immune status, it is argued that even one unit of pathogen is enough to induce illness, given the proper circumstances and hence all individuals are vulnerable (Teunis et al., 2000). Furthermore, epidemiological studies often do not evaluate a specific pathogen within a population, so outcomes are non-specific. An exception to this is Enger et al.'s (2012) study which included 3 specific pathogens to estimate the risk (Enger et al., 2012). This is problematic given that QMRA models are designed to predict the risk related to a single pathogen (Mara et al., 2007). Additionally, epidemiological studies do not include non-reported cases and may include non-exposed individuals (Rose et al., 1991b). Hence, both epidemiological studies and QMRA risk can both over- and underestimate the risk of disease in a population.

As seen in the summary table (Table 11) of all identified published studies reporting the relationship between epidemiological study results and QMRA risk, epidemiological data and QMRA models can agree, if the assumptions used to calculate the theoretical risk of the QMRA resembles the conditions which occurred during the epidemiological investigation (Eisenberg et al., 2006; Enger et al., 2012; Mara et al., 2007). In the Mara et al study (2007), the causative pathogen was undetermined. However, when assuming the causal pathogen was a rotavirus as opposed to *Giardia* or *Cryptosporidium*, the results of the QMRA more closely resembles the observed risk indicating it was the likeliest causative pathogen (Mara et al., 2007). Eisenberg's study highlights the inefficiency of epidemiological studies to assess low-estimate risks and hence, QMRA models with low risk estimates may be difficultly validated with epidemiological results.

Table 11. Epidemiological investigations and QMRA models

Author, Year, Country	Objective	Method	Water supply	Population	Models	Results	Comment
Zmirou-Navier, 2006, France	To determine if non-epidemic epidemiological data is comparable to the risk estimates from a *Giardia* dose-response model in the general population	-volunteer based study -chosen among 4 public water supplies . -completed daily health diaries -alert noted when two events happened in one community in 48hrs -episodes must be separated by 48hr to be distinct -drinking water consumption self-reported -tap water sampled monthly, 100L tested for *Cryptosporidium* and *Giardia,* USEPA method 1623 -virology detected using RT-PCR -bacteria analysis done for thermo tolerant faecal coliforms, faecal streptococci	-4 water sources: 1. one pristine groundwater 2. two vulnerable ground water 3. one compromised surface water, livestock and urban contamination 4. one surface water, close to a recreational lake -all chlorinated except pristine ground water	-544 volunteers -27.5% children, 12.1% over 60 -case definition: acute digestive condition: abdominal pain, nausea, vomiting and/or diarrhoea -diarrheic episode: episode of diarrhoea and fever or other digestive condition -gastro-enteritis: diarrhoea with fever or vomiting	- Exponential dose response curve $P_i=1^{-exp(-rCV)}$ r=0.02 (95% CI: 0.0098-0.036) C= 10 cyst/100L V=2L Risk=I_o x RR_i I_o=2.4 cases per person year -used abatement factor on cyst counts to compensate for the fact that not all are viable or infectious: 1/1, 1/2 and 1/5 -Covariates: Community, age, compliance with bacterial criteria, viral markers	-ADC:2.8 cases per person-year (95% CI: 2.6 -3.0) -GE: 0.2 cases per person-year -OR for one unit increase of *Giardia dose:* 1.76 (95% CI: 1.21-2.55), p-value=0.003 -model risk values over estimated incident rate in relation to abatement factor by: 6.5-3.0 for 1/1; 3.3-1.5 for 1/2; 1.6 for 1.5. -RR overestimated by 12% according to the model	-30.6% positive samples for either protozoan -*Giardia* found in higher concentration in tap water than *Cryptosporidium* -model best correlated with 1.5 abatement factor highlighting lack of certainty when it comes to the pathogen capacity to induce illness -assume 20% of the detected cyst can induce disease
Mara DD 2007, Mexico	Estimate human health risk associated with the use of wastewater for unrestricted and restricted crop irrigation and compare it to the outcomes of epidemiological studies by Blumenthal and Peasy 2003	-risk of individuals eating wastewater-irrigated salad crops or working in wastewater irrigated fields -calculated the annual risk of infection -project the risk for restricted irrigation in two scenarios:	-wastewater irrigation -non potable water	-field workers -children playing in field	-Haas QMRA, 10 000 trial Monte Carlo simulation -Beta Poisson dose-response model for rotavirus and *Campylobacter* infections -Exponential dose-response model for *Cryptosporidium* infections	Restricted: -risk of annual rota virus infection is higher than 10^{-2} pppy with a soil quality of 10^6 *E. coli* -risk of *Campylobacter* and *Cryptosporidium* did not surpass 10^{-2} (10^{-3} - 10^{-5}) Unrestricted:	-annual risk of infection does not consider the probability that an individual may be infected more than once. -lower standard of risk than is acceptable by the WHO

		1. highly mechanized agriculture (ingestion of 1-10mg wastewater soil) 2.labour-intesive agriculture (ingesiotn of 10-100mg wastewater soil) -unrestricted regulations -100g/d of lettuce Reference level of risk is 10-2 per person per year -Transformed the excess weekly prevalence of disease in Bluementhal et al(2003 and 2001) study into the risk of diarrhoeal disease per person per five months			-used the annual risk of infection $P_{1(A)}(d) = 1 - [1 - P_1(d)]^n$ $D=10^{m-D-7}VN$ for unrestricted irrigation N=number of pathogens, V=volume of water on 100g of lettuce after irrigation 10^m= concentration of *E.coli*	-10^{-2}ppy when for water of 10^4-10^5 *E.coli* -*Campylobacter* and *Cryptosporidium* meet acceptable risk (10^{-2}-10^{-7}) (10^{-2} – 10^{-8}) -Blumenthal et al found risk of 0.14 and 0.23 per person per 5 months in one study and 0.37 in the second (2003). The estimated field data are 1 order of magnitude lower or equivalent for rotaviruses (1.4 x 10^{-2} or 0.33). -*Campylobacter and Cryptosporidium*, risk were always lower (1 and 3 order of magnitude) -unrestricted water irrigation -rotavirus closely resembled the estimated risk (0.39 to 0.38 for 10^3-10^5 *E.coli)* -*Campylobacter and Cryptosporidium*, risk were always lower (1 and 3 order of magnitude)	-risk models are effective for predicting the risk for rotavirus, but tend to overestimate the risk of *Campylobacter* and *Cryptosporidium* -different approached to assess risk lead to different results
Eisenberg 2006 United states	Compare and contrast two approaches to obtain risk estimates of drinking water for coinciding data	-assessed attributable risk from an randomized, 6 month crossover, intervention trial -information recorded in health diaries.	-drinking water -raw water has a log normal distribution of *Cryptosporidium* and *Giardia*	-1 296 subjects in 456 households	-risk assessment model evaluated daily for 1 year -Exponential and Beta-Poisson dose-response model -include source water concentration, treatment efficiency (CT values estimate for *Giardia*), water consumption, probability of disease	-estimated attributable risk -365 (95% CI= -2,555 to 1,825) -mean risk of illness varied from 2.1 to 3.4 -predict risk (combining *Cryptosporidium, Giardia* and enteric viruses):13.9 per 10 000 person per person year(2.5, 97.5	-more cases were reported from sham group than active group

						percentiles: 1.6; 37.7) at 4 log removal -the trial observed a maximum 1,825 cases per 10,000 ppy, risk assessment model predicted 2-14 cases per 10,000 ppy	
Enger, 2012, Congo	Calibrate QMRA models to evaluate the efficiency of household water treatments in developing countries	-developed a QMRA model based on three pathogens (*E. coli*, *Giardia*, rotavirus) -simulated the study population and simulated a monthly survey. -calibrated the QMRA model in 1000 000 simulations. -assigned infection to individual according the probability of infection -estimate diarrhoeal illness according to a morbidity ratio (based on the literature) -calibrated the risk model by simulating the risk model repeated and using many input and parameter value.	-drinking water	-simulated children under 5 years of age -life straw HWT treatment	-the model considered which pathogen the individual would be infected (0, 1, 2, 3) -compliance to treatment is included -environmental concentration and daily dose evaluated according to concentration in untreated water (d), proportion of water treated (w), liters of water consumed (d), log reduction value (r) -Dose(d)=cd[(1-w) + $w10^{-r}$)] -dose response converted to probability of infection -durations of infection if estimated and morbidity is assigned according to proportion infected with diarrhoea) -immunity is included in model (7 days after recovery from infection -total of 33 parameters included in the model, 26 coming from the litterature	-predicted LPR 0.5 (2.5-97.5 percentile: 0.33-0.77) for high compliance to 0.86 (2.5-97.5 percentile: 0.68-1.09) for low compliance. -observed LPR 0.84 (95% CI: 0.61 -1.14) -distribution of the predicted and the estimated LPR differed significantly according to the Wilcoxon rank sum test p=0.02)	-compliancy was key for intervention effectiveness regardless of calibration -cannot take into account various transmission route -could not take into account viability of pathogen -less the 0.3% of the simulated models were compliant with the epidemiological data

ADC=acute digestive condition, C=concentration by liter of cysts in tap water, log transformed, D=daily dose of ingested parasite, GE=gastroenteritis, I_0= baseline incident rate, LPR= longitudinal prevalence ratio, OR=Odds ratio, P_i=probability of infection, r=organism specific infectivity parameter=0, RR= relative risk, RR_i= relative risk associated with dose (C*V), SD= standard deviation, V=individual consumption of tap water

1.7 Guideline establishment

The rules regarding water treatment for *Giardia* are fairly standard throughout Canada and the United States. This is logical, given that North American surface waters generally all test positive for *Giardia*, (LeChevallier et al., 1991b). Fittingly, the main threats to Canadian drinking water according to the Canadian drinking water guide are: *E. coli, Cryptosporidium* and *Giardia.* It is proposed, that *Giardia* cysts undergo a 99.9% elimination, which corresponds to a 3-log removal (Health Canada, 2009, 2012). This recommended reduction is comparable to that of Cryptosporidium, (99%, 2.5-log removal) and viruses (99.99%, 4-log removal). Generally, the guideline help define maximum acceptable concentrations, interim maximum acceptable concentrations, and aesthetic objectives (Krewski et al., 2004). For certain microbial pathogens, there is no tolerable lower limit, as it is assumed a single infection may lead to illness in vulnerable individuals (Krewski et al., 2004).

To established guidelines, norms need to be explored, guidelines implemented and rules delimited. Traditionally, members of a committee create norms through the discussion and revision of the best evidence. In Canada, this group is the Federal-Provincial-Territorial Committee on Drinking Water. The committee includes scientists, stakeholders, government officials, regulators, consultants, and facility operators that contribute to the knowledge pool (Health Canada, 2009). Sectors involved include: natural resource management, land use planning, environmental protection and public health (Health Canada, 2009). Guidelines are established through five stages: identification, assessment, evaluation and decision-making, approval, and re-evaluation (Krewski et al., 2004). The Committee on Drinking Water will also review the current drinking water standards and determine whether the guideline needs to be modified, especially following an important outbreak (Health Canada, 2009). Regional health departments can help report on the occurrence of disease within their city, by means of ordained or non-ordained medication and hospital records (Health Canada, 2009). Before prescribing a regulation, members balance health risks, costs and potential benefits (Health Canada, 2009). The proposed document is then revised by a panel of experts and then released to the general public. Afterwards, each province and

territory can adopt a legislation to protect its source water and sanitization measures (Health Canada, 2009).

An example of a current guideline revision is the Québec water quality standard. The guideline was updated in February 2012; the documents were made public from November 2010 to January 2011. Most of the update pertained to renewing water regulation according to recent research, improving water monitoring -including audits, and improving qualification of water operators. Another guideline recently update is the protozoan guideline, which had 8 years between updates. In January 2011, public consultation of the newly proposed guideline had finished and was published in 2012 (Health Canada, 2012). The decision to review the 2004 guideline was taken in October 2006 with special attention given to outbreaks, detection, transmission, water treatment, recovery methods, effectiveness of UV treatment and risk analysis. With regards to this project, May 2011 marked the acceptance of the proposal to integrate QMRA models in Canadian guidelines using *Cryptosporidium* and *Giardia* as reference pathogens (Health Canada, 2012). This reflects the global trend of integrating QMRA in water regulation framework adopted by the WHO, the European Commission, the Netherlands, Australia and the United States, especially with regards to health regulations and the necessity for site-specific regulation (Health Canada, 2012; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011).

In the United States, one of the main guidelines concerning the treatment of water for protozoan parasites is the Surface Water Treatment Rule for the USEPA (1989). It remains the key document explicitly describing the regulations concerning *Giardia,* despite being revised approximately every six years (Pontius, 2002). In the last 21 years there have been four documents pertaining to the regulation of *Giardia*, written in the United-States: surface water treatment rule (SWTR) 1989, Interim Enhanced Surface Water Treatment Rule (IESWTRE) 1998, Long Term 1 Enhanced Surface Water Treatment Rule (LT1ESWTR) 2002, Long Term 2 Enhanced Surface Water Treatment Rule (LT2ESWTR) 2005 (Federal Register Reference, 1989, 1998, 2002, 2006; Pontius, 2002). Albeit, the later focuses on *Cryptosporidium* and turbidity, believing that the changes will also affect *Giardia*. Hence,

the aforementioned documents provide the established guideline (Betancourt et al., 2004). *Giardia* was not updated as of November 2010 because of current ongoing second review (United States Environmental Protection Agency, 2011) a recent risk assessment guideline has been published further elaborating *Giardia's* purpose in risk management (Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). Despite the LT2ESWTR being a dated document, its continued use is likely in part because the USEPA took a conservative approach to their regulations.

The initial document (SWTR) was created following a stipulation to promulgate a drinking water regulation concerning the efficiency and use of filtration, (Federal Register Reference, 1989). The purpose of this was to determine a maximum contaminant levels (also revised in the IESWTR and the LT2ESWTR) which established that 0 mg/L of *Giardia* was the non-enforceable public health goal (Federal Register Reference, 1998; Pontius, 2002). Over twenty years later, the keystone document that played a pivotal role in establishing water norms, with regards to human health effects, is Rose et al.'s 1991 paper (Rose et al., 1991b). It was among the first articles to characterize the occurrence of *Giardia* in pristine and contaminated drinking water sources, showing that peak cyst concentration in clean water may be the same as polluted water (albeit less frequent). Additionally, it evaluated infection rates following *Giardia* waterborne outbreak (50 per 10 000). The SWTR also estimated the daily risk of *Giardia* infections from diverse concentrations of cysts in drinking water (exponential risk assessment models), and found that a minimum of 3-log removal (99.9%) will generally result in less than 10^{-4} daily risk for a worst case scenario (250 cyst/100L) although it would be inefficient at concentrations levels of 750 cysts per 100L (Federal Register Reference, 1989). This regulation is uniformly applied for all water source and systems and is equally reflected in the Canadian drinking water regulations.

Chapter 2: Pertinence and study objectives

2.1 Pertinence

The goal of Canadian water authorities, with regards to drinking water, is to ensure the distribution of water devoid of microbiological and chemical contamination, while maintaining a pristine physical appearance and a palatable taste. Consequently, water is evaluated in order to ensure its compliance to microbial, chemical, and physiological norms (Aidun et al., 2004). The performance evaluation of water treatment plants, in turn, allows plant operators as well as public health officers to determine if the end water is fit for consumption and that most microbiological risk has been eliminated. Hence, there are measures that survey, evaluate and review water treatment plants drinking water plans (Health Canada, 2009). Depending on the plants' performance, changes may need to be implemented in order to ensure minimal risk, or, in terms more commonly used by the Canadian government, a risk that does not exceed 10^{-6} DALY per person per year. This risk is nearly 0, that is 0.000 001 year lost due to health issues caused by *Giardia*. For *Giardia, w*ater quality is expressed in terms of risk as it is impractical to determine an acceptable concentration threshold for treated water as a single organism is sufficient to cause illness. Operators must instead rely on minimum log removal in order to respect the risk threshold through plant optimisation; this ensures that even if risk assessment measurements are not exact, the risk present in the drinking water will be negligible. Water treatment plants' performance takes into accounts its ability to disinfect, filter, and remove pathogens with the purpose of eliminating consumers' exposure to contaminants.

Despite this different communities are still afflicted with endemic gastroenteritis following the consumption of water and outbreaks also occur. Parasites such as *Giardia*, which are nearly ubiquitous in Canadian water catchment sources, challenge the water treatment plants due to their resistance to desiccation following exposure to chlorine (Levallois et al., 1999). This emphasises the importance of having highly efficient coagulation, sedimentation and filtration components as they are not fail proof. To verify treatment efficiency, laboratory test on water samples are required. The evaluation through laboratory testing for *Giardia* is particularly expensive, making it impractical for water treatment plants to sample their water

and test for the presence of that protozoan. Additional, the lab tests results cannot always confirm the viability and the pathogenicity of the parasites; the infectious fraction may be ambiguous.

To replace the requirement of frequent water testing of raw and treated water for pathogen loads, QMRA models have been proposed to potentially estimate yearly risk of giardiasis or other waterborne diseases. However, as these models are recent, they have not yet been widely adopted by policy makers. Indeed, QMRA details were only elaborated in the Canadian protozoan guidelines since the 2010 update (Federal-Provincial-Territorial Committee on Drinking Water, 2010). Concentration and achievable removal goals have been implemented and used for a far greater period of time in developed countries, especially with regards to chemicals (first regulation adopted in 1986 in Canada, 2006 for *E. coli*). Naturally, threshold values are better understood and applied. The interpretation of the predicted consequences generated by QMRA models has yet to be perfected. Nonetheless, in order to create and apply norms and regulations derived from the models, it is crucial that the models and their results are properly understood and interpreted. As of now, there are very few studies that have compared QMRA's predicted risk with observable risk. By doing so, the efficiency of the QMRA models and their predictive limits (all while bearing in mind surveillance limits), will permit a more thorough interpretation of the model's results. This will allow a synergy between decision makers and end users, an element highly encouraged by the Canadian multi-barrier approach to water sanitation.

2.2 Study objectives

The study's overarching objective is to evaluate the association between the presence of *Giardia* cysts in untreated water, sampled at the entrance of three drinking water treatment plants within the province of Québec, and the prevalence of gastroenteritis or giardiasis, whether endemic, sporadic or epidemic, within the three provided municipalities.

2.2.1 Specific objectives

1. Explore the association between the incidence of gastroenteritis, as well as giardiasis, and the concentration of *Giardia* cyst in raw drinking water.

2. Study gastroenteritis' temporal or seasonal variations using Info-Santé CLSC's database.

3. Evaluate the association between the rate of giardiasis and the predicted probability of illness generated by Health Canada's QMRA model.

4. Determine whether QMRA models can predict the occurrence of giardiasis in drinking water consumers provided by the community's drinking water treatment plant.

Chapter 3: Article

Drinking water quantitative microbial risk assessment: can the estimated risk predict the incidence of giardiasis and gastroenteritis

Short title: QMRA and epidemiological risk

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Abstract

Canada has multiple provincial and regional water regulations and policies to control potential health hazard associated with drinking water. Despite these guidelines, outbreaks and individual illness caused by pathogens in Canadian drinking water occur. The risk associated with pathogens in drinking water, such as *Giardia*, can be estimated using quantitative microbial risk assessment (QMRA). We used QMRA models to predict the probability of illness of giardiasis in communities supplied by three municipal water treatment plants, in the province of Quebec, Canada. Data from a notifiable diseases database (2005-2010) and the Info-Santé telehealth database (2007-2010) allowed us to determine the incidence of giardiasis and gastroenteritis within the three municipalities. General additive models were used to assess the relationship between predicted probability of illness and observed illness; only sex and turbidity were retained in the final model. While municipalities with the higher yearly mean incidence rate (IR) was associated with a higher yearly probability of illness (P_{ill}) (IR 0.13, P_{ill} $5.84x10^{-5}$ vs IR 0.0, P_{ill} $3.99x10^{-11}$ for giardiasis), a higher weekly or monthly probability of illness was negatively associated to an increase in weekly or monthly IR. An increase in predicted risk did not correspond to an increase in observed risk. For QMRA models to be used for predicting epidemiological data, more population and physical-chemical data is needed to generate risk estimation.

Key words*: Giardia*, gastroenteritis, notifiable disease, telehealth, quantitative microbial risk analysis, water

Acronyms*:*
AIC: Akaike information criterion
CI: confidence interval
FSA: Forward Sortation Area
WBD: waterborne disease
WTP: water treatment plant
QMRA: Quantitative microbial risk analysis

Résumé

Le Canada est muni de plusieurs réglementations et normes qui encadrent le traitement d'eau potable. Toutefois, la contamination microbiologique d'eau est possible malgré les traitements. L'importance de cette contamination peut être évaluée utilisant l'évaluation quantitative du risque microbien (ÉQRM). L'incidence de gastroentérite et de giardiase pouvant être d'origine hydrique, dans trois municipalités québécoises, fut comparée aux résultats de l'analyse de risque ÉQRM. Des modèles généraux additifs et des corrélations de Spearman ont servi pour modéliser cette relation. Le risque prédit, ajusté pour la turbidité et le sexe, est significativement associé à l'augmentation de cas de giardiase. Cependant, la relation entre le taux hebdomadaire et mensuelle et les risque prédit sont négatives, pareillement pour les corrélations, indiquant qu'une augmentation du risque prédit ne correspond pas à une augmentation du risque observé. Les modèles ÉQRM surestiment le risque et nécessitent des données populationnelles et physico-chimiques détaillées pour mieux refléter le risque épidémiologique.

Introduction

Potable drinking water is a precious commodity and its availability is essential to the development and health of a nation. To ensure its availability and adequate water safety, treatment technologies have been implemented to reduce the risk of disease associated with water consumption. Despite the presence of state-of-the-art water treatment systems, waterborne diseases (WBD) occur in developed countries. If symptomatic, WBDs will often manifest as gastroenteritis, generally an infectious diarrhoeal illness. On average, every person living in Canada has one episode of gastroenteritis annually, with over 200 community outbreaks occurring over 30 years (Federal-Provincial-Territorial Committee on Drinking Water, 2012; Payment, 2003). Although the etiologic agent is generally unknown, the most commonly identified causal pathogens in outbreaks are protozoan parasites (21%) and, more precisely, *Giardia* (Adam, 1991; Farthing, 1996). As for *Giardia,* 940 individual cases were reported in the province of Quebec during 2010 (Ministère de la Santé et Services sociaux, 2011) although the incidence has declined in Canada from about 35 to 13 cases per 100 000 persons from 1990 to 2004 (Public Health Agency of Canada, 2006).

The cysts and oocysts of intestinal parasites present in raw water are of particular concern for water sanitation as they are highly resistant to chemical disinfection, unlike their bacterial and viral counterparts (LeChevallier et al., 1991). Parasites enumeration and identification are problematic due to laboratory analysis cost, poor cysts recovery and wide measurement errors in these tests (United States Environmental Protection Agency, 2005).

The United States Environmental Protection Agency (USEPA) has established current drinking water regulations for two parasites since 1989 for *Giardia* cysts and 1998 for *Cryptosporidium* oocysts (Federal Register Reference, 1989, 1998). The European Drinking Water Directive has no defined regulations for parasites but has underlined since 1980 and formalized in 1998, that (oo)cysts should be absent from drinking water (Council Directive, 1980, 1998). Proposed revisions to ensure pertinence and effectiveness suggest that the emphasis should shift from relying on pathogens concentration alone to understanding pathogens' effect on human populations (Hellard et al., 1997). Quantitative microbial risk analysis (QMRA) models (Haas et al., 1999), have largely been adopted by scientists and

regulators as a method of assessing microbial risk associated with drinking water (van Lieverloo et al., 2007; World Health Organization, 2008). These models quantify risk and may even estimate the potential consequences associated with water consumption by integrating water treatment plant (WTP) operational and pathogens data to quantify potential health risk. The measurement error of these models is generally unknown and their acceptability and ease of use or implementation are still ill defined (Macgill et al., 2001; Schijven et al., 2011). Improvement in these areas would facilitate and encourage regulatory authorities' to use QMRA models. However, QMRA has infrequently been contrasted to epidemiological results, and as a consequence, its validity in a public health context is still open for debate.

The primary purpose of this study is (i) to evaluate the relationship between the incidence of giardiasis and the predicted probability of illness generated by Health Canada QMRA model and (ii) to determine if QMRA models can predict with sufficient reliability the occurrence of giardiasis of drinking water consumers in non-outbreak settings. The probability of illness in communities was evaluated for three drinking water treatment plants by integrating data on *Giardia* cysts concentrations in raw water with water treatment process performance data. The association between the incidence rate of gastroenteritis and estimated health risk was analysed in three communities using notifiable diseases and telehealth databases.

Method

Water samples

The selected WTP were previous included in a Canadian project aiming to assess waterborne health risk through quantitative risk assessment models (Payment, 2014). The sites were included in as they regularly tested for *Giardia* cysts, their microbiologically challenged water source (no zero cysts counts confirmed through historical data) continuous on-line computerized monitoring for CT-values and access to an electronic database for physical-chemical data (Table 12). The project included three water treatment plants in the province of Québec, Canada. They consented to provide physical and chemical

performance data on their treatment processes. The included WTP also provided weekly or monthly *Giardia* cysts concentrations in raw (untreated) water samples within the years 2005-2010. We had approached six plants and all consented, however one municipality declined to provide epidemiological data and was not included, excluding 3 plants.

Table 12 Water treatment plant characteristics

	Source water	Average population	Contamination	Treatment	Samples provided and frequency	Sampling date	Other WTP
WTP A	Great River	1 551 776	No main source	Direct filtration, sedimentation, post-chlorination	67 monthly	January 2005 - October 2010	6*
WTP B	River	90 776	Wastewater treatment plant and sewer overflow	Coagulation flocculation, filtration, sedimentation, and post-chlorination	31 weekly	September 2009 - July 2010	0
WTP C	River	43 204	Agricultural and animal (avian)	Coagulation flocculation, filtration, sedimentation, inter-ozonation and post-chlorination	30 weekly	December 2008 - June 2009	0

WTP: Water treatment plant

*The selected main WTP is subject to a higher concentration of urban contamination and has a water treatment process without coagulation or ozone

Biological, physical, and chemical data collection

All 128 water samples were processed using the USEPA 1623 method (filtration, immunofluorescence, immunomagnetic separation, impregnation and quantitative evaluation) to enumerate *Giardia* cysts and to determine their concentration within the raw source water (United States Environmental Protection Agency, 2005). Water volume

filtered varied between 1 L to 100 L per sample, depending on water pressure and turbidity. Spike matrix recoveries were available for WTP B and Cs samples were processed at the BC-CDC laboratory, Vancouver, British-Columbia while WTP A analyzed their samples in their own laboratory. Samples from WTP B and C were shipped by courier the day following filtering. Genotyping was not performed on observed cysts. Other data obtained included: chlorine concentrations, ozone concentration, contact time, raw water pH, raw water temperature, and raw water turbidity.

Census information

Sample population information was obtained from the Canadian Census 2006 (Statistic Canada, 2009). We delimited WTP geographical area by forward sortation area (FSA) (geographical delimitation defined by the first three characters of the Canadian postal service). Hence, socio-economic information was gathered according to FSA. We included: the total population, number of males and females, number of individuals within 18 predetermined age categories, prevalence of the after tax low income cut off (LICO) for census family and non-family, unemployment and absence of high school certification or equivalent. LICO describes an income threshold below which households allocate most of their income to basic necessities. A census family is a married or common-law couple with or without children, or a lone parent living with children; a non-family are individuals living in a private dwelling who do not correspond to a census family (Statistic Canada, 2013).

We excluded FSA regions that were not listed in the census, fictional postal codes, postal codes that were created after the 2006 census, sectors with insufficient census respondents, or on census suppression list (Statistics Canada, 2011).

Epidemiological data

The study population data was obtained from two Canadian provincial databases: Info-santé (a telehealth system) and Quebec's notifiable diseases database (Institut national de santé publique du Québec, 2013; Ministère de la Santé et Services sociaux, 2009). No restriction

was placed on age or sex. The only inclusion criterion required individuals to be located within the territory supplied by the WTP.

The telehealth system provided the number of calls requesting information for acute gastrointestinal illness—identified by the code 5801—for our three municipalities from January 2007 until December 2009 (Ministère de la Santé et Services sociaux, 2009). Gastroenteritis is defined by the telehealth system as vomiting, diarrhoea, nausea, abdominal cramps, stomach burns, constipation and black stool or any symptoms related to the gastrointestinal tract, excluding post surgery and pregnancy cases.

After obtaining ethic approval from each of the participating municipalities the notifiable disease database information was provided by the Direction des ressources informationelles de l'Institut et Laboratoire national de santé publique du Québec for giardiasis cases dating from January 2006 to December 2010. These are laboratory confirmed cases of *Giardia* after stool analysis.

Both databases included: grouped age, sex, postal codes to three positions (FSA) and call date/episode reception date. Notifiable diseases database cases were validated — presence of cysts in clinical sample or *Giardia lamblia* antigens identified in stool. If the giardiasis episode date was unavailable, the stool sample date was used. Cases for which sex, age or FSA data were absent were excluded from the study (less than 10%).

Quantitative Microbial Risk Analyses (QMRA)

The QMRA model used was developed by Health Canada. It is a probabilistic model to estimate annual risk of illness & disability adjusted life years (DALYs) based on source water pathogens and treatment barriers performance (Health Canada, 2011). This QMRA model, using Excel algorithms, allows users to evaluate the probability of infection and illness as well as DALYs for a set of five pathogens including *Giardia*. For this pathogen, an exponential model was used where r, the infectivity parameter is 0.01982 (Rose et al., 1991a), V is the volume of water consumed and μ the mean concentration per litre (equation

1). The probability of infection was multiplied by 0.24 to obtain the probability of illness (Eisenberg et al., 2006).

$P_{infection} = 1\text{-}e^{-\mu Vr}$ (equation 1)

Variables included in the model are: the population size, daily water intake (fixed at a conservative 1.0 L/day), fraction of infectious cysts (fixed at 1.00), weekly arithmetic mean of residual chlorine, ozone, disinfectant contact time, pH and temperature which are used to evaluate disinfection performance. The model is conceived to include the mean and standard deviation of raw water pathogen concentrations. For the purposes of the project, the mean and standard deviation were deemed to be identical as only weekly *Giardia* point estimates were sampled and no true distribution was available. However, a sensitivity analysis using the standard deviation from the observed variations over five years, including monthly values of physical chemical data and *Giardia* concentration in source waters, was done for municipality A.

Process performances are granted according to fixed log credits given to filtration processes or variable log inactivation for disinfection processes which are granted based on CT values. Coagulation processes, filtration methods and types of disinfection can be specified in the model. Each coagulation or filtration treatment process is associated with specific log reduction parameters and these parameters are included in an Excel macro. This macro generates a yearly/daily probability distribution function (PDF) of infection or illness. These PDF only accounts for the variability of source water pathogen concentrations and exclude treatment process variability. The probability of illness was used instead of infections, which are often asymptomatic and absent from public health databases. The daily probability of individual illness provided by the model was transformed into weekly probability in order to reflect the water sampling frame.

For WTP A, the monthly pathogen concentration was transformed into weekly information as only a single sample was taken per month; we deemed it representative of the monthly water quality. Physical-chemical information was available on a weekly basis. For WTP B

and C, in order to have a nearly complete year of data, *Giardia* concentration was estimated for missing weeks by averaging the concentration of the preceding and succeeding weeks; consecutive missing months were not estimated (Levesque et al., 2013). A post-hoc sensitivity analysis was done excluding weeks for which *Giardia* concentration estimates were absent as concentration estimation is often inexact; the association between the predicted probability of illness and incidence of giardiasis remained unchanged.

Analysis

Analyses were conducted using SAS 9.3 (SAS Institute Inc). Descriptive analyses were first performed to verify trends, normality and outliers. Our main analysis consisted of a Generalized Additive Models (GAM), using a Poisson distribution, were used to evaluate the relationship between the weekly predicted risk of giardiasis by QMRA to the observed number of cases of *Giardia* identified in the notifiable diseases database. Smoothing splines were used to control for seasonal variances (Aramini et al., 2000; Fung et al., 2003).

The dependent variable was the number of *Giardia* cases reported in the notifiable diseases database within a specific time frame and location. Cases were then aggregated according to either week and FSA or week and municipality. In order to take into account giardiasis incubation period and water transit time, four different models were created. These models translated the probability of illness by seven days. The probability of illness was compared to cases reported at 0 week, one week, two weeks, three weeks and four weeks. While the incubation period of *Giardia* cysts may be longer than a month, 7-10 days is considered to be the median incubation time however the duration may vary from 3 to 25 days (Heymann, 2008; Rendtorff, 1954).

Independent variables considered for model inclusion were the following: weekly probability of illness according to QMRA, turbidity, national holidays, average income, prevalence of non high school diploma, prevalence of unemployment, prevalence of LICO for census families and non-census families, dummy variables for population proportion of males (four categories: 0-25%, 26-50%, 51%-75%, 76-100%), and proportion of cases' age

(in four categories: 0-4, 5-19, 20-55, ≥60) (Moore et al., 2011). The probability of illness controls for population size and the different water treatment methods, as these are variables included within the QMRA model. The holidays were: New Year 's Day, Easter, Victoria Day, St-Jean-Baptiste Day, Canada Day, Labour Day, Thanksgiving day, and Christmas day. Due to a small sample size, a parsimonious model was favoured. Variables were selected for inclusion in the model according to their significance (α=0.05) and the most appropriate model was selected according to the smallest Akaike information criterion (AIC) value and deviance (Akaike, 1981).

Secondary analysis, in order to explore the relationship between the probability of illness and incidence rate per 100 000 people-year of giardiasis or gastroenteritis, included the use of Spearman correlation and the Durbin-Watson coefficient. The incidence rates were calculated based on weekly, monthly and yearly cases. The probability of illness was then evaluated for weekly, monthly and yearly risks.

A further visual comparison of monthly and weekly incidences was done in order to understand temporal trends. The number of predicted cases was obtained by multiplying the probability of illness with the population size.

This project obtained consent from 9 ethics committees, including regional health departments, the national concertation table for infectious disease, Info-Santé CLSC, SOGIQUE, and the Comité d'Éthique de la Recherche de l'Université Laval (CÉRUL), with permission being renewed annually upon revision.

Results

Descriptive

The notifiable diseases and telehealth databases recorded 1 685 giardiasis and 212 425 gastroenteritis cases respectively during the study period; however, only 61% of giardiasis cases and 59% of gastroenteritis cases could be paired with microbial risk prediction generated from the environmental samples (Table 12). Thus no risk analysis was available for the periods without water samples. No *Giardia* case was reported in municipality C

during the corresponding water sampling period. Municipality B had only 4 corresponding samples, whereas municipality A had 244.

Both populations significantly differed from the census population in regards to sex and age (Table 13). The proportion of males among giardiasis cases was more elevated than in the census population. In contrast, the proportion of females among gastroenteritis cases was greater in the telehealth database than in the census population. In both databases the recorded numbers of cases were predominantly either between 0-4 years of age (notifiable diseases 14.3%; telehealth 38.2%) or between 25-34 years of age (notifiable diseases 13.7%; telehealth 8.4%). The proportion of elderly individuals (notifiable diseases 2.2%, telehealth 7.0%) was similar in both databases but was not the most prevalent age group.

Table 13. Sociodemographic characteristics of cases and source population

Characteristic		Census population n(%)	Notifiable disease cases n (%)	Telehealth cases n (%)
Cases		-	1685	212425
Age * †	Age 0-4	84 250 (5.0)	147 (14.3)	48 245 (38.2)
	Age 5-9	81 750(4.8)	93 (9.0)	5 645 (4.5)
	Age 10-14	87 630 (5.2)	46 (4.5)	2 523 (2.0)
	Age 15-19	88 695 (5.3)	39 (3.8)	3 626 (2.9)
	Age 20-24	122 255 (7.3)	88 (8.6)	8166 (6.5)
	Age 25-29	144 265 (8.6)	141 (13.7)	10 612 (8.4)
	Age 30-34	128 285 (7.6)	119 (11.6)	8 868 (7.0)
	Age 35-39	124 495 (7.4)	75 (7.3)	5 641 (4.5)
	Age 40-44	129 290 (7.7)	81 (7.9)	4384 (3.5)
	Age 45-49	126 090 (7.5)	65 (6.3)	4081 (3.2)
	Age 50-54	115 205 (6.8)	55 (5.3)	4184 (3.3)
	Age 55-59	102 483 (6.1)	28 (2.7)	3660 (2.9)
	Age 60-64	82 060 (4.9)	20 (1.9)	3587 (2.8)
	Age 65-69	66 940 (4.0)	9 (0.8)	3042 (2.4)
	Age 70-74	62 785 (3.7)	12 (1.2)	2768 (2.2)
	Age 75-79	55 800 (3.3)	5 (0.5)	2866 (2.3)
	Age 80-84	41 895 (2.5)	1 (0.1)	2468 (1.9)
	Age ≥85	33 685 (2.0)	4 (0.4)	2081 (1.6)
Sex * †	Male	808 465 (48.0)	623 (60.6)	48 601 (38.4)
	Female	871 750 (52.0)	405 (39.4)	77 818 (61.5)

* † Statistically different from the census population with $p < 0.001$

Probability of illness

The observed overall yearly probability of infection of *Giardia* (Table 14), throughout a year corresponded to a lower probability of infection than the USEPA goal for annual risk of infections ($1x10^{-4}$ infection per year). The predicted monthly and weekly probabilities of *Giardia* infection for municipality B and C were below this threshold. However,

municipality A's monthly and weekly probability of infection were above the threshold (Table 14). This breach mainly occurred in winter months (November - March) (Figure 4 and Figure 6).

Table 14. Incidence, incidence rate of giardiasis and estimated probability of illness for all municipalities based on yearly, monthly and weekly water treatment plant agglomerated values

		Notifiable disease database mean (SD)		
		Municipality A	**Municipality B**	**All**
Year				
	Incidence	$1.32x10^{-4}$ ($2.11x10^{-5}$)	$2.20x10^{-5}$ ($1.55x10^{-2}$)	$1.01x10^{-4}$ ($5.68x10^{-5}$)
	IR/100 000ppl-yrs	13.22 (21.08)	22.03 (15.58)	100.75 (56.82)
	Individual yearly probability of illness	$5.84x10^{-5}$ ($2.05x10^{-5}$)	$3.99x10^{-11}$ ($2.40x10^{-11}$)	$4.17x10^{-5}$ ($3.31x10^{-5}$)
Month				
	Incidence	$1.2x10^{-5}$ ($4.29x10^{-6}$)	$1.10x10^{-5}$ (-)	$1.2x10^{-5}$ ($4.71x10^{-6}$)
	IR/100 000ppl-yrs	13.90 (3.92)	13.53 (0.59)	13.88 (3.92)
	Individual yearly probability of illness	$4.69x10^{-4}$ ($1.00x10^{-4}$)	$2.30x10^{-11}$ ($1.67x10^{-11}$)	$4.38x10^{-4}$ ($9.71x10^{-4}$)
	Individual Monthly probability of illness	$3.85x10^{-5}$ ($8.20x10^{-5}$)	$1.89x10^{-12}$ ($1.37x10^{-12}$)	$3.60x10^{-5}$ ($7.99x10^{-5}$)
Week				
	Incidence	$2.71x10^{-6}$ ($1.53x10^{-6}$)	$1.10x10^{-5}$ (0)	$2.84x10^{-6}$ ($1.84x10^{-6}$)
	IR/100 000ppl-yrs	14.12. (7.97)	57.44 (0)	14.82 (13.44)
	Individual yearly probability of illness	$4.49x10^{-4}$ ($9.61x10^{-4}$)	$1.96x10^{-11}$ ($1.65x10^{-11}$)	$4.42x10^{-4}$ ($9.55x10^{-4}$)
	Individual weekly probability of illness	$8.59x10^{-6}$ ($1.84x10^{-5}$)	$3.76x10^{-13}$ ($1.51x10^{-12}$)	$8.45x10^{-6}$ ($1.83x10^{-5}$)

IR: incidence rate; ppl: people; NDD: notifiable diseases database

Table 15. Incidence, incidence rate of gastroenteritis and estimated probability of illness for all municipalities based on yearly, monthly and weekly water treatment plant agglomerated values

		Telehealth database mean (SD)			
		Municipality A	**Municipality B**	**Municipality C**	**All**
Year					
	Incidence	0.02 (0.004)	1.06×10^{-2} (6.92×10^{-3})	0.02	1.76×10^{-2} (6.31×10^{-3})
	IR/1 000ppl-yrs	233.80 (48.40)	125.36 (81.53)	1.43×10^{-3}	207.14 (74.31)
	Individual yearly probability of illness	6.20×10^{-5} (2.18×10^{-5})	3.98×10^{-11} (2.40×10^{-11})	264.07	3.50×10^{-5} (3.66×10^{-5})
Month					
	Incidence	1.76×10^{-3} (6.87×10^{-3})	1.94×10^{-3} (8.37×10^{-4})	4.07×10^{-3} (2.10×10^{-3})	2.05×10^{-3} (1.19×10^{-3})
	IR/1 000ppl-yrs	21.18 (8.30)	23.27 (10.07)	49.21 (25.93)	(24.66) (14.40)
	Individual yearly probability of illness	4.20×10^{-5} (1.26×10^{-6})	5.03×10^{-11} (5.15×10^{-11})	1.33×10^{-13} (1.85×10^{-13})	3.65×10^{-4} (9.30×10^{-4})
	Individual monthly probability of illness	5.11×10^{-4} (1.50×10^{-5})	4.11×10^{-12} (4.23×10^{-12})	1.10×10^{-14} (1.52×10^{-14})	3.00×10^{-5} (7.64×10^{-5})
Week					
	Incidence	4.05×10^{-4} (1.56×10^{-4})	4.95×10^{-4} (1.69×10^{-4})	9.19×10^{-4} (4.82×10^{-4})	4.79×10^{-4} (2.73×10^{-4})
	IR/1 000ppl-yrs	21.13 (8.17)	25.82 (8.81)	47.93 (25.13)	24.95 (14.23)
	Individual yearly probability of illness	4.96×10^{-4} (1.03×10^{-3})	4.81×10^{-10} (2.92×10^{-9})	1.94×10^{-13} (2.94×10^{-13})	3.60×10^{-4} (9.00×10^{-4})
	Individual weekly probability of illness	9.50×10^{-6} (1.97×10^{-5})	9.23×10^{-12} (5.60×10^{-11})	3.72×10^{-15} (5.64×10^{-15})	6.9×10^{-6} (1.73×10^{-5})

IR: incidence rate; ppl: people

The total incidence rate per 100 000 people-years of *Giardia* or gastroenteritis (Table 15) and probability of illness were significantly correlated whether on a weekly or monthly scale (Table 16). The weekly and monthly rates did have a significant positive auto-correlation respectively amongst each time frame, according to the Durbin-Watson statistic. A sensitivity analysis (data not shown) excluding all but municipality A identified a monthly correlation for telehealth reported cases with higher reporting occurring during the winter months (January-March) (Figure 5).

Table 16. Correlation between incidence-rate per 100 000 people years and the QMRA's yearly predicted probability of illness

	Time	Municipality	n	Spearman correlation (*p*-value)	Durbin-Watson (*p*-value positive; *p*-value negative)
Notifiable disease database					
	Weekly	All municipalities	248	-0.14 (0.02)	1.15 (<0.001; 1.00)
		Municipality B C	4	na	na
		Municipality A	244	-0.14 (0.03)	1.54 (<0.001; 0.99)
	Monthly	All municipalities	61	-0.260 (0.043)	1.53 (0.03; 0.97)
		Municipality B C	4	0.632 (0.367)	2.08 (na)
		Municipality A	57	-0.287 (0.032)	1.54 (0.03;0.96)
	Yearly	All municipalities	7	0.750 (0.052)	1.32 (0.07;0.93)
		Municipality B C	3	na	na
		Municipality A	4	0.40 (0.505)	0.65 (0.04;0.96)
Telehealth database					
	Weekly	All municipalities	270	0.30 (<0.01)	0.95 (<0.01;1.00)
		Municipality B C	74	-0.10 (0.39)	0.22 (<0.01;1.00)
		Municipality A	196	0.45 (<0.01)	0.10 (<0.01;1.00)
	Monthly	All municipalities	63	-0.00 (0.98)	1.04 (<0.01;1.00)
		Municipality B C	18	-0.08 (0.75)	0.45 (na)
		Municipality A	45	0.40 (0.06)	0.55 (<0.001;1.00)
	Yearly	All municipalities	7	0.39 (0.38)	2.83 (0.82;0.16)
		Municipality B C	3	na	na
		Municipality A	4	0.40 (0.60)	1.78 (0.05;0.94)

na = not available

Observed number of cases of *Giardia* ranged from 1-12 cases per week, gastro-enteritis ranged from 1-1127, while the QMRA predicted case range was <1-156. Figures 5 and 7 illustrate the increase of telehealth cases occasionally corresponded to higher probability of

risk. No measurable trend was confirmed with visual analysis or modelling. For the giardiasis cases, increase in QMRA predicted risk did not follow the same tendency as the observed risk of *Giardia*.

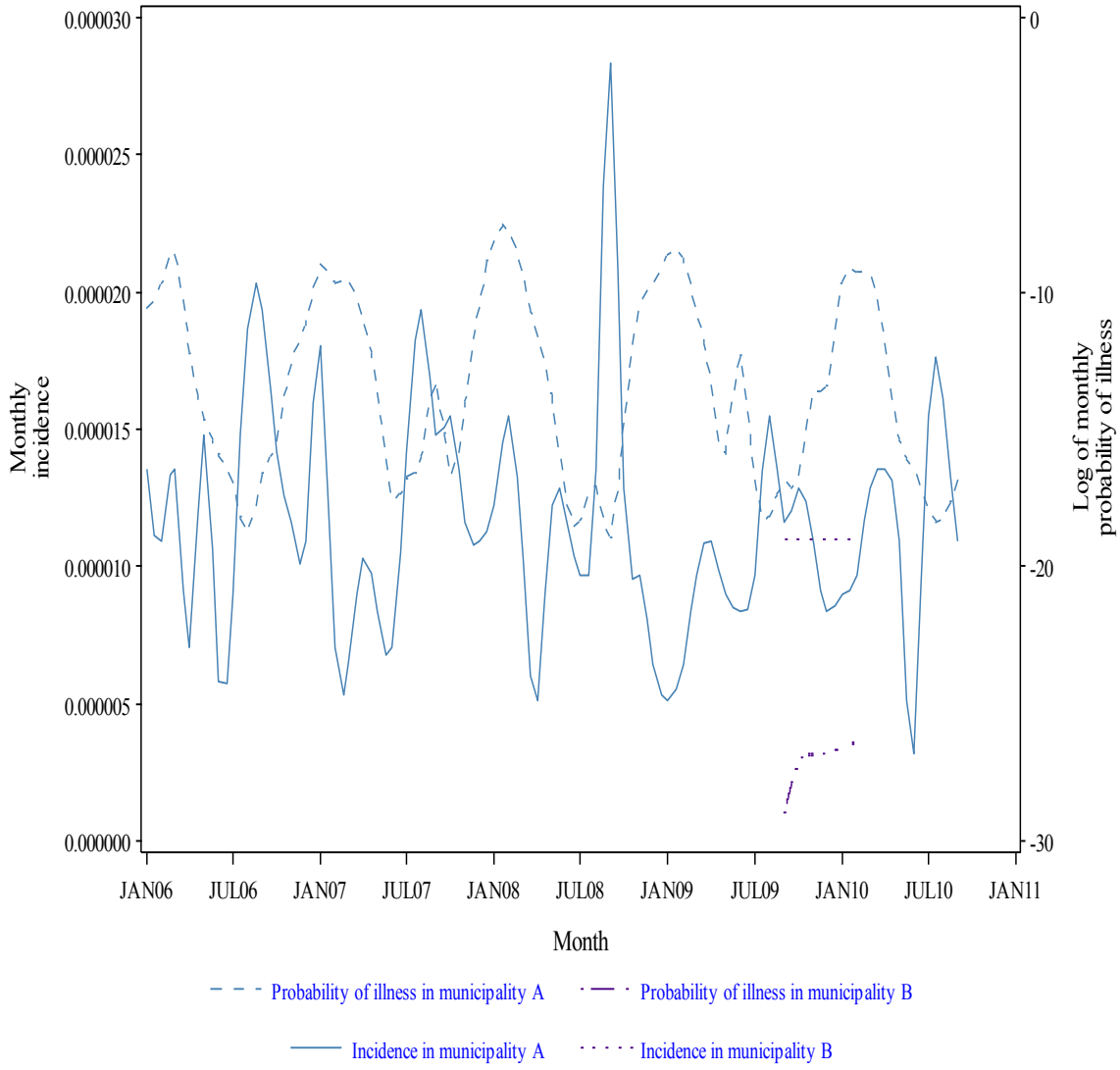

Figure 4. Monthly giardiasis incidence from the Notifiable diseases database and their associated probability of illness

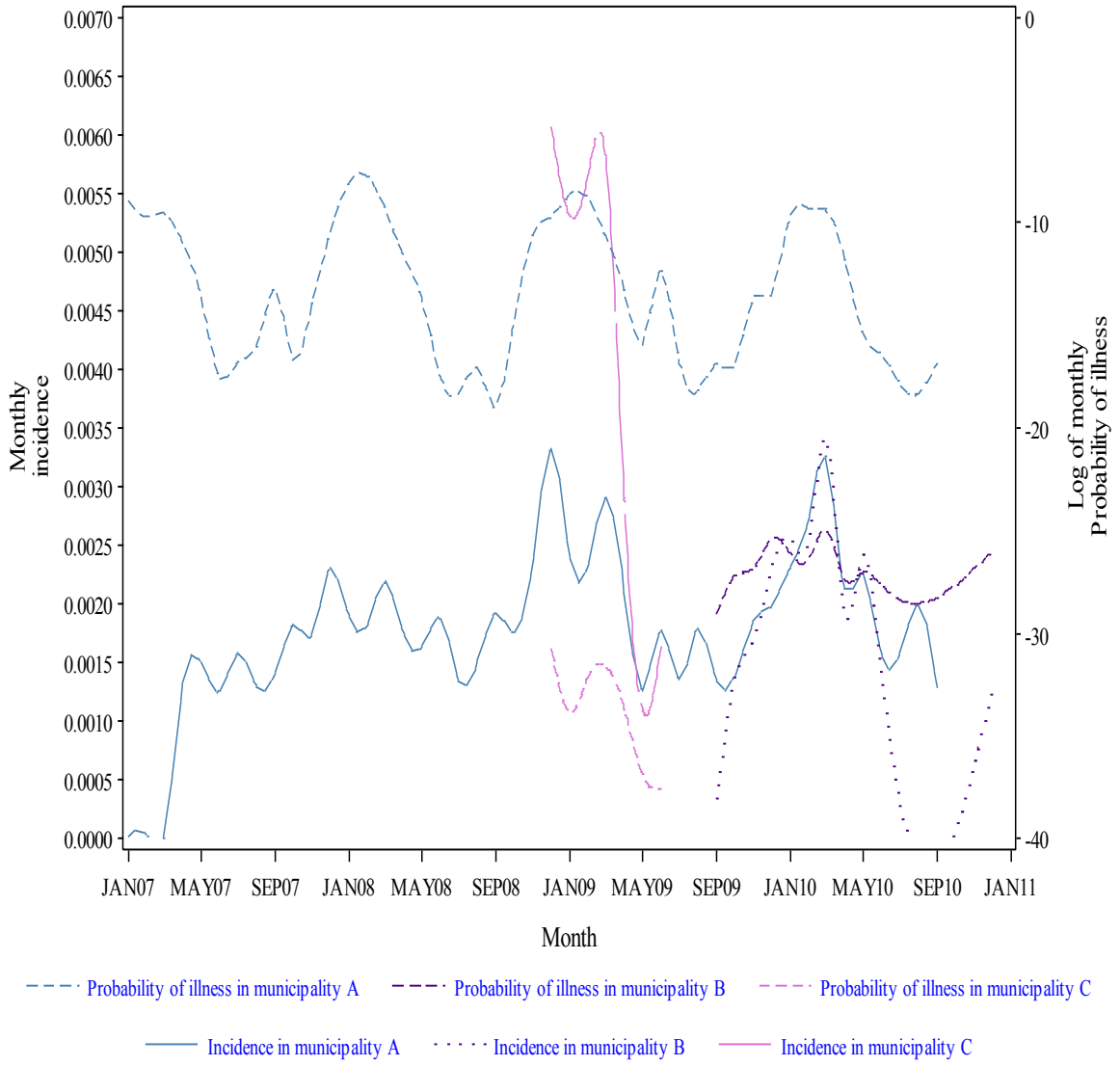

Figure 5. Monthly gastroenteritis incidence from the Info-Santé database and their associated probability of illness

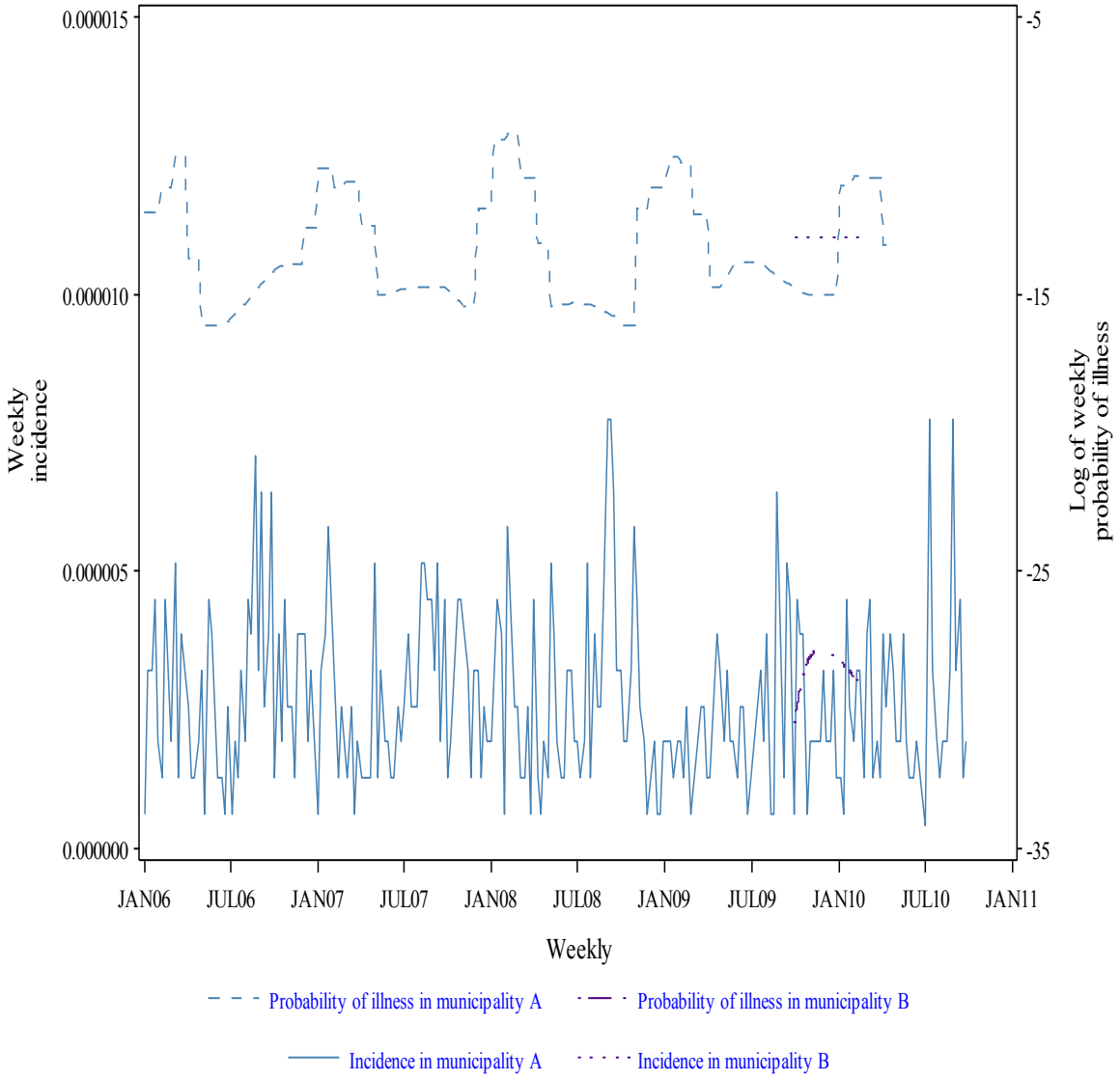

Figure 6. Weekly incidence of giardiasis from the Notifiable diseases database and their associated probability of illness

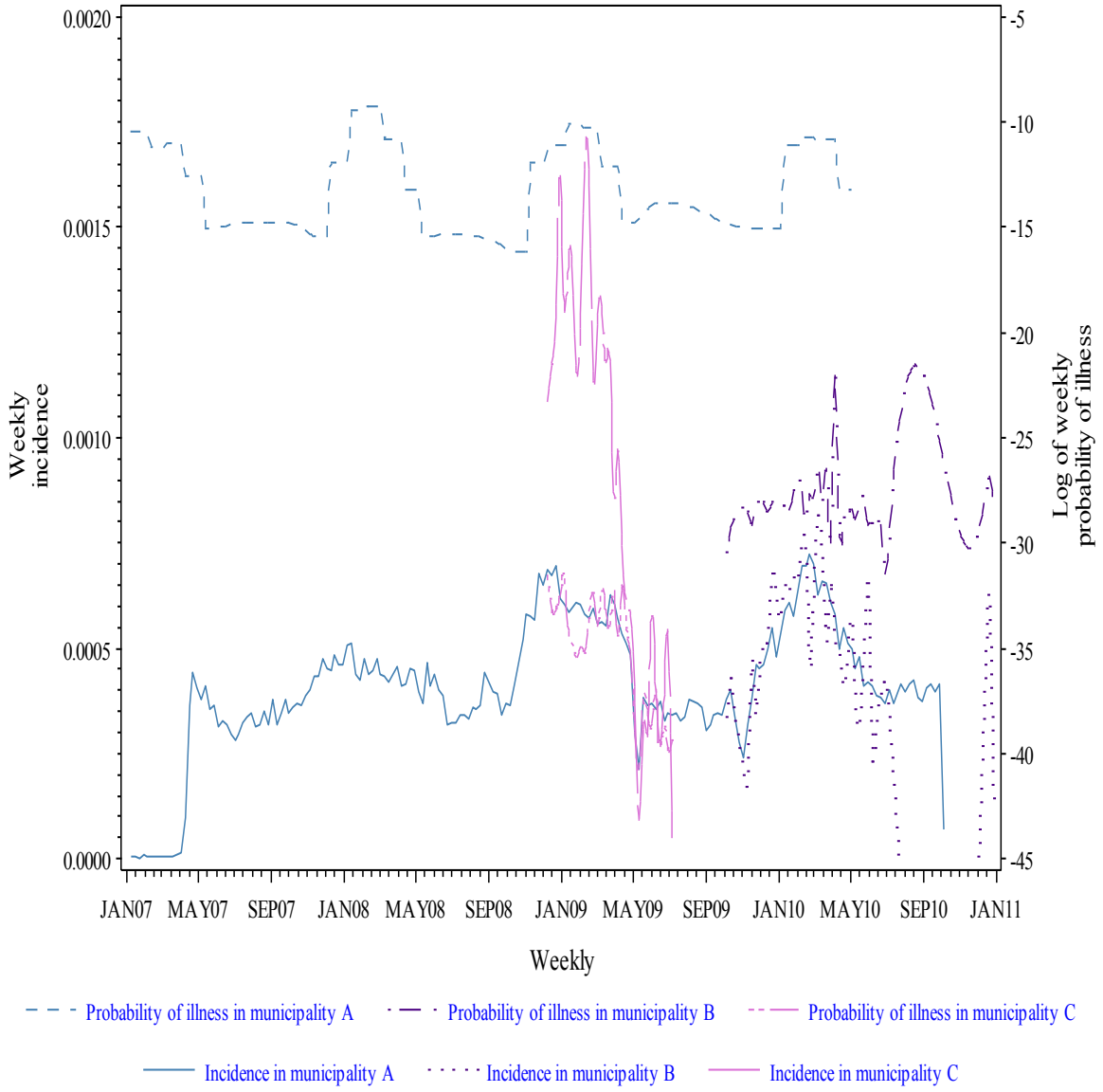

Figure 7. Weekly incidence of gastroenteritis and their associated probability of illness

***General Additive Model and* Giardia**

The relationship between QMRA predictions and observed giardiasis was further evaluated using GAM. Only two co-variables were statistically significant ($p \leq 0.005$) and retained in the model: sex ($p \leq 0.005$) and raw water turbidity ($p \leq 0.001$). These variables remained even when stratifying by municipality. Both the probability of illness and the turbidity were log transformed; however, this did not improve normality and untransformed values were retained. The final model selected is presented in equation 2.

No. notifiable diseases cases per municipality ~ Spline (Probability of illness weekly) + $Z_{Sex26\text{-}50\%}$ + $Z_{Sex51\text{-}75\%}$ + $Z_{Sex76\text{-}100\%}$ + Spline (Turbidity) (equation 2)

For the first three incubation periods, all models were significant when agglomerating cases by week and municipality. Regardless of whether or not models were smoothed with splines, the models remained significant. Models tested by agglomerating cases by week and FSA were not statistically significant. When evaluating the probability of illness for giardiasis, excluding all cities but municipality A model significance and included covariables remained.

At 1 week of incubation, the GAM probability of illness parameter estimate was positive. For all other time the parameter was negative suggesting an inverse relationship between an increase of cases and the predicted risk of illness using QMRA models. This was also observed in the Spearman correlation analysis as the probability of illness and incident rate had a negative relationship.

The GAM models AIC value was higher for 0 week of incubation (weekly deviance: 1 133, AIC: 27 194; yearly deviance: 1 128, AIC: 27 069), 1 week incubation (weekly deviance: 1 133, AIC: 27 186; yearly deviance: 1 127 AIC 27 048) and 3 weeks of incubation (weekly deviance: 1 136, AIC: 27 274; yearly deviance: 1 134, AIC: 27 219). The most adequate model was for 2 weeks of incubation (weekly deviance: 1 128, AIC: 27 076; yearly deviance: 1 124, AIC: 26 983) or 4 weeks (weekly deviance: 1 122, AIC: 26 938; yearly

deviance: 1 120, AIC: 26 876). This may reflects time for the water to be distributed within the municipalities (< 7 days) and a minimal number of incubation days for giardiasis.

Discussion

Quantitative microbial risk analysis estimates have a limited relationship with epidemiological databases, which represents only a fraction of the true number of cases. While we observed a significant association using a model including turbidity and sex, an increase in epidemiological cases did not consistently correspond with weekly or monthly risk. QMRA models are mainly used to estimate the number of infected individuals and not to evaluate symptomatic individuals which are the tip of the iceberg. It thus apparently overestimates the risk, suggesting that the Health Canada QMRA model, when compared to a notifiable diseases database, may not be valid for predicting population health risk using epidemiological methods.

When modelling correlations, annual predicted risk of giardiasis was strongly associated with yearly incidence rate of giardiasis cases, but only 7 years were available to determine the annual incidence rate. Weekly telehealth data suggested a stronger positive correlation with weekly gastroenteritis incidence rates. Monthly and weekly correlations were strongest for municipality A which had the highest population size and incidence of giardiasis and gastroenteritis.

The observed annual risk of giardiasis is within the range of annual risk of infection previously reported in the literature concerning Quebec water sources, which is 1.1×10^{-1} to 1.0×10^{-14} risk of infection per year (3.08×10^{-2}-2.8×10^{-15} yearly probability of illness) (Payment et al., 2000). This may in part be due to more precise water sampling data or improvements to WTP. Indeed, in the past 13 years, longer chlorine contact time and the addition of ozonation have been incorporated into the WTPs of municipality B and municipality C respectively.

With the exception of two sharp increases in risk, the observed risk for *Giardia* trend was generally lower than the predicted probability of illness for all municipalities. This is congruent with the epidemiological observations of previous studies, which suggest that the predicted risk of illness overestimates the actual burden of illness found in the population (Eisenberg et al., 2006; Mara et al., 2007; Zmirou-Navier et al., 2006). Zmirou-Navier et al. (2006) reported a 12% difference, whereas Mara et al. (2007) observed a difference of one order of magnitude between predicted and observed risk. Our weekly estimates were not sufficiently precise to determine the number of cases. The proposition that daily data would be the most efficient to predict risk may only be effective with a highly sensitive epidemiological tool (Enger et al., 2012; Signor et al., 2006). Most *Giardia* cases will be under-reported in generalized databases (Flint et al., 2004; MacDougall et al., 2008; Majowicz et al., 2005).

In Canada, approximately 1 of every 300 cases is confirmed by laboratory tests, emphasising the difference between unreported and reported cases (MacDougall et al., 2008; Majowicz et al., 2005). This has a strong impact on the reliability of our results as the true risk predicted by QMRA models is unable to be ascertained using traditional surveillance databases. It is likely that we underestimated the observed risk and unduly penalize QMRA models for overestimating the risk. Moreover, in our particular context, even reported *Giardia* samples often did not occur within our sampling period, and within the municipalities having a smaller population size, the number of cases ranged from 0 to 5, with only 4 weeks being able to correspond to the environmental sampling frame and limit our ability to reject the null hypothesis.

Nonetheless, epidemiological data can be properly explained by QMRA models (Enger et al., 2012). Prior research has successfully compared risk calibrated using parameters from three pathogens to test the effectiveness of a household water treatment to prevent gastroenteritis in a randomized control trial. The observed longitudinal prevalence ratio (LPR) was 0.84 for low compliance with the predicted LPR being 0.86 (Enger et al., 2012). Quantitative risk models need to be calibrated according to specific populations' health information, unlike current QMRA models, which are generalized and do not contain

population data such a gender, age, or previous immune status (Eisenberg et al., 2006; Enger et al., 2012; Mara et al., 2007; Rose et al., 1991b). Another argument supporting the notion that QMRA models overestimate the risk is the uncertainty and variability in the water sample's infectious fraction and dose-pathogen recovery (Petterson et al., 2007). Additionally, our weekly estimates were point estimates (no distribution), reducing the model's performance (Karavarsamis et al., 2010). Other methods, such as Bayesian analysis, need to be considered as dynamic corrections and explanation and is not limited to a priori analyses (Greiner et al., 2013; Hunter et al., 2011; Pintar et al., 2012; Schmidt et al., 2013).

Finally, the two significant co-variables, sex and turbidity are only partially supported by the literature. Recent studies evaluating risk suggest that age and sex may not be-significantly associated with predicted risk of infection (Pintar et al., 2012). In this study, age is unexpectedly not significantly associated with predicted risk of illness; however this is likely explained by the lack of individual water consumption, immune status and dose-response value. The dose-response value was evaluated in healthy volunteers and do not reflect the more vulnerable population (Rendtorff, 1954). Turbidity has been associated with an increase of gastroenteritis prevalence, although there are conflicting results. It is unlikely that a higher concentration of particulate matter corresponds to an increase in water contamination, unless it is within a rural area, or a sector prone to industrial or sewage run-off, where pathogens are more plentiful (Allen et al., 2008; Febriani et al., 2009; Proctor et al., 1998). While one WTP was in a rural zone, the two others were under the influence of wastewater. Therefore, the association may be realistic (Beaudeau et al., 2010; Gilbert et al., 2006; Tinker et al., 2010). It is also possible that the turbidity effect may hide the effects of water temperature on treatment performances and pathogen persistence in source waters. For all three systems investigate, the highest source water turbidity is observed during the snow melt season occurring in the spring.

One of this study's main advantages is the usage of the probability of illness to evaluate the risk of giardiasis associated with drinking water quality as opposed to the traditional probability of infection. This has successfully been used in beach water studies (Ashbolt et

al., 2010; Schoen et al., 2010; Soller et al., 2006). Infections can be asymptomatic and consequently unreported. This would be problematic given that our epidemiological data derive from both a notifiable diseases database and a telehealth database, and only record symptomatic illness. The notifiable diseases database includes only laboratory confirmed cases of giardiasis which includes potential asymptomatic carriers. The telehealth database augments this study's sensitivity as it includes all reported gastroenteritis cases. Water was sampled weekly from two WTP for less than a year and monthly for nearly five years in order to be able to compare point estimates. This allowed us to evaluate the estimated risk on a narrower scale and gave us the opportunity to visualize point source events.

Additionally, the three WTPs have large differences with respect to the concentration of protozoan parasites in their source waters. We observed that the WTP with the lowest predicted risk had no detectable reported giardiasis cases. This suggests that if the risk is infinitesimally small, the value of QMRA to predict a single pathogen impact on the population lessens and the risk estimation may be mainly valuable, in an epidemiological context, for higher risks.

QMRA model calibration was not possible in the study due to the ecological study design; no individual host factors were available. Consequently genetics, weight, immune status, metabolic capacity, and co-morbidities were not taken into consideration (Hynds et al., 2012; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). This information is not typically found within databases and would require thorough medical documentation and serological test, as done by Zmirou-Navier et al. (Zmirou-Navier et al. 2006). Alternative, non-negligible, routes of transmission, including secondary transmission, are also absent from the model (Eisenberg et al., 2005; Interagency Microbiological Risk Assessment Guideline Workgroup, 2011; Li et al., 2009; Li et al., 2009). The lack of specificity and infectious origin in the telehealth data also caused an overestimation in the number of infectious gastro-intestinal illnesses (Gilbert et al., 2006). Certain cyst counts were absent and needed to be estimated, leading to an imprecise risk projection. Cysts were not genotyped and thus we are uncertain of their infectious origin and cysts were enumerated using two different methods leading to potential discrepancies

between counts. Information concerning WTP efficiency was not available for all treatment plants and consequently, the QMRA model used was for general log removal and not specific log removal. The evaluation of treatment performance on a weekly basis may bear significant limitations. Considering that treatment performances vary on a log-scale, short-term (e.g. several hours) underperformances may be important to correctly characterize the actual pathogen removal or inactivation. In addition, site-specific process performance may be inaccurately described by Health Canada QMRA model. More precise treatment plant information integrated into the QMRA model will lead to a more precise reflection of observable risk (Jaidi et al., 2009; Sokolova et al., 2012).

Conclusion

This project aimed to provide insight into the relationship between the theoretical risk models and epidemiological data. The notifiable disease database recorded the observed risk of giardiasis and Info-Santé telehealth reported observed cases of gastroenteritis. Both were compared to weekly predicted probability of giardiasis illness. While a weekly association was identified, there was a negative relationship between observed and predicted risk; it is not informative from a public health perspective. The observed incidence of gastroenteritis and giardiasis measured in this study could not validate QMRA models in an epidemiological context using secondary databases; population data and individual health status are not readily available. While QMRA analyses are a useful tool for improving WTP measures it has limited epidemiological validity. Given QMRA's recent integration into the Canadian Drinking Water Guidelines, understanding its relevance to public health will further support its usefulness in regulating water treatment quality.

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Chapter 4: Supplementary analysis

4.1 Methodology

Three other data explorations were done in the context of this project. These were contrasting predicted number of cases to observed number of cases, geo-spatial and temporal evaluation to observe how cases were distributed through time and space.

4.1.1 Geospatial

Additional information concerning the three municipalities included in the study is present here, as opposed to the article, in order to maintain municipality anonymity. The geospatial evaluation was done using ESRI ArcGIS 9.3 to create character maps. Giardiasis (2005-2010) and gastroenteritis (2007-2010) cases were tallied according to FSA for all three water treatment plants' (WTP) health region. Maps were generated using DMTI Spatial Inc.'s Platinum Postal Code Suit, published in August 2011.

4.1.2 ARIMA

Temporal analyses were accomplished using autoregressive integrated moving average (ARIMA) models. They were done using both the notifiable diseases data base and the telehealth database in order to describe seasonality and to be able to control for potential auto-correlative values. The main unit of analysis was the prevalence of gastrointestinal or giardiasis cases reported weekly or monthly. Covariables tested for cross correlation included: the probability of illness, sex and turbidity. Temporal trends were described numerically and graphically in order to identify potential lags and seasonal variations. Significant lag times were noted and the model was retested until significant lags and seasonal trends were accounted. Co-variables were assessed for the significance across time. Models were iteratively evaluated in order to determine the most adequate auto-regressive and moving-average terms, the best AIC value and the best predictive fit. Once a

model was selected it was used to predict the incidence of gastroenteritis 20 weeks forecast or giardiasis 10 months forecast.

4.2 Supplementary results

4.2.1 Number of predicted cases

Incidence rates and the number of predicted cases for the notifiable diseases database and telehealth database were computed in order to facilitate comparison with the observed incidence rates per thousand people-years (Table 17). The predicted estimated numbers of cases of giardiasis for the notifiable diseases database are higher than the observed number of cases by one order of magnitude. The telehealth observable incident rate per thousand people-years of gastrointestinal disease is at least two orders of magnitude higher than the predicted incidence risk of giardiasis.

Table 17. Predicted incidence rate and range or predicted cases

	Notifiable disease database			Telehealth database		
	Predicted IR/1000 ppl-yrs mean (SD)	Predicted no. cases min-max	Observed no. cases min-max	Predicted IR/1000 ppl-yrs	Predicted no. cases min-max	Observed no. cases min-max
Year	0.04 (0.03)	0-136	1-232	0.03 (0.04)	0-136	522 - 36 358
Month	0.44 (0.97)	0-668	1-44	0.36 (0.93)	0-668	30 - 516
Week	0.44 (0.96)	0-156	1-12	0.36 (0.90)	0 - 156	1 - 1127

SD : standard deviation
IR : incidence rate
ppl : people

4.2.2 Geospatial location of cases

Figures 8-11 allow visualization of the cases within the regions. It is observed that generally regions that had a higher density of *Giardia* cases reported also tended to have a greater density of individuals using the telehealth system. The older and denser sectors of these regions and adjoined regions have a similar number of cases as their nearest neighbours for giardiasis.

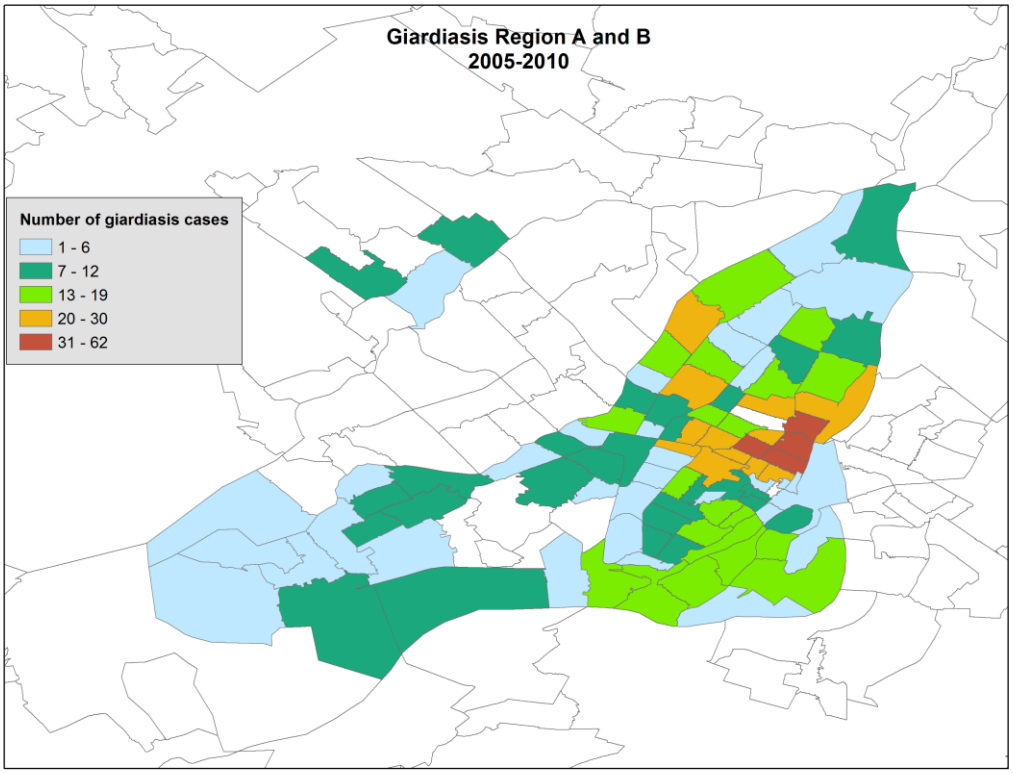

Figure 8. *Giardia* cases in region services by water treatment plant in municipalities A and B

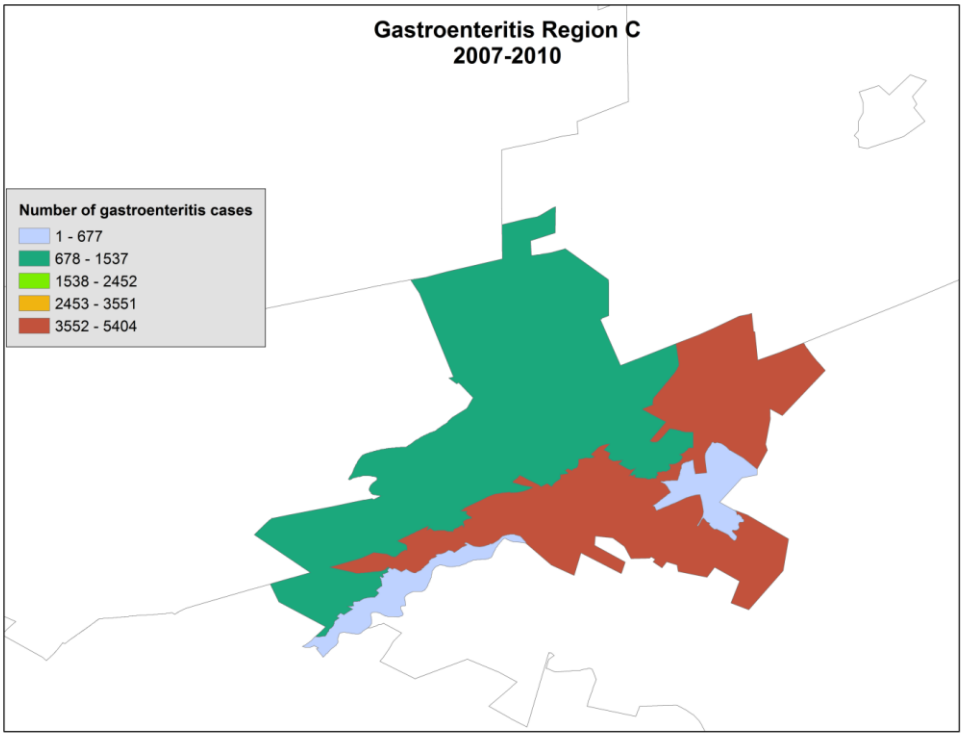

Figure 9. *Giardia* cases in region services by water treatment plant in municipality C

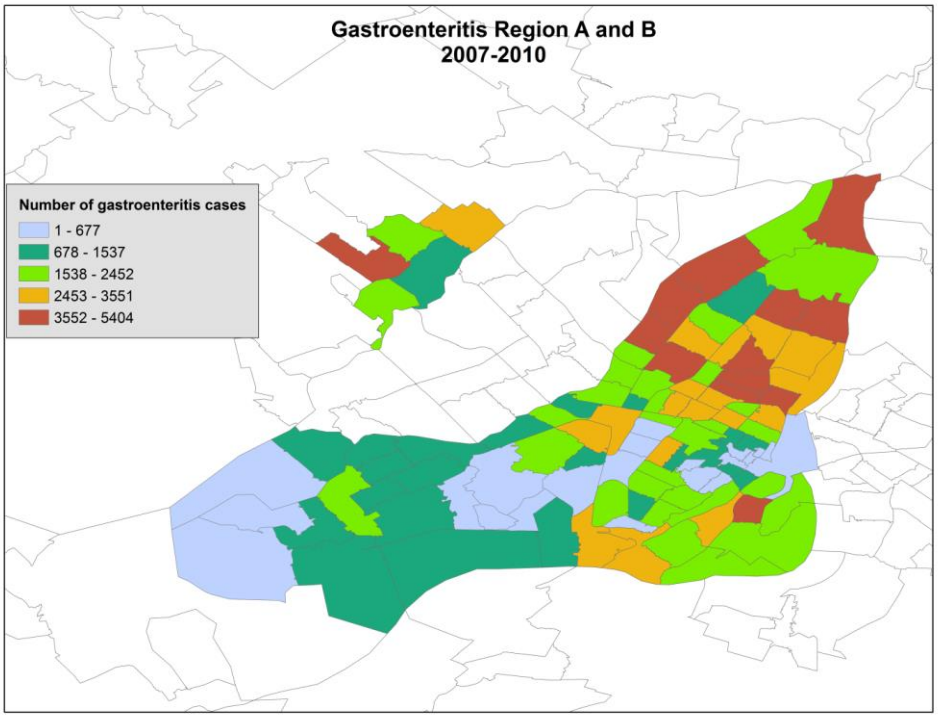

Figure 10. Gastroenteritis cases in region services by water treatment plant in municipality A and B

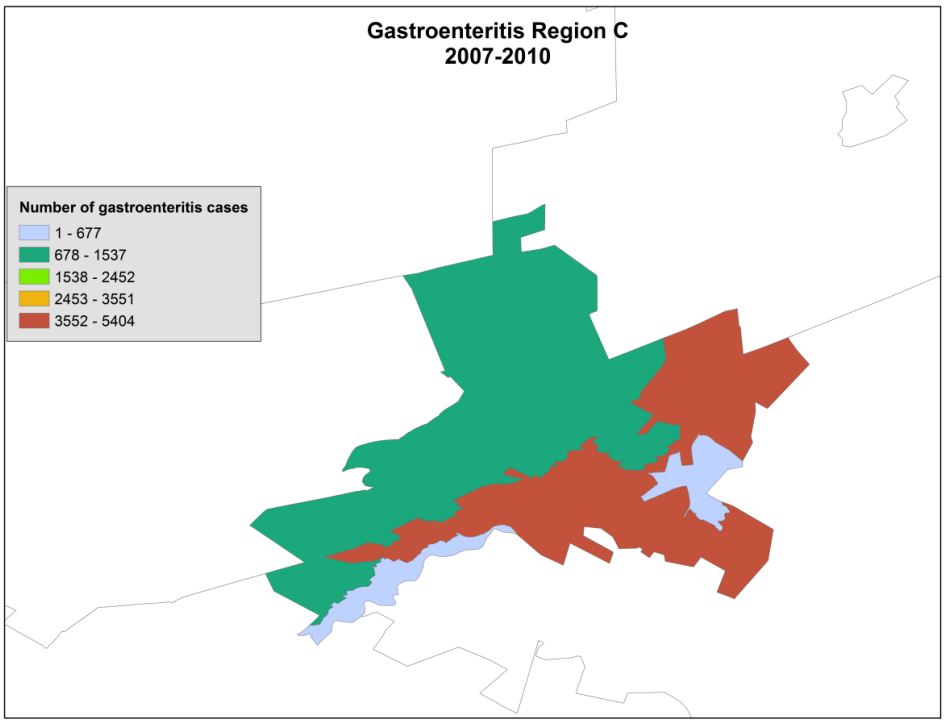

Figure 11. Gastroenteritis cases in region services by water treatment plant in municipality C

4.2.3 Temporal analysis

Weekly and monthly seasonal ARIMA models were successfully constructed for the telehealth database. For the notifiable diseases database only monthly ARIMA models were possible due to the low weekly risk. Info-santé datasets were initially non-stationary and required to be differentiated in order to respect ARIMA models postulates. The notifiable diseases database model was stationary; however, without first order differentiation the forecasted incidence of giardiasis did not follow the actual incidence. All models needed to be differentiated in order to consider seasonal effects (Figure 12 and Figure 13).

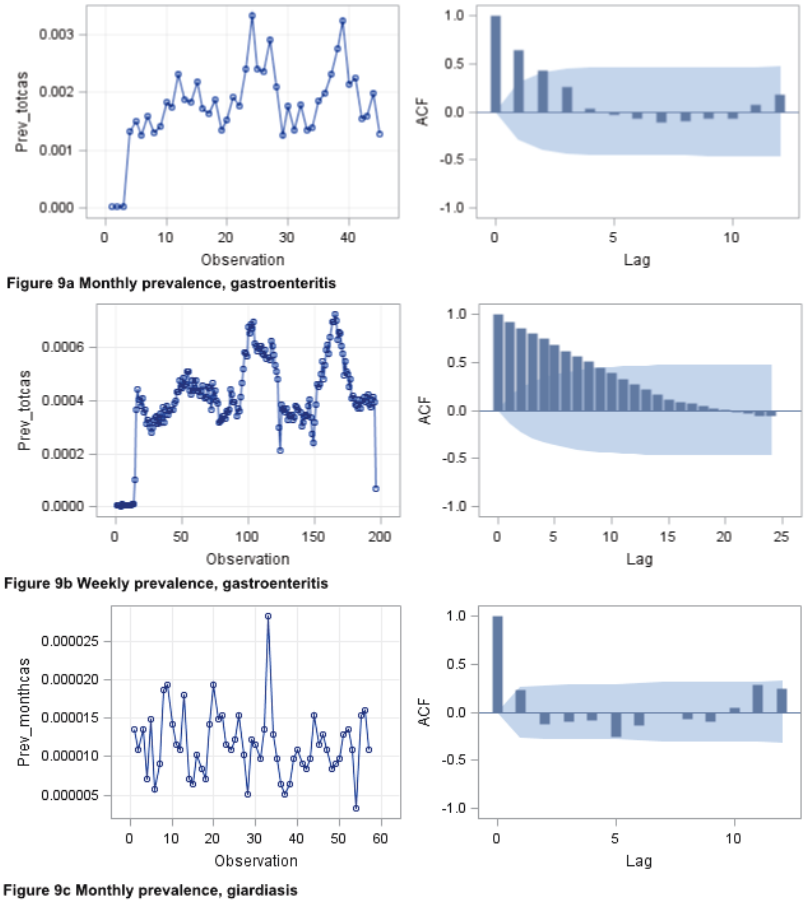

Figure 12. Scatterplot matrix and autocorrelation function to determine stationarity and seasonality before differencing

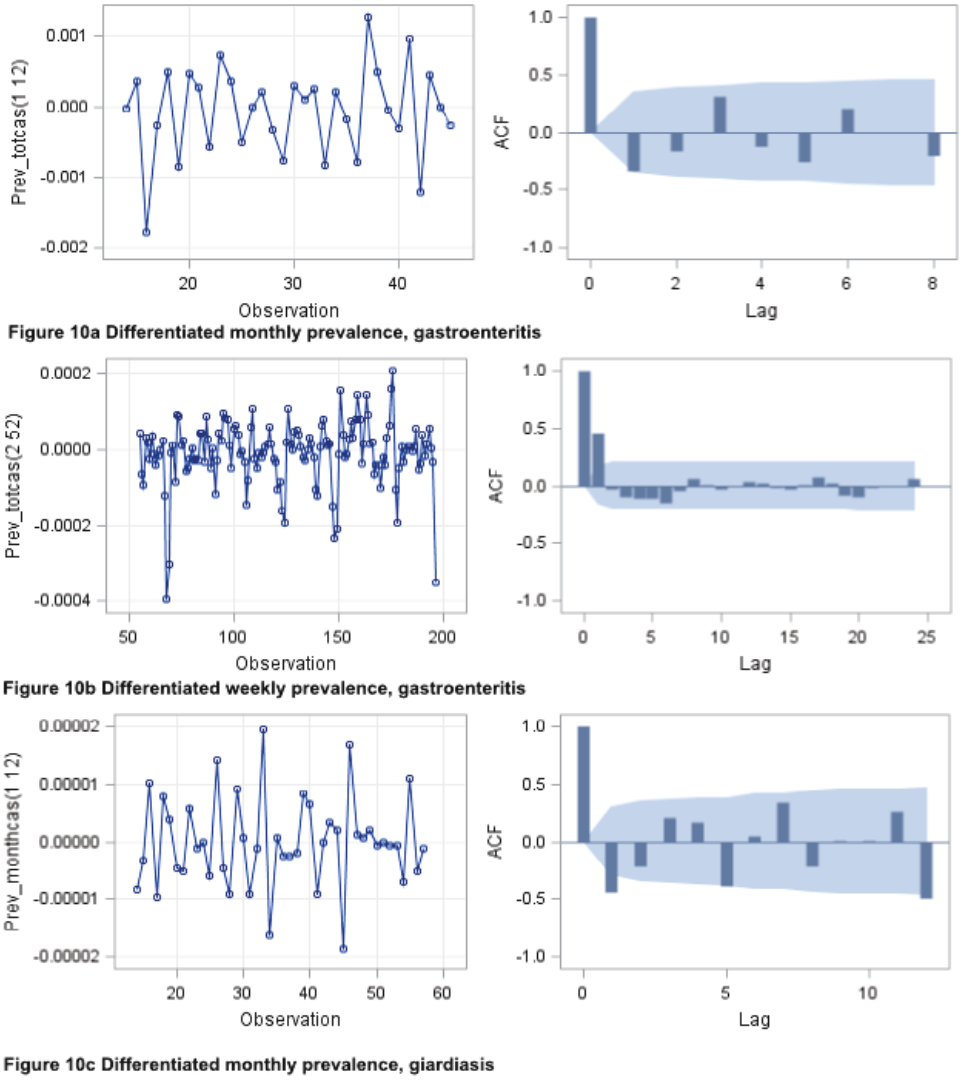

Figure 13. Scatterplot matrix and autocorrelation function to determine stationarity and seasonality after differencing

Monthly models were seasonal differentiated according to a 12-month trend and weekly models according to a 52-week trend. Monthly gastroenteritis and giardiasis models were differentiated at time 1 and 12 for seasonal effects, indicating that results are closely influenced by the cases present in the previous month and associated with those from the previous year. Weekly gastroenteritis models required a second non-seasonal differentiation suggesting an exponential relationship. Cross-correlation variables deviance was unsuitable

in the forecasted models. However, the non-forecasted models were statistically significantly associated with the probability of illness, turbidity and sex.

When forecasting the estimated ARIMA model, gastroenteritis models resulted in the most exact predictions (Figures 15-16). The ARIMA models have more precise confidence intervals and fit the observed data trend more exactly than giardiasis models (Figure 14-16). We note a general peak in the prevalence of giardiasis during the fall and a decrease in the winter, however, the forecasted portion does not follow the seasonal trend as closely (Figure 11). Figure 15 and 16 highlight an increase in gastroenteritis cases in the late fall and early winter month with the summer period being generally lower. This trend is maintained in the forecasted data. Table 18 presents the models that were compared to determine best forecasting fit and the chosen models.

Table 18. ARIMA model fit

	Model (P,D,Q)s	**Selected**	**AIC**	**Significant White noise**	**Forecast precise**	**Forecast followed trend**
Monthly Notifiable Diseases						
	(0,0,1)	No	-1248.35	No	No	No
	(0,0,1)12	No	-974.497	No	Yes	No
	(5,1,1)(0,1,0)12	Yes	-937.752	No	No	yes
Weekly Telehealth						
	(1,1,1)	No	-3303.2	No	No	No
	(1,1,1)(0,1,0)52	No	-2357.14	No	Yes	No
	(1,2,1)(1, 2,0)52	yes	-2330	No	No	Yes
Monthly Telehealth						
	(2,1,1)	No	-539.522	No	Yes	No
	(1,1,1)(1,1,0)12	Yes	-378.706	No	Yes	Yes

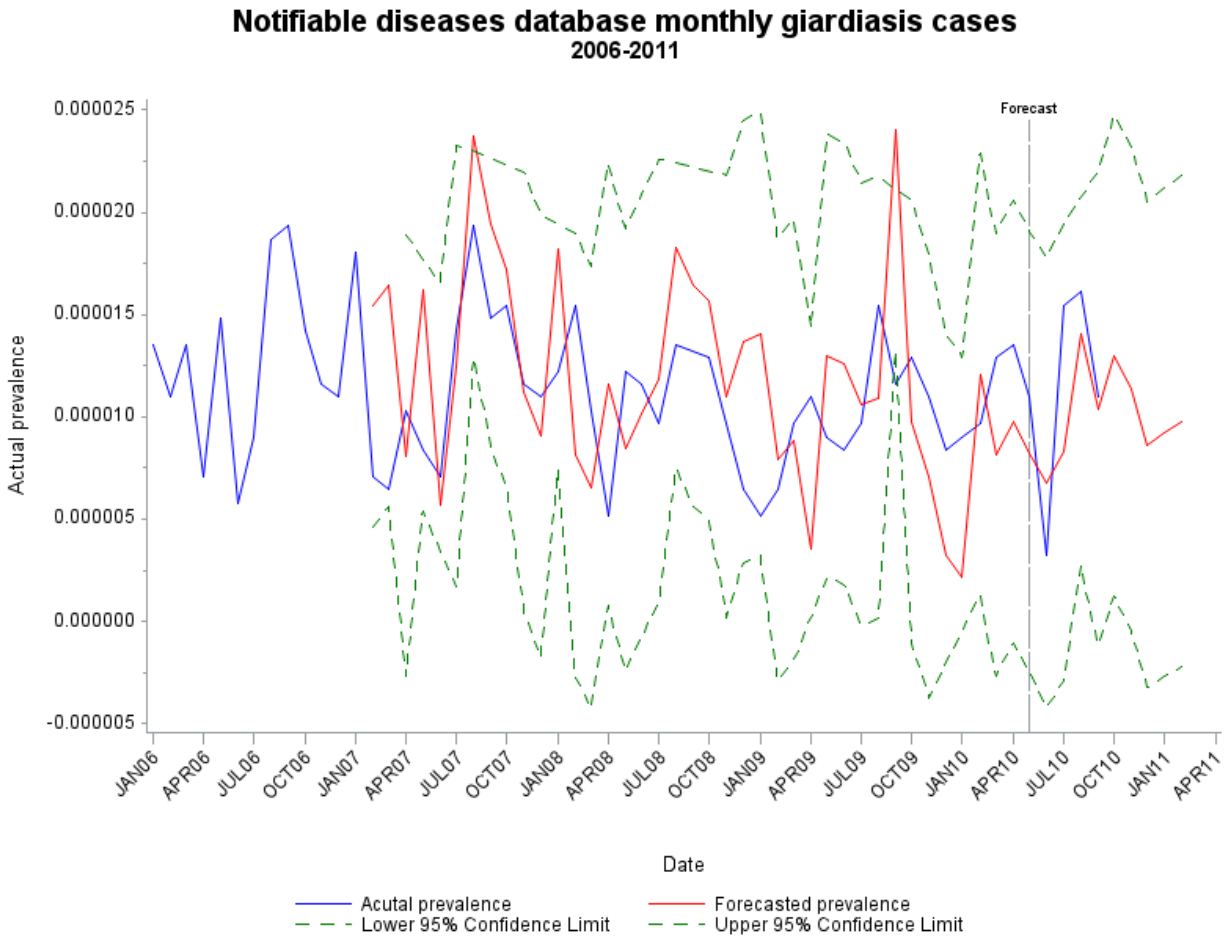

Figure 14. Forecasted incidence of giardiasis

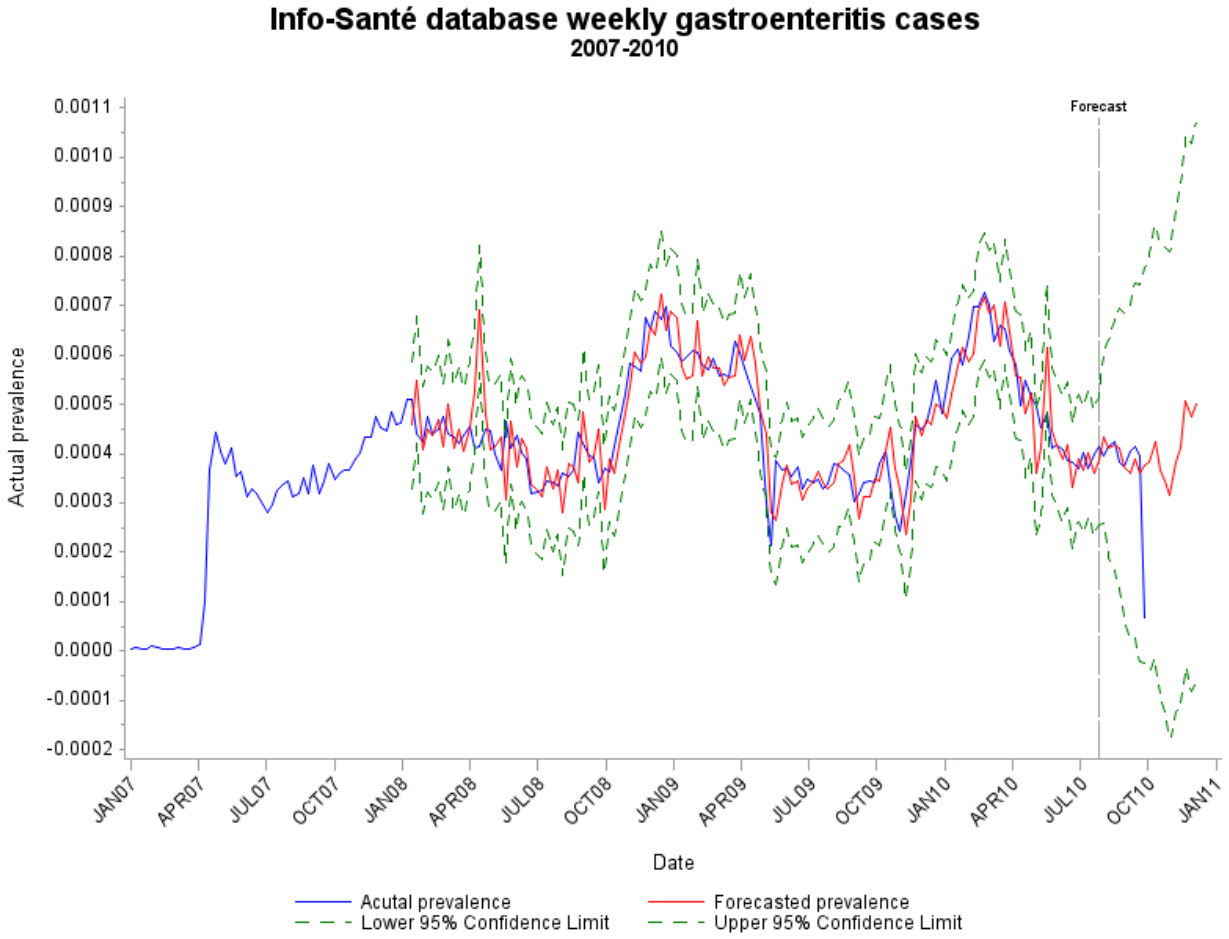

Figure 15. Forecasted weekly incidence of gastroenteritis

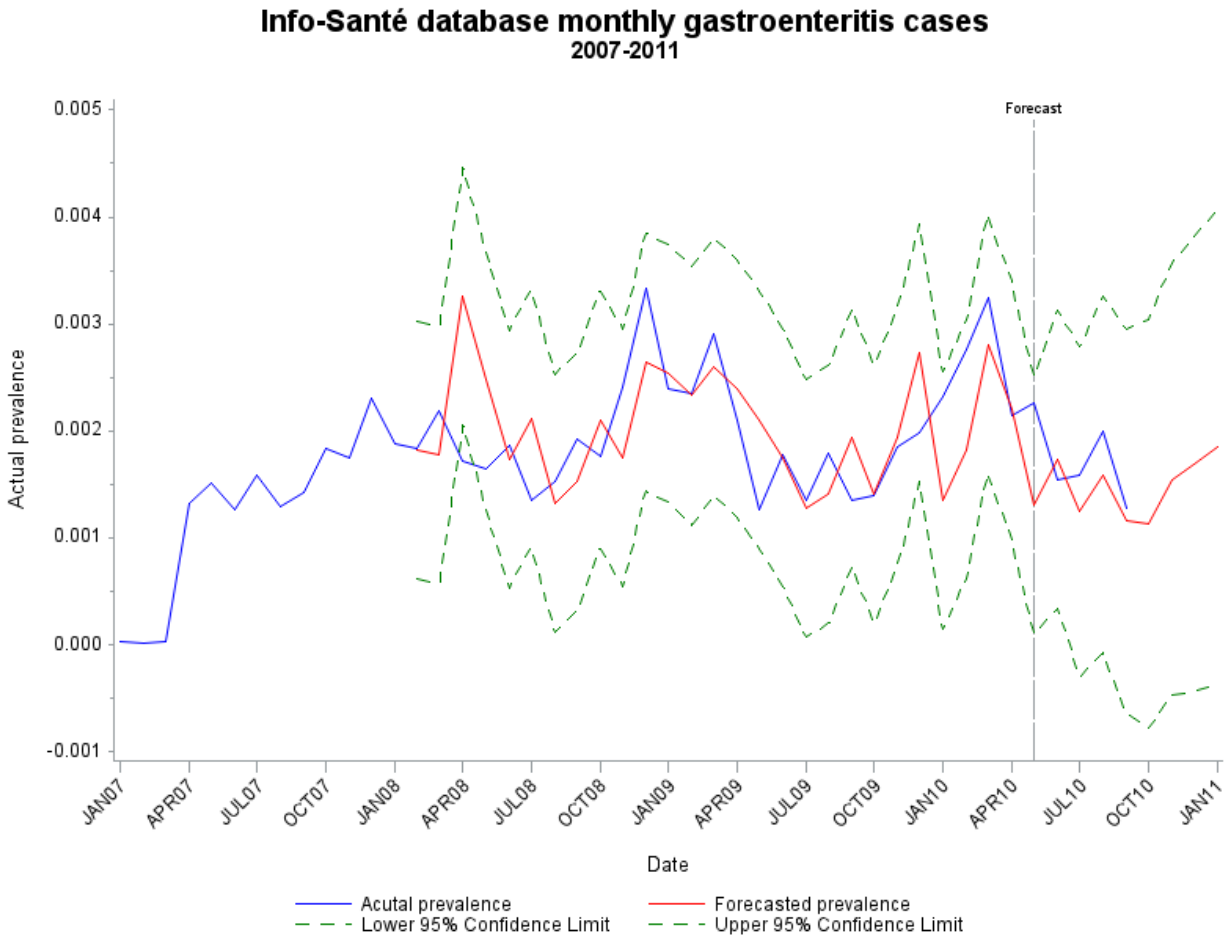

Figure 16. Forecasted monthly incidence of gastroenteritis

Chapter 5 Discussion

5.1 Main results

The mean annual IR of giardiasis from 2005-2010 for the MADO database, that is laboratory confirmed cases, is 2.20 x 10^{-2} cases per 1000 people-year. This rate is much lower than that reported IR of gastrointestinal disease identified using the Info-Santé CLSC database which reported 207.4 cases per 1 000 people-year. The corresponding probabilities of illness were 4.17×10^{-5} and 3.50×10^{-5} for the notifiable diseases database and telehealth database respectively. A significant relationship was identified using the notifiable diseases database when evaluating whether the probability of illness could successfully predict the number of cases of giardiasis within the population consuming tap water. As this relationship was inverted, QMRA use in an epidemiological context is not recommended.

Most socio-economic variables were not significant in the GAM model and were not appropriate to predict the number of *Giardia* cases within the three municipalities included in the study. Only the proportion of male and mean daily turbidity had a significant relationship with the number of laboratory confirmed cases. No particular lag time appeared to be more significant, as all 4 one week lag period resulted in a significant model. Lag time at weeks 2 and 4 had the smallest AIC value (26 982 and 26 938).

When integrated in the general additive models the probability of illness had a negative parameter estimate, suggesting that for every decrease in predicted risk there was an increase in observed risk. This could potentially be cause by the presence of unadjusted confounding variables, a lack of statistical power and incomplete databases which could not consider personal data including unknown transmission pathway. A simple analysis between the incidence-rate per 1000 people-years and the probability of illness showed a negative significant relationship for weekly estimates. Yearly estimates were positively correlated however, there were only 7 data points included in the model and therefore this needs to be interpreted with caution. For municipality A, with 4 data points there were no correlations with the predicted estimates. Both database appeared to have significant auto-correlation according to the Durbin-Watson value and consequently ARIMA models were

explored. There appeared to be a need to differentiate the data and adjust for lag at time 5 for giardiasis and time 1 for telehealth data (weeks). Models corrected for seasonal also appeared to be better adjusted to explain the distribution of gastroenteritis in a temporal fashion.

5.2 Study's advantages and limits

This study evaluated the association between probability of illness and risk of disease on a narrower timescale than the usual annual frame and using existing databases compares to works that had been previously done (Eisenberg et al., 2006; Enger et al., 2012; Mara et al., 2007). Limits of the risk predicted by the QMRA model will be elaborated in section 6.3.1. The method is not without precedent as it has been previously used to evaluate turbidity in relation to gastrointestinal illness (Beaudeau et al., 2008; Gilbert, 2004; Lim et al., 2002; Schwartz et al., 1997). GAMs have indeed been used to determine the effectiveness of different parameters in explaining the association between cases of gastroenteritis and explanatory value. Statistical models are often determined for fit using AIC to identify whether a statistical model is desirable (Interagency Microbiological Risk Assessment Guideline Workgroup, 2011). Although, GAM models can be used to estimate temporal factors, an ARIMA model was preferred to evaluate the temporal association between gastroenteritis reported by Info-Santé. This has been a method utilized to evaluated gastroenteritis, mortality indicators and respiratory disorders (Abraha et al., 2009; Soebiyanto et al., 2010).

Other methodological advantages of this project include evaluating events on a narrow time scale. Generally, yearly estimates are reported (Eisenberg et al., 2006; Karavarsamis et al., 2010; Mara et al., 2007; Pintar et al., 2012), however this study deliberately evaluated the association between risk of illness and observed cases of illness on a weekly scale. This provided us with the opportunity to investigate if risk was more accurate on a smaller scale, as proposed by Signor and Ashbolt (2006). It is suggested that daily values, allowing accurate spatial distribution of parasites, chlorine variation and contact time, are more

efficient. Our yearly risk estimates were the most similar to the observed risk, with weekly and monthly risk overestimating the risk, particularly for the notifiable diseases database.

Lastly, our study's findings benefit from relying on two databases. The notifiable diseases database contains laboratory confirmed, validated giardiasis infections. This provides the study with strong specificity to identify individual infected by *Giardia*, upon which the probability of illness was constructed. The Info-Santé database, maintained by the CLSC, contributed an additional sensitivity to detect a greater number of cases (Gilbert et al., 2006). For mild symptoms such as gastroenteritis it is unlikely that people will seek medical consultation, rather, if they require wish to obtain medical information, and are aware of the service, they would call for help (Flint et al., 2004).

With regards the database use, they also have some weaknesses. The Info-Santé teleheath database is non-specific and will catalogue gastrointestinal cases even of non-infectious or waterborne origins (Ministère de la Santé et Services sociaux, 2009). As the model is based on a sole pathogen, *Giardia,* it will not properly estimate the number of cases, as there will be many viral and bacterial causes, even when disregarding constipation. The notifiable disease database underreported true burden of illness as most individuals will not seek medical consultation and not all stool samples will be suitable for analysis (Flint et al., 2004).

Other study's limits lie within the inability to consider additional individual factors within the QMRA models making. These include gender, bodyweight, occupation, genetic and acquired susceptibility, co-morbidities overall risk of specific drinking water source and transmission source (Eisenberg et al., 2005; Hynds et al., 2012; Li et al., 2009b). There are also limits regarding the exactitude of the exposure: water consumption. While this study estimate water consumption typical for the region it was impossible to confirm the precise quantity of water consumed provided by a specific WTP. The WTP of municipality B and C have a portion of the population using well water and municipality A had other WTPs distributing water throughout the region. Risk will change depending on water consumed given the dose response component of QMRA models.

Albeit, our current study did not show strong support of our weekly point estimates likely because of a lack a description of the pathogen's distribution. Risk analyses are more precise when provided with a distribution rather than point estimate. The lack of diversity in our weekly pathogen samples did not permit a suitably diverse estimation as may be needed to accurately describe the water source pathogen load (Karavarsamis et al., 2010). Additionally, genetic testing was not performed to determine whether the *Giardia* present in the water was infectious to humans; consequently, the assumed pathogenicity of the *Giardia* parasite is not definitive.

5.3 Literature comparison

Generally, our study agrees with the literature that epidemiological information does not accurately reflects estimates predict by QMRA. Our results showing an inverse relationship between the predicted risk and the observed risk may be caused by the limited information available in the pre-existing databases. While certain studies have found the Monte Carlo simulation underestimated the risk (Eisenberg et al., 2006; Soller, 2006) most other studies have found the risk tends to be overestimated (Mara et al., 2007; Rose et al., 1991b; Zmirou-Navier et al., 2006). Our studies' yearly estimates for giardiasis were twofold greater than the observed risk. Consequently, it is closer to Mara's (2007) 1 order of magnitude rather than the 12% excess risk described by Zmirou-Navier (2006) (Mara et al., 2007; Zmirou-Navier et al., 2006). The more conservative estimate of the Zmirou-Navier (2006) study is likely due to the presence of serological information allowing the greatest number of cases to be predicted. The weekly observed incident rate is greater than the predicted incidence; this may be due to a lack of distribution explored by the exponential model. As our study had only a single sample per week, we do not incorporate any notion of dispersion. This would have been possible by taking into account the yearly distribution; however the focus of the study was to understand if weekly associations were possible.

5.3.1 QMRA

QMRA models have many limitations due to uncertainty and variability of the component used to evaluate risk. The most precise QMRA model will need to describe with great accuracy the water being consumed by the population. The best estimators to understand the risk is a probably 365 daily risk estimate which allows for the most accurate distribution of risk (Signor et al., 2006).

Different models need to be considered to have more accurate risk management strategy, including hierarchical models (Schmidt et al., 2013a) and Bayesian models (Pintar et al., 2012; Schmidt et al., 2013a; Schmidt et al., 2013b). The advantage of Bayesian models as oppose to discrete models, with probability distributions or the Monte-Carlo method, are their ability to integrate feedback in the various models components. Bayesian inferences can take into account joint probability distributions, which can be corrected or adjusted using a backwards reasoning easily visualised in a network graph (Greiner et al., 2013). Bayesian models would be able to, for example, take into account multi-directionality of different source of infection and describe the importance of peak events.

Other limitations of QMRA models, again which may be corrected with Bayesian models, is their ability to retrofit information. This is of particular importance when trying to identify the overall risk of a water source, including its vulnerably to fluctuations in pathogen loads (Sokolova et al., 2012). However given that our model measured fecal contamination load directly at the WTP input site, knowing the main pathogenic load is important for public health purpose but will not result in modifying system changes.

If we are to use QMRA models for comparison with epidemiological data it would be wiser not to directly model the estimated risk in statistical models. Enger et al. (2012), suggested calibrating QMRA models according to the microbial risk present in the population (Enger et al., 2012). This is, to a certain extent, already done by including the quantity of water consumed and the pathogen's probability of causing illness. Albeit, as previously discussed, the Health Canada QMRA model does not take into account individual factors of the exposed population (i.e., age, immunity, comorbidites). The infectivity of the pathogen

strain may also be time-dependent. It would be interesting to include these factors in a Monte-Carlo simulation in order to obtain more precise distributions. As it stands, QMRA models are principally developed to optimize water treatment plants. The included measurement and factors integrated in QMRA models revolve around WTP performance including their ability to filter, to coagulate, to sediment and to disinfect the water. If QMRA models are to be more relevant to epidemiologic field, it seems essential to include more population data in order to better reflect the mechanics of the water consumers. A barrier, however, exist when attempting to calibrate the model, as tried by our study and Enger et al. (2012)'s study. It is very difficult to match the information provided in epidemiological studies to risk models. Enger et al. (2012) took numerous simulations and only 0.3% of the models to properly reflect the epidemiological data (Enger et al., 2012). A substantial amount of population data must be available and, a sufficient number of yearly data must be available to have sufficient power in order to apply models to generate reliable conclusions.

5.4 Future research

It would be useful to try to calibrate Health Canada QMRA directly within the risk model as opposed to attempting to calibrate the information within regression models. Proposed additions would include immunity, potentially accomplished by surveying the population for household immunity, presence of symptomatic illness, included a background presence of diarrhoeal illness not associated with infection, duration of illness, duration of immunity, duration of asymptomatic infection, and number of individuals in different age categories. These are all factors that could vary in time and could potentially be modified within a Monte Carlo simulation. Fitting age and gender specific daily water consumption is a possible method of adjustment that would improve models as done by Pintar et al. (2012). Although, the overall risk in that particular population was not affected by neither gender nor age within the 5th and 95th percentile range. This calibration will likely not be generalized for all populations and will likely need to be done according to regions as personal characteristics will change. Our current model will need to use data not included in

the model's development to be validated (Interagency Microbiological Risk Assessment Guideline Workgroup, 2011).

Conclusion

This project aimed to evaluate the validity of QMRA models in an epidemiological context. The predicted probability of illness was generated to determine the risk associated with *Giardia* cysts concentration found in the water of three municipalities in Quebec. The notifiable diseases database and the Info-Santé CLSC database were used to determine the number of reported cases of giardiasis and gastroenteritis. Generalized additive models and Spearman correlations were used to analyze and estimate the relationship between the predicted risk and the observed risk. ARIMA models were used to confirm temporal trends of gastroenteritis

Our results suggest that while there is a significant relationship between the probability of illness and giardiasis, it is not sufficiently precise to confirm QMRA models validation. The relationship is negative, indicating that an increase in probability of illness estimated by QMRA is associated with a decrease in incidence of giardiasis in the target population. The Spearman correlations were also negative. These findings are impractical from a public health perspective. The seasonal peaks, confirmed by ARIMA models, were overestimated by the probability of illness.

Nonetheless, QMRA models remain an important tool for regulating water treatment plant performance and setting benchmarks for drinking water regulations. The risk tends to overestimate the actual burden of disease encouraging a conservative approach to drinking water safety. For QMRA tool to be efficiently used in a public health or epidemiological context they will need to include more individual risk factors of the study population and more precise physico-chemical information of the treated water. As QMRA models currently stand, they are best used for their current prescribed purpose of optimizing water treatment plants.

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Appendices

Appendix A. Autorisation from the Comité d'éthique de la recherche de l'Université Laval

UNIVERSITÉ LAVAL

Vice-rectorat à la recherche et à la création
Comité d'éthique de la recherche

APPROBATION DE L'ÉTHIQUE

Projet de recherche impliquant des êtres humains ou
la consultation de renseignements personnels

Ce projet de recherche a été examiné en conformité avec les
Modalités de gestion de l'éthique de la recherche sur des êtres humains de l'Université Laval,
par le Comité sectoriel d'éthique de la recherche sciences de la santé

Projet intitulé :	*Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par six usines de traitement d'eau au Québec*
Nom du chercheur :	Madame Michèle Shemilt
Nom du directeur de recherche :	Monsieur Patrick Levallois
Numéro d'approbation :	2010-304 / 19-01-2011
Date de décision :	19 janvier 2011
Date d'expiration de l'approbation :	1er février 2012

Après examen des informations et des documents qui lui ont été transmis, le Comité a constaté que ce projet respecte les principes d'éthique de la recherche avec des êtres humains. Il prend acte de la confirmation écrite de la chercheure à l'effet qu'elle a pris connaissance des mesures de suivi[1] associées à l'émission de l'approbation éthique de son projet et qu'elle accepte de les appliquer. Par conséquent, le Comité approuve ce projet pour un an.

Mahmoud Rouabhia, président
Comité d'éthique de la recherche en sciences de la santé

Date

[1] Rappel des mesures de suivi au verso

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UNIVERSITÉ LAVAL

Vice-rectorat à la recherche et à la création
Comité d'éthique de la recherche

Québec, le 13 janvier 2012

Madame Michèle Shemilt
(Directeur : monsieur Patrick Levallois)
2087, rue du Parc-Gomin
Québec (Québec) G1T 1A6

Objet : Projet de recherche intitulé : Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec
(Numéro d'approbation : 2010 - 304 A-1 R-1/ 16-01-2012)

Madame,

Le Comité d'éthique de la recherche en sciences de la santé a pris connaissance de votre demande de renouvellement au projet cité en objet. Après étude, le Comité constate le bon déroulement du projet. Il a pris connaissance également de votre demande d'amendement et vous remercie des précisions et des documents fournis. Il comprend que cet amendement consiste à ajouter ou modifier certaines variables à l'étude, à réduire la taille de l'échantillon ainsi que la période d'étude. Après étude, le Comité approuve l'amendement et il renouvelle le projet jusqu'au 1er février 2013.

Au nom du Comité, je vous remercie d'avoir soumis votre demande d'approbation d'amendement et de renouvellement à son attention. Je vous souhaite le plus grand succès dans la poursuite de vos travaux de recherche et je vous prie d'accepter, Madame, mes salutations distinguées.

[redacted]

Mahmoud Rouabhia, président
Comité d'éthique de la recherche en sciences de la santé

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....2

UNIVERSITÉ LAVAL

Vice-rectorat à la recherche et à la création
Comité d'éthique de la recherche

Québec, le 21 janvier 2013

Madame Michèle Shemilt
2087, rue du Parc-Gomin
Sillery (Québec) G1T 1A6

Objet : Projet de recherche intitulé : Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec
(Numéro d'approbation : 2010-304 R-2 / 21-01-2013)

Madame,

Le Comité d'éthique de la recherche en sciences de la santé a pris connaissance de votre demande de renouvellement de l'approbation éthique pour le projet cité en objet et du rapport d'étape qui l'accompagne. Le Comité prend acte que ce projet utilise des bases de données secondaires déjà existantes et que vous avez obtenu les approbations des Directions de santé qui seront sollicitées pour cette étude. Après étude, le Comité constate que le projet se déroule tel qu'approuvé. Par conséquent, il **approuve le renouvellement** de l'approbation éthique de ce projet pour une période d'un an, soit **jusqu'au 1er février 2014.**

Au nom du Comité, je vous remercie d'avoir soumis cette demande de renouvellement à son attention. De plus, je vous souhaite le plus grand succès dans la poursuite de vos travaux de recherche et je vous prie d'accepter, Madame, mes salutations distinguées.

[redacted]

Mahmoud Rouabhia, président
Comité d'éthique de la recherche en sciences de la santé

c.c. Monsieur Patrick Levallois, directeur de recherche

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[redacted]

UNIVERSITÉ LAVAL

Vice-rectorat à la recherche et à la création
Comité d'éthique de la recherche

Québec, le 22 janvier 2014

Madame Michèle Shemilt
5-2126, Benoît XV
Québec (Québec) G1L 3A2

Objet : Projet de recherche intitulé : Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec
(Numéro d'approbation : 2010-304 R-3 / 22-01-2014)

Madame,

Le Comité d'éthique de la recherche en sciences de la santé a pris connaissance de votre demande de renouvellement de l'approbation éthique pour le projet cité en objet et du rapport d'étape qui l'accompagne. Le Comité prend acte que cette demande a pour but de maintenir l'autorisation d'entreprendre des analyses selon les modifications ou précisions requises. Après étude, le Comité constate que le projet se déroule tel qu'approuvé. Par conséquent, il **approuve le renouvellement** de l'approbation éthique de ce projet **jusqu'au 1er février 2015,** date anniversaire de l'approbation initiale.

Au nom du Comité, je vous remercie d'avoir soumis cette demande de renouvellement à son attention. De plus, je vous souhaite le plus grand succès dans la poursuite de vos travaux de recherche et je vous prie d'accepter, Madame, mes salutations distinguées.

[redacted]

Mahmoud Rouabhia, président
Comité d'éthique de la recherche en sciences de la santé

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Appendix B. Autorisation from the Table de concertation nationale en maladies infectieuses

RE : Projet de recherche Giardiase - demande accès MADO

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À : Michèle Shemilt
Cc : Joane.Desilets.reg14@ssss.gouv.qc.ca; Helene_Dupont@ssss.gouv.qc.ca
Pièces jointes : pic26153._____); _____)[Ouvrir sous forme de page Web]; Protocole IAF MSHEMILT 190~_____)[Ouvrir sous forme de page Web]; _____)[Ouvrir sous forme de page Web];

Bonjour Mme Shemilt,

Après consultation des régions interpellées, je joins leur réponse à mon courriel.
Vous constaterez que 3 des 4 régions acceptent de collaborer à votre projet de recherche.
Toutefois, avant de donner leur autorisation officielle via leur directeur, nous souhaitons voir le rapport d'un comité d'éthique.
Une fois cette étape franchie, je vous ferai suivre une lettre type que vous pourrez adapter à votre projet et que je pourrai faire suivre aux directeurs de santé publique.

J'attend donc de vos nouvelles...

Marie-Josée Archetto, B. Sc inf.
Professionnelle en soutien à la TCNMI
Table de concertation nationale en maladies infectieuses (TCNMI)

Direction de santé publique de la Montérégie
1255 Beauregard
Longueuil, Qc, J4K 2M3
Tél: 450 928-6777 poste 3164
Téléc.: 450 928-3023
courriel: mj.archetto@rrsss16.gouv.qc.ca

04 Mauricie -Centre du Québec : Après avoir revu le protocole et en avoir discuté, la Région Mauricie et Centre du Québec est d'accord avec la pertinence du projet ainsi que pour y participer selon le protocole reçu et à la condition que le projet soit soutenu par un comité d'éthique. **Fernand Guillemette**

06 Montréal: Voici les commentaires de Dr Robert Allard au sujet de la demande de Mme Shemilt:

"Après avoir lu le protocole, je pense qu'il s'agit d'un projet dont la valeur scientifique est suffisante pour qu'il mérite d'être soumis à un comité d'éthique de la recherche et pour que les DSP y participent selon les modalités qui seront déterminées par le comité."

Par conséquent, nous jugeons ce projet recevable et y collaborerons selon les modalités qui seront établies .**Louise Valiquette,**

13 Laval: Après discussion, nous avons décidé **de ne pas participer** à cette étude et refuser le transfert des données du registre MADO de la région de Laval. **Alejandra Irace-Cima**

15 Laurentides: Tel que demandé, nous avons pris connaissance de la demande du projet cité en titre.

Nous considérons cette demande recevable. Les données demandées en lien avec le fichier MADO sont non nominales à l'exception du code postal (qui peut être considéré comme une donnée nominale même à trois caractères).

Cependant, il est important de souligner que le nombre de cas de giardiase rapportés dans la région des Laurentides pour les municipalités visées par l'étude est relativement faible pour permettre des analyses statistiques avancées (8 à 14 cas par année, répartis dans 7 municipalités).

Nous sommes néanmoins prêt à mettre à la disposition des chercheurs les données non nominales des cas de giardiase saisis au registre MADO pour la MRC demandée, en autant que le projet soit accepté par un comité d'éthique.

Nous apprécierions être informé en temps opportun des conclusions de ce projet de recherche en lien avec les cas signalés dans la région des Laurentides.

Appendix C. Autorisation from the Departement de santé publique

Agence de la santé
et des services sociaux
de Montréal
Québec
Direction de santé publique

Le 25 mai 2011

Madame Michèle Shemilt
Unité de Recherche en Santé Public du CHUQ
2875 boulevard Laurier
Québec (Québec) G1V 2M2

Objet : Autorisation d'extraction des données MADO régionales

Madame Shemilt,

Par la présente, nous autorisons l'extraction des données MADO pour la région socio-sanitaire 06 pour votre projet intitulé « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par six usines de traitement d'eau au Québec ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de part sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard le 30 novembre 2012.

Nous vous souhaitons la meilleure des chances dans la réalisation de votre projet.

Je vous prie d'agréer, Madame, l'expression de mes sentiments distingués.

La directrice adjointe de santé publique,

[redacted]

Terry-Nan Tannenbaum

TNT/jn

GARDER notre monde ENSANTÉ
1301, rue Sherbrooke Est
Montréal (Québec) H2L 1M3
Téléphone : 514 528-2400
www.santepub-mtl.qc.ca

Agence de la santé
et des services sociaux
de Montréal
Québec
Direction de santé publique

Le 3 décembre 2012

Madame Michèle Shemilt
Unité de Recherche en Santé Publique du CHUQ
2875, boulevard Laurier
Québec (Québec) G1V 2M2

Objet : Renouvellement des autorisations d'extraction des données MADO régionales

Madame Shemilt,

Par la présente, nous renouvelons l'autorisation d'extraction des données MADO pour la région socio-sanitaire ci-dessous indiquée pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard en 31 décembre 2013.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Veuillez agréer nos salutations distinguées.

Le directeur de santé publique,

[redacted]

Richard Massé, M.D.

GARDER notre monde ENSANTÉ

1301, rue Sherbrooke Est
Montréal (Québec) H2L 1M3
Téléphone : 514 528-2400
www.santepub-mtl.qc.ca

Agence de la santé
et des services sociaux
de Montréal
Québec
Direction de santé publique

Le 7 novembre 2013

Madame Michèle Shemilt
Axe Santé des populations et pratiques optimales en santé
Centre de recherche, CHU de Québec
2875 boulevard Laurier
Édifice Delta II, 6e étage, bureau 600
Québec G1V 2M2

Objet : Renouvellement des autorisations d'extraction des données MADO pour la région 06 (Montréal)

Madame Shemilt,

Par la présente, nous renouvelons l'autorisation d'extraction des données MADO pour la région socio-sanitaire mentionnée en objet **jusqu'au 1er février 2014** pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ». **L'accès aux données au-delà de cette date, soit jusqu'au 31 décembre 2014, vous sera autorisée après réception de l'approbation du comité d'éthique.**

Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard le 31 décembre 2014.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Veuillez agréer nos salutations distinguées.

Le directeur de santé publique,

[redacted]

Richard Massé, M.D.

GARDER notre monde ENSANTÉ
1301, rue Sherbrooke Est
Montréal (Québec) H2L 1M3
Téléphone : 514 528-2400
www.santepub-mtl.qc.ca

Agence de la santé
et des services sociaux
de Montréal
Québec

Direction de santé publique

Le 7 mai 2014

Madame Michèle Shemilt
Axe Santé des populations et pratiques optimales en santé
Centre de recherche, CHU de Québec
2875, boulevard Laurier
Édifice Delta II, 6e étage, bureau 600
Québec (Québec) G1V 2M2

Objet : Renouvellement des autorisations d'extraction des données MADO pour la région 06 (Montréal)

Madame,

Par la présente, nous renouvelons l'autorisation d'extraction des données MADO pour la région socio-sanitaire mentionnée en objet **jusqu'au 1er février 2015** pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ».

Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard le 31 décembre 2015.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Veuillez agréer nos salutations distinguées.

Le directeur de santé publique,

[redacted]

Richard Massé, M.D.

RM/jd

vivre
une île
en santé

1301, rue Sherbrooke Est
Montréal (Québec) H2L 1M3
Téléphone : 514 528-2400
www.santemontreal.qc.ca

Agence de la santé et des services sociaux des Laurentides
Québec
Direction de santé publique

Saint-Jérôme, le 10 mai 2011

Mme Michèle Shemilt
Unité de recherche en santé publique du CHUQ
2875, boulevard Laurier
Québec, Qc G1V 2M2

Objet : Autorisation d'extraction des données MADO régionales

Madame,

Par la présente, nous autorisons l'extraction des données MADO pour la région socio-sanitaire 15-Laurentides pour votre projet intitulé « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par six usines de traitement d'eau au Québec ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de part sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard le 30 novembre 2012.

Nous vous souhaitons la meilleure des chances dans la réalisation de votre projet et vous prions d'agréer, Madame, nos salutations distinguées.

Le directeur de santé publique par intérim,

[redacted]
Eric Goyer, M.D. M.Sc., C.S.P.Q

EG/dc

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1000, rue Labelle, bureau 210
Saint-Jérôme (Québec) J7Z 5N6
Téléphone : (450) 436-8622
Télécopieur : (450) 436-1761
www.rrsss15.gouv.qc.ca

Agence de la santé
et des services sociaux
des Laurentides
Québec
Direction de santé publique

Saint-Jérôme, le 22 novembre 2012

Mme Michèle Shemilt
Unité de recherche en Santé publique du CHUQ
2875, boulevard Laurier
Québec, Qc G1V 2M2

Objet : Renouvellement de l'autorisation d'extraction des données MADO pour la région sociosanitaire 15-Laurentides

Madame,

Par la présente, la Direction de santé publique (DSP) renouvelle, jusqu'au 31 décembre 2013, l'autorisation d'extraction des données MADO pour la région sociosanitaire mentionnée ci-haut pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ». La DSP considère que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

J'aimerais profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et je vous demande de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard le 31 décembre 2013.

Je vous souhaite la meilleure des chances dans la continuation de votre projet.

Veuillez agréer, Madame, mes salutations distinguées,

Le directeur de santé publique,

[redacted]
Eric Goyer, M.D., M. Sc., FRCPC

EG/dc

m:\8215 mado\corresp\2012\renouvellement autorisation extraction données mado_2012-11-14.docx

1000, rue Labelle, bureau 210
Saint-Jérôme (Québec) J7Z 5N6
Téléphone : (450) 436-8622
Télécopieur : (450) 436-1761
www.rrsss15.gouv.qc.ca

Agence de la santé et des services sociaux des Laurentides
Québec

Direction de santé publique

Saint-Jérôme, le 28 octobre 2013

Madame Michèle Shemilt
Axe Santé des populations et pratiques optimales en santé
Centre de recherche, CHU de Québec
2875, boulevard Laurier
Édifice Delta II, 6e étage, bureau 600
Québec (Qc) G1V 2M2

Objet : Renouvellement des autorisations d'extraction des données MADO régionales pour la région sociosanitaire 15-Laurentides

Madame,

Par la présente, nous renouvelons l'autorisons l'extraction des données MADO pour la région socio-sanitaire ci-dessous indiquée pour votre projet intitulé « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de part sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard en 31 décembre 2014.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Veuillez agréer, Madame, nos salutations distinguées,

Le directeur de santé publique,

[redacted]

Eric Goyer, M.D., M. Sc., FRCPC

EG/sn

1000, rue Labelle, bur. 210
Saint-Jérôme (Québec) J7Z 5N6
Téléphone : (450) 436-8622
Télécopieur : (450) 436-1761
www.santelaurentides.qc.ca

Michèle Shemilt
Unité de Recherche en Santé Public du CHUQ
2875 boulevard Laurier,
Québec, Qc
G1V 2M2

Objet : Autorisation d'extraction des données MADO régionales

Mme Michèle Shemilt

Par la présente, nous autorisons l'extraction des données MADO pour les régions socio-sanitaires ci-dessous indiquée pour votre projet intitulé « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par six usines de traitement d'eau au Québec ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de part sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard en30 Novembre 2012.

Nous vous souhaitons la meilleure des chances dans la réalisation de votre projet.

Veuillez agréer nos salutations distinguées,

[redacted]

Signature du directeur de santé publique

Gilles W. Gagnier

Nom du directeur de santé publique

04

Région socio-sanitaire

13/05/2011

Date

Agence de la santé et des services sociaux de la Mauricie et du Centre-du-Québec
Québec
Direction de santé publique

Le 20 novembre 2012

Madame Michèle Shemilt
Unité de Recherche en Santé Publique du CHUQ
2875, boulevard Laurier
Québec, Qc G1V 2M2

Objet : Renouvellement des autorisation d'extraction des données MADO régionales

Madame,

Par la présente, nous renouvelons l'autorisons l'extraction des données MADO pour la région socio-sanitaire ci-dessous indiquée pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard en 31 décembre 2013.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Nous vous prions d'agréer, Madame, nos salutations distinguées.

Le directeur,

[redacted]

GWG/JF/LL

Gilles W.Grenier, M.D.
Région de la Mauricie et du Centre-du-Québec

550, rue Bonaventure
Trois-Rivières (Québec) G9A 2B5
Téléphone : 819 693-3636
Télécopieur : 819 373-1627
www.agencesss04.qc.ca

Bureau
350, rue Saint-Jean
Drummondville (Québec) J2B 5L4
Téléphone : 819 477-6221
Télécopieur : 819 477-9443

Agence de la santé et des services sociaux de la Mauricie et du Centre-du-Québec
Québec

Direction de santé publique

Le 31 octobre 2013

Madame Michèle Shemilt
Axe Santé des populations et pratiques optimales en santé
Centre de recherche, CHU de Québec
2875 boulevard Laurier
Édifice Delta II, 6e étage, bureau 600
Québec (Québec) G1V 2M2

Objet : Renouvellement des autorisation d'extraction des données MADO régionales

Madame,

Par la présente, nous renouvelons l'autorisons l'extraction des données MADO pour la région socio-sanitaire ci-dessous indiquée pour votre projet intitulé « *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec* ». Nous considérons que votre projet est pertinent pour l'atteinte de nos objectifs de santé publique, de par sa contribution à l'avancement des connaissances épidémiologiques pouvant être utiles au Québec.

Nous aimerions profiter de l'occasion pour vous rappeler vos obligations et votre engagement à protéger la confidentialité de ces données, et nous vous demandons de détruire le fichier de données, ainsi que toute copie partielle ou complète, au plus tard en 31 décembre 2014.

Nous vous souhaitons la meilleure des chances dans la continuation de votre projet.

Nous vous prions d'agréer, Madame, nos salutations distinguées.

L'adjointe médicale à la protection,

[redacted]

LMJF/LL

Linda Milette, M.D.
en remplacement du Dr Gilles W Grenier,
directeur de santé publique

550, rue Bonaventure
Trois-Rivières (Québec) G9A 2B5
Téléphone : 819 693-3636
Télécopieur : 819 373-1627
www.agencesss04.qc.ca

Bureau
350, rue Saint-Jean
Drummondville (Québec) J2B 5L4
Téléphone : 819 477-6221
Télécopieur : 819 477-9443

Appendix D. Autorisation from SOGIQUE

1. SOMMAIRE DE LA DEMANDE DE CHANGEMENT APPLICATIF

La demande consiste à obtenir des données statistiques de l'application ISW, des 5 dernières années pour une chercheure qui travaille en collaboration avec l'INSPQ.

1.1 IDENTIFICATION

Titre de la DDC :	ISW- DDC 20110209 – Étude GIARDIA	N° DDC :	20110209
N° des DDC connexes :	N/A		
Demandée par :	Michèle Shemilt [redacted]	Demandée le :	17 décembre 2010
Téléphone :	[redacted]	Poste :	
Établissement :	Université Laval [redacted]	Courriel :	michele.shemilt.1@ulaval.ca

1.2 DESCRIPTION

Description du changement :	Demande d'accès à des statistiques	Documents inclus :	Deux documents sont disponibles pour consultation et proviennent de Madame Shemilt de l'université de Laval.

Une chercheure demande l'accès à des statistiques liées au code de raison 5810 pour effectuer une étude en lien avec la concentration de GIARDIA.

Demande :
« Le modèle que nous utilisons intègre la concentration de Giardia à l'eau brute à l'entrée de six usines de traitement d'eau au Québec, et génère des probabilités de maladies spécifiques à la giardiase. L'objectif ultime est de déterminer si les probabilités de maladies générées par le modèle reflètent de façon juste l'état de santé observé au niveau de la population desservie par les usines.

Afin de pouvoir identifier les cas de gastroentérites potentiellement liés à l'eau, j'aimerais utiliser les données répertoriées dans les fichiers d'Info-Santé. Celles-ci sont de nature syndromique, représentant la seule source de données ayant des cas confirmés par des tests de laboratoire.

Je recherche les cas de giardiase correspondant au code d'Info-Santé 5810, au cours des années 2006-2010 (inclusivement) triés par les villes qui suivent :

DSP 15 (Laurentides) [redacted]
DSP 13 (Laval): MRC [redacted]
DSP 04 /17 (Mauricie et Centre Sud du Québec): [redacted]
DSP 06 (Montréal): [redacted]

1. La date de naissance : L'âge sera utilisé comme variable de contrôle dans le modèle de régression. Il est connu que l'âge est un facteur potentiellement confondant avec la giardiase en raison que les personnes à certains âges sont plus susceptibles à développer une giardiase.

2. **Date de l'appel** : La date de prélèvement permettra d'identifier les cas dans la chaîne temporelle de la survenue de giardiase.

3. Code postal: Le code postal permet à la fois de cerner géographiquement les cas dans le territoire des usines d'eau et de générer l'indice de défavorisation globale de Pampalon, ce qui permet de contrôler les variations socio-économiques de la population à l'étude.

À aucun moment, lors de la dissémination du projet, les données individuelles ou localisations seront dévoilées à des individus non-impliqués dans le projet. Seuls les chercheurs principaux auront accès aux données. Chaque individu sera assigné un numéro d'immatriculation individuel pour préserver l'anonymat. Les fichiers seront maintenus à un endroit unique sécurisé par un mot de passe. Les données seront détruites 1 an après la terminaison du projet. »

Cette demande a été approuvée par Madame Isabelle Poulin (MSSS) pour les droits d'accès aux statistiques mais à condition qu'aucune donnée nominative ne soit fournie.

Les coûts inhérents à la demande sont aux frais du demandeur soit madame Michèle Shemilt.

Justification et incidence si non réalisée :				
Aucune incidence sur ISW si cette demande n'est pas réalisée.				
Type :	Urgent ( )	Correction ( )	Amélioration fonctionnelle ( )	Amélioration technique ( )
# erreur(s) connue(s) :				
Demande de changement préautorisée ( )				

Approbation de l'implantation du changement urgent :		**Date :**	

2. ÉVALUATION PAR LE COMITÉ CONSULTATIF DES CHANGEMENTS (CAB)

Comité tenu le :		Présences :	
Demande jugée recevable :		Oui ( ) Non ( )	
Raison pour laquelle la demande est non recevable :			
Priorité proposée par le comité :			

3. ÉVALUATION ET APPROBATION DE LA DEMANDE DE CHANGEMENT PAR SOGIQUE ET LE FOURNISSEUR

3.1 SOLUTION RECOMMANDÉE

Description :	Analyser les coûts de la demande et de la faisabilité d'extraite les données demandées depuis 2006 jusqu'à 2010.
Détails	Exemple de présentation des données : (données fictives) Date RSS Terr Municip CP Groupe_age Sexe 2009-01-07 1 1081 14055 G0L 55-59 2009-01-07 1 1081 14025 J0H F 2009-01-07 1 1071 12072 G5R 1-4 M 2009-01-07 1 1021 9025 G0K 45-69 F 2009-01-07 1 1031 8005 G0J 55-59 F 2009-01-07 1 1011 10043 G5L 15-19 F Les données seront fournies sous le format Excel, une ligne par appel fait au service Info-Santé, un fichier par région et par année. Le nombre de fichiers pourraient varier selon le volume de données. Il est possible de devoir faire plusieurs fichiers pour une région et pour une année étant donné le nombre élevé d'appels.

Détails (suite)	**Code de raison d'appel** Le seul code normatif fourni sera le 5810 au cours des années (2006-2010 inclusivement) de 5 régions différentes (le tri sera fait par région et par année). Le code de raison d'appel ne figurera pas dans le fichier de données. Tous les appels ayant un code de raison 5810 sreront pris en compte, que cette raison ait été codée comme principale ou secondaire. Date **de début d'appel**: Une décision doit nous parvenir de madame Shemilt concernant l'année 2006 (plus difficile à fournir pour SOGIQUE, ce qui demande des efforts supplémentaires en temps pour obtenir les données. Madame Shemilt a confirmé par courriel que les données 2007 à 2010 seront suffisantes : Extrait du courriel du 7 mars 2011 : « Bonjour Mme ThériaultJ'ai reçu la confirmation que l'extraction des données 2007-2010 sera suffisante pour le projet. Je vous remercie infiniment pour votre patience. Bonne Journée, Michèle Shemilt » Donc les fichiers comprendront les appels dont la date de début d'appel se situe entre le 1er janvier 2007 et le 31 décembre 2010. Le format de date sera le suivant (Date-mois-jour). RSS : (Région sociosanitaire) Une sélection se fera sur la région de résidence des usagers. Seules les régions suivantes seront fournies : - Région 04 - Région 06 - Région 15 - Région 13 La région 17 demandée pour l'étude, est incluse dans les données de la région 04. Pour ce qui est de la région 06, tous les arrondissements sont inclus dans la demande. Territoire de CLSC : Le code de territoire du CLSC est affiché (code selon les fichiers M34 du MSSS) La liste M34 pour ces codes sera fournie au demandeur. Municipalité : Le code de municipalité est affiché (code selon les fichiers M34 du MSSS) La liste M34 pour ces codes sera fournie au demandeur. Code postal : Pour ce qui est du code postal, il n'y aura que les trois premières positions qui seront fournies. **Groupe d'âge** : La date de naissance ne peut pas être fournie en raison de la protection des données nominatives. Les données seront donc établies par groupe d'âge : Moins de 1 an – (1-4) – (5-9) – (10-14) – (15-19) – (20-24) – (25-29) – (30-34) – (35-39) – (40-44) – (45-49) – (50-54) – (55-59) – (60-64) – (65-69) – (70-74) – (75-79) – (80-84) – (85 et plus). Sexe Le sexe n'était pas demandé par le demandeur, mais madame Shemilt mentionne que c'est un oubli. Le sexe sera donc ajouté aux données. (M, F ou vide) Anonymes : Les données des usagers traités comme Anonyme, sont aussi demandées, et seront utilisés selon les besoins de l'étude. Il faut toutefois que la région de résidence soit identifiée comme faisant partie des régions visées. Les appels des anonymes ne fournissant aucune donnée sur leur région de résidence ne seront

ISW
F-P

Exclusions :	La notion de MRC ne sera pas traitée dans les fichiers produits.		
Recommandée par :	Jacinthe Thériault et François Maillé	Date :	2011-02-09
Composantes touchées :	Aucune composante n'est touchée par ce changement.		
Impacts et risques :	Aucun	**Évaluateur :**	Jacinthe Thériault et Véronique Dupont (Analyste)
Bénéfices :		**Évaluateur :**	

Coûts et effort :

Estimation des coûts		2011-04-08
	HRE	$
Secrétaire	1	30,00 $
Conseiller (ère)	0	0,00 $
Analyste	14	1 820,00 $
Pilote de système	2	160,00 $
Programmeur	4	520,00 $
Total	21	2 530,00 $
Niveau de complexité		3
$ ajouté selon le niveau de complexité		75,90
Heures - GRAND TOTAL	21	2 605,90 $

Estimé par :	Jacinthe Thériault	Date :	2011-02-09	Effort (heures) :	21H
Instructions de **retour à l'état initial :**	N/A				

Recommandations du gestionnaire **de l'actif** et du pilote :

Effecteur la requête suite à l'approbation des coûts.

Priorité d'implantation suggérée :	N/A
Période d'observation recommandée pour le changement implanté :	N/A

3.2 DÉCISION CONCERNANT **L'APPROBATION**

Approuvée par :		Tél. :		Date :	
Décision:	Approuvée (X)	Rejetée ( )	Reportée ( )	Autre :	
Priorité d'implantation :					
Conditions ou justifications :	Cette analyse est approuvée à condition de s'entendre sur les dates pour fournir les statistiques demandées. Un échéancier trop serré vient à l'encontre des travaux actuellement en cours par l'équipe Info-Santé Web.				
	Le demandeur devra respecter l'entente en ce qui concerne les données et les détruire 1 an après la fin du projet.				
	Les données sont requises pour le 1 avril 2011				

4. PLANIFICATION ET SUIVI DE LA DEMANDE DE CHANGEMENT (LORSQUE LE CHANGEMENT EST APPROUVÉ)

4.1 PLANIFICATION

N° de version associée :		**Date planifiée d'implantation**	
Date reportée d'implantation		N° de version associée	
Liste des principaux jalons :			
Courte description		Date de début planifiée	Date de fin planifiée
Secrétaire			
Analyste - Dossier fonctionnel P490 - Contrôle qualité - Extraction des données (16 fichiers)			
Pilote de système – P891			
Développeur			

4.2 SUIVI

Observations et commentaires :			
Auteur :		Date :	

Appendix E. Autorisation from Info-Santé CLSC

Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

CERTIFICAT DE CONFORMITÉ ÉTHIQUE

Le 15 novembre 2011

Madame Michèle Shemilt
Axe Santé des populations et environnementale
2875, boulevard Laurier, Édifice Delta II, 6e étage, bureau 600
Québec (Québec)
CANADA G1V 2M2

Objet : Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec (Madame Michèle Shemilt)

Madame Shemilt,

Le projet cité en rubrique a été évalué par le comité restreint lors de la réunion du 24 octobre 2011.

Il me fait plaisir de vous informer que le projet cité en rubrique a été approuvé, quant à sa forme et son contenu actuels. Le chercheur s'engage toutefois, comme elle en fait mention, à collecter et utiliser que des renseignements rendus anonymes (sans identifiants). Aussi, **l'autorisation de la Direction des services professionnels sera requise.** Le projet rencontre les autres critères d'importance et de mesures de sécurité pour minimiser les risques.

Liste des documents évalués et approuvés :

- Protocole (2011-09-27)
- Extraction des données 5810 Sogique (sans date)
- Courriel d'engagement du superviseur de l'étudiant (2011-11-11)
- Approbation conditionnelle du comité d'éthique dede l'Université Laval (2011-01-19) (sans signature)
- Lettre de Frédérique Paquet précisant le besoin de consentement des régions incluses dans l'étude (sans date) (sans signature)

Le Comité d'éthique vous rappelle que vous êtes responsable de la qualité scientifique de votre projet, du respect des personnes impliquées dans celui-ci ainsi que de l'utilisation correcte des ressources affectées à votre projet.

Il est entendu que vous vous engagez aux termes suivants :

1. Si, au cours du déroulement du projet, un changement relatif aux éléments suivants :
   - Méthodologie utilisée;
   - Critères d'inclusion et d'exclusion des sujets de recherche;
   - Formulaire de consentement ou tout autre document remis pour cette demande de recherche;

ou si un événement externe défavorable à l'avancement du projet et/ou si une information pouvant avoir une incidence sur le désir de participer des sujets devaient survenir au cours du déroulement du projet, le chercheur devra en aviser, dans les plus brefs délais, le Comité d'éthique de la recherche et ce, sous la forme d'un rapport d'étape.

Coalition canadienne pour un système de santé écologique

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514 934-0354

☐ CLSC DE PARC-EXTENSION
7085, rue Hutchison
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H3N 1Y9
514 273-9591

2. Afin de se conformer à une exigence du ministère de la Santé et des Services sociaux de mettre en place un mécanisme permettant de retracer les personnes qui prêtent leur concours à des activités de recherche, nous vous rappelons que vous devez maintenir une liste de sujets de recherche qui comprend notamment les informations suivantes : le nom ou système de codification en tenant lieu, les coordonnées permettant de retracer la personne, le numéro de projet et la date de début et de fin de participation. Les mesures de protection de la confidentialité s'appliqueront à cette liste.

3. Ce certificat est valide pour une période d'un (1) an à compter de la date de son émission. Un mois avant l'expiration de ce délai, le chercheur devra soit aviser le Comité d'éthique de la recherche de la fin du projet de recherche, soit soumettre une demande de renouvellement de ce certificat (voir Rapport envoyé par courriel). Les faits justifiant la fin du projet ou le renouvellement de la présente seront alors mentionnés.

4. Ce certificat d'éthique est valable dans les sites de recrutement qui font partie du CSSS de la Montagne. Pour ce qui est des autres sites, votre projet pourra procéder dès que ces sites auront effectué leur propre évaluation ou feront leur le présent certificat par une approbation administrative.

5. Avant de mettre en œuvre votre étude au CSSS de la Montagne, vous devez aviser Mme Spyridoula Xenocostas, Directrice des activités de recherche et de formation au (514) 934-0505 poste 7610 de la date du début de vos travaux de recherches.

Nous vous prions d'agréer, Madame Shemilt, l'expression de nos sentiments les meilleurs.

[redacted]

Marie Hirtle, LL.B., LL.M.,
Présidente du Comité d'éthique de la recherche

p.j. (rapport)

Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

Le 22 novembre 2011

Madame Michèle Shemilt
Axe Santé des populations en santé environnementale
2875 boulevard Laurier
Édifice Delta II, 6e étage, Bureau 600
Québec (Québec) G1V 2M2

Objet : Accès au fichier nominal du registre d'Info-santé dans le cadre de votre projet de recherche : *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec*

Madame,

Suivant l'étude de votre demande d'accès au fichier nominal du registre d'Info-santé de la région sous la responsabilité du CSSS de la Montagne, la présente vous autorise à consulter les données nécessaires au projet de recherche cité en rubrique, qui seront extraites par la SOGIQUE.

Notre autorisation est valide pour une période d'un an, soit du 22 novembre 2011 au 22 novembre 2012 et elle est conditionnelle au respect de votre engagement et à celui de votre équipe de recherche à ne collecter et n'utiliser que des renseignements rendus anonymes (sans identifiants).

Cette autorisation est donnée en vertu de l'article 19.2 de la *Loi sur les services de santé et services sociaux*, conditionnellement au respect du caractère confidentiel des renseignements obtenus, de même qu'à celui des normes éthiques et d'intégrité scientifique généralement reconnues.

Veuillez recevoir, Madame, l'expression de nos sentiments les meilleurs.

La directrice des services professionnels et médicaux,

[redacted]

Dre Vania Jimenez

c.c : Mme Suzanne Walsh, responsable de l'accès, CSSS de la Montagne
Me Marie Hirtle, présidente du Comité d'éthique de la recherche du CSSS de la Montagne
Mme Andréanne Boisjoli, agente de recherche, Centre de recherche et de formation du CSSS de la Montagne
Mme Chantal Cloutier, coordonnatrice, services des archives

Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

Le 9 janvier 2013

Renouvellement
Certificat de conformité éthique

Madame Michèle Shemilt
Axe Santé des populations et environnementale
2875, boulevard Laurier, Édifice Delta II, 6e étage, bureau 600
Québec (Québec) CANADA G1V 2M2

Objet : PE 795 - 24.10.2011 : « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec » (Madame Michèle Shemilt)

Madame Shemilt,

La demande de renouvellement de certificat d'éthique pour le projet cité en rubrique et les documents soumis ont été évalués en comité restreint le 9 janvier 2013. Nous vous remercions de nous avoir fait parvenir le complément d'information demandé. Il me fait plaisir de vous informer que le certificat de conformité éthique a été renouvelé, quant à sa forme et son contenu actuels, et sera valide du 15 novembre 2012 au 15 novembre 2013. Le chercheur s'engage, comme elle en a fait mention, à collecter et utiliser que des renseignements rendus anonymes (sans identifiants). Le projet rencontre les autres critères d'importance et de mesures de sécurité pour minimiser les risques. Aussi, **l'autorisation de la Direction des services professionnels sera requise**, et le chercheur devra demander le renouvellement de l'autorisation d'accès aux dossiers, laquelle est échue depuis le 22 novembre 2012.

Documents évalués et approuvés :

Lettre de Michèle Shemilt (2012-11-11)
Rapport et demande de renouvellement (2012-11-11)
Lettre de Mahmoud Rouabhia, président du comité d'éthique de la recherche en sciences de la santé de l'Université Laval (2012-01-13)
Lettre de Michèle Shemilt (2012-12-29)
Lettre de demande d'amendement de Michèle Shemilt (2012-01-10)
Protocole (2011-12-19)

Le Comité d'éthique vous rappelle que vous êtes responsable de la qualité scientifique de votre projet, du respect des personnes impliquées dans celui-ci ainsi que de l'utilisation correcte des ressources affectées à votre projet.

Il est entendu que vous vous engagez aux termes suivants :

1. Si, au cours du déroulement du projet, un changement relatif aux éléments suivants :
    - Méthodologie utilisée;

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- Critères d'inclusion et d'exclusion des sujets de recherche;
- Formulaire de consentement ou tout autre document remis pour cette demande de recherche;

ou si un événement externe défavorable à l'avancement du projet et/ou si une information pouvant avoir une incidence sur le désir de participer des sujets devaient survenir au cours du déroulement du projet, le chercheur devra en aviser, dans les plus brefs délais, le Comité d'éthique de la recherche et ce, sous la forme d'un rapport d'étape.

2. Afin de se conformer à une exigence du ministère de la Santé et des Services sociaux de mettre en place un mécanisme permettant de retracer les personnes qui prêtent leur concours à des activités de recherche, nous vous rappelons que vous devez maintenir une liste de sujets de recherche qui comprend notamment les informations suivantes : le nom ou système de codification en tenant lieu, les coordonnées permettant de retracer la personne, le numéro de projet et la date de début et de fin de participation. Les mesures de protection de la confidentialité s'appliqueront à cette liste.

3. Ce certificat est valide pour une période **d'un (1) an**. Un mois avant l'expiration de ce délai, le chercheur devra soit aviser le Comité d'éthique de la recherche de la fin du projet de recherche, soit soumettre une demande de renouvellement de ce certificat (voir **Rapport** envoyé par courriel). Les faits justifiant la fin du projet ou le renouvellement de la présente seront alors mentionnés.

4. Ce certificat d'éthique est valable dans les sites de recrutement qui font partie du CSSS de la Montagne. Pour ce qui est des autres sites, votre projet pourra procéder dès que ces sites auront effectué leur propre évaluation ou feront leur le présent certificat par une approbation administrative.

5. Avant de mettre en œuvre votre étude au CSSS de la Montagne, vous devez aviser Mme Spyridoula Xenocostas, Directrice des activités de recherche et de formation au (514) 934-0505 poste 7610 de la date du début de vos travaux de recherches.

Nous vous prions d'agréer, Madame Shemilt, l'expression de nos sentiments les meilleurs.

Marie Hirtle, LL.B., LL.M.,
Présidente du Comité d'éthique de la recherche

P.j. Rapport

Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

Le 13 février 2013

ENVOI PAR COURRIER ÉLECTRONIQUE

Madame Michèle Shemilt
Axe Santé des populations en santé environnementale
2875, boulevard Laurier
Édifice Delta II, 6e étage - Bureaux 600
Québec (Québec) G1V 2M2

Objet : Renouvellement d'accès au fichier nominal du registre d'Info-santé dans le cadre de votre projet de recherche : *Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec*

Madame,

Suivant votre demande de renouvellement d'accès au fichier nominal du registre d'Info-santé de la région sous la responsabilité du CSSS de la Montagne, la présente vous autorise à consulter les données nécessaires au projet de recherche cité en rubrique, qui seront extraites par la SOGIQUE.

Notre autorisation est valide pour une période d'un an, soit du 13 février 2013 au 13 février 2014 et elle est conditionnelle au respect de votre engagement et à celui de votre équipe de recherche à ne collecter et n'utiliser que des renseignements rendus anonymes (sans identifiants).

Cette autorisation est donnée en vertu de l'article 19.2 de la *Loi sur les services de santé et services sociaux*, conditionnellement au respect du caractère confidentiel des renseignements obtenus, de même qu'à celui des normes éthiques et d'intégrité scientifique généralement reconnues.

Veuillez recevoir, Madame, l'expression de nos sentiments les meilleurs.

[redacted]
Vania Jimenez, M.D.
Directrice des services professionnels et médicaux

VJ/ll

c. c Mme Suzanne Walsh, responsable de l'accès, CSSS de la Montagne
Me Marie Hirtle, présidente du Comité d'éthique de la recherche, CSSS de la Montagne
Mme Andréanne Boisjoli, agente de recherche, Centre de recherche et de formation CSSS de la Montagne
Mme Chantal Cloutier, coordonnatrice, services des archives, CSSS de la Montagne

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Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

Le 24 octobre 2013

Renouvellement
Certificat de conformité éthique

Madame Michèle Shemilt
Axe Santé des populations et environnementale
2875, boulevard Laurier, Édifice Delta II, 6e étage, bureau 600
Québec (Québec) CANADA G1V 2M2

Objet : PE 795 - 24.10.2011 : « Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec » (Madame Michèle Shemilt)

Madame Shemilt,

La demande de renouvellement de certificat d'éthique pour le projet cité en rubrique et les documents soumis ont été évalués en comité restreint le 24 octobre 2013. Il me fait plaisir de vous informer que le certificat de conformité éthique a été renouvelé, quant à sa forme et son contenu actuels, et sera valide du 15 novembre 2013 au 15 novembre 2014. Le chercheur s'engage, comme elle en a fait mention, à collecter et utiliser que des renseignements rendus anonymes (sans identifiants). Le projet rencontre les autres critères d'importance et de mesures de sécurité pour minimiser les risques. Aussi, le chercheur pourra demander le renouvellement de l'autorisation d'accès aux dossiers avant qu'elle ne vienne à échéance le 13 février 2014. Le formulaire de demande d'accès est en pièce jointe.

Documents évalués et approuvés :

Courriel de Michèle Shemilt (2013-10-24)
Rapport de suivi et demande de renouvellement (2013-10-17)
Renouvellement de l'approbation éthique du Comité d'éthique de la recherche en sciences de la santé de l'Université Laval [jusqu'au 1er février 2014](2013-01-21)
Protocole (2011-12-19)
Analyse utilisé pour le projet PE 795 24.10.2011 (sans date)

Le Comité d'éthique vous rappelle que vous êtes responsable de la qualité scientifique de votre projet, du respect des personnes impliquées dans celui-ci ainsi que de l'utilisation correcte des ressources affectées à votre projet.

Il est entendu que vous vous engagez aux termes suivants :

1. Si, au cours du déroulement du projet, un changement relatif aux éléments suivants :

   Méthodologie utilisée;
   Critères d'inclusion et d'exclusion des sujets de recherche;
   Formulaire de consentement ou tout autre document remis pour cette demande de recherche;

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ou si un événement externe défavorable à l'avancement du projet et/ou si une information pouvant avoir une incidence sur le désir de participer des sujets devaient survenir au cours du déroulement du projet, le chercheur devra en aviser, dans les plus brefs délais, le Comité d'éthique de la recherche et ce, sous la forme d'un rapport d'étape.

2. Afin de se conformer à une exigence du ministère de la Santé et des Services sociaux de mettre en place un mécanisme permettant de retracer les personnes qui prêtent leur concours à des activités de recherche, nous vous rappelons que vous devez maintenir une liste de sujets de recherche qui comprend notamment les informations suivantes : le nom ou système de codification en tenant lieu, les coordonnées permettant de retracer la personne, le numéro de projet et la date de début et de fin de participation. Les mesures de protection de la confidentialité s'appliqueront à cette liste.

3. Ce certificat est valide pour une période d'un (1) an. Un mois avant l'expiration de ce délai, le chercheur devra soit aviser le Comité d'éthique de la recherche de la fin du projet de recherche, soit soumettre une demande de renouvellement de ce certificat (voir Rapport envoyé par courriel). Les faits justifiant la fin du projet ou le renouvellement de la présente seront alors mentionnés.

4. Ce certificat d'éthique est valable dans les sites de recrutement qui font partie du CSSS de la Montagne. Pour ce qui est des autres sites, votre projet pourra procéder dès que ces sites auront effectué leur propre évaluation ou feront leur le présent certificat par une approbation administrative.

5. Avant de mettre en œuvre votre étude au CSSS de la Montagne, vous devez aviser Mme Spyridoula Xenocostas, Directrice des activités de recherche et de formation au (514) 934-0505 poste 7610 de la date du début de vos travaux de recherches.

Nous vous prions d'agréer, Madame Shemilt, l'expression de nos sentiments les meilleurs.

Marie Hirtle, LL.B., LL.M.,
Présidente du Comité d'éthique de la recherche

P.j. Rapport de suivi
Demande d'autorisation d'accès aux banques de données et aux dossiers cliniques (et demande de renouvellement)

Centre de santé et de services sociaux
de la Montagne

Centre affilié universitaire

Le 14 février 2014

Madame Michèle Shemilt
Axe Santé des populations et environnementale
2875, boulevard Laurier, Édifice Delta II, 6e étage, bureau 600
Québec (Québec) CANADA G1V 2M2

Objet : Renouvellement d'accès au fichier nominal du registre d'Info-santé dans le cadre de votre projet de recherche PE 795 - 24.10.2011 : ***Évaluation de la validité des modèles de risque pour prédire l'incidence de giardiase et de gastroentérites d'origine hydrique dans une population desservie par trois usines de traitement d'eau au Québec***

Madame,

Suivant votre demande de renouvellement d'accès au fichier nominal du registre d'Info-santé de la région sous la responsabilité du CSSS de la Montagne, la présente vous autorise à consulter les données nécessaires au projet de recherche cité en rubrique.

Notre autorisation est valide pour une période d'un an, soit du 13 février 2014 au 13 février 2015 et elle est conditionnelle au respect de votre engagement et à celui de votre équipe de recherche à ne collecter et n'utiliser que des renseignements rendus anonymes (sans identifiants).

Cette autorisation est donnée en vertu de l'article 19.2 de la *Loi sur les services de santé et services sociaux*, conditionnellement au respect du caractère confidentiel des renseignements obtenus, de même qu'à celui des normes éthiques et d'intégrité scientifique généralement reconnues.

Veuillez recevoir, Madame, l'expression de nos sentiments les meilleurs.

[redacted]

Vania Jimenez, M.D.
Directrice des services professionnels et médicaux

c.c : Mme Suzanne Walsh, responsable de l'accès, CSSS de la Montagne
Me Marie Hirtle, présidente du Comité d'éthique de la recherche du CSSS de la Montagne
Mme Andréanne Boisjoli, agente de recherche, Centre de recherche et de formation du CSSS de la Montagne
Mme Chantal Cloutier, coordonnatrice, services des archives

RE Demande d'autorisation d'extraction des données Info-Santé régionales
jacques_berube@ssss.gouv.qc.ca [jacques_berube@ssss.gouv.qc.ca]

Date d'envoi : 20 octobre 2011 08:36
À : Michèle Shemilt
Cc : Patrick Levallois; frederic.paquet@ssss.gouv.qc.ca
Pièces jointes : _____)[Ouvrir sous forme de page Web]; _____)[Ouvrir sous forme de page Web], _____)[Ouvrir sous forme de page Web], _____-_____)[Ouvrir sous forme de page Web]

Bonjour Mme Shemilt,

Demande d'autorisation d'extraction des données Info-Santé régionales,

Demande acceptée pour le service régional Info-Santé et Info-social des Laurentides, région 15.

Jacques Bérubé
Coordonnateur
Service régional Info-Santé et Info-Social des Laurentides
Tél: 450-420-4170 #2202
www.jacques_beurbe@ssss.gouv.qc.ca

RE : RE Demande d'autorisation d'extraction des données Info-Santé régionales

jacques_berube@ssss.gouv.qc.ca [jacques_berube@ssss.gouv.qc.ca]

Date d'envoi : 13 novembre 2012 09:37

À : Michèle Shemilt

Pièces jointes : ❑ (3)

[Ouvrir sous forme de page Web]

Bonjour Mme Shemilt,

Demande d'autorisation d'extraction des données Info-Santé régionales,

Demande acceptée pour le service régional Info-Santé et
Info-social des Laurentides, région 15.

Jacques Bérubé
Coordonnateur

Service régional Info-Santé et Info-Social des Laurentides

Tél : 450-420-4170 # 2202

Courriel : jacques_berube@ssss.gouv.qc.ca

RE : RE : RE Demande d'autorisation d'extraction des données Info-Santé régionales

jacques_berube@ssss.gouv.qc.ca [jacques_berube@ssss.gouv.qc.ca]

Date d'envoi : 24 octobre 2013 08:10
À : Michèle Shemilt
Cc : Anne-Marie.Larose.tdb@ssss.gouv.qc.ca
Pièces jointes :)[Ouvrir sous forme de page Web]

Bonjour Mme Shemilt,j'asume présentement un intérim à direction des services aux adultes et des services généraux. Le service Info-santé est dans la même direction. J'autorise donc l'extraction des données Info-Santé régionales des Laurentides, pour les raisons d'appels mentionnées dans votre courreil. Je mets en copie conforme Mme Anne-Marie Larose qui est présentement à l'intérim comme coordonnatrice du service régional.

Jacques Bérubé
Directeur Intérim
Direction des services aux adultes et des services généraux
CSSS Thérèse De-Blainville
125 rue Duquet,
Ste-Thérèse,QC, J7E 0A5
Tél: 450-430-4553 #5138

Centre de santé et de services sociaux
de Bécancour–Nicolet-Yamaska

Le 30 mars 2012

Madame Francine Courchesne
Directrice de la santé physique et des services diagnostiques
CSSS de Bécancour–Nicolet-Yamaska
Service régional Info-Santé Info-Social
625, avenue Godefroy, bureau 200
Bécancour (Secteur Saint-Grégoire) G9H 1S3

Objet : Demande d'autorisation

Madame,

Par la présente, j'autorise une prolongation de l'accès aux bases de données d'Info-Santé de SOGIQUE dans le cadre du projet de recherche universitaire de Mme Michèle Shemilt, étudiante à la maîtrise au Centre de recherche du CHUQ.

La loi permet effectivement que le directeur des services professionnels accorde une telle autorisation, c'est-à-dire avoir accès à des renseignements personnels contenus dans un dossier sans le consentement des personnes concernées à des fins d'étude, d'enseignement ou de recherche.

Je vous rappelle que cette autorisation est valide seulement si les critères établis par l'article 125 de la Loi sur l'accès aux documents des organismes publics et sous la protection des renseignements personnels sont satisfaits.

De plus, cette autorisation doit être limitée dans le temps. Dans ce contexte, la présente autorisation prendra fin le 31 décembre 2012.

Nous vous prions d'accepter, Madame, nos salutations les meilleures.

[redacted]
Docteur Dominique Tardif
Directeur des services professionnels

c.c. Mme France Flageol, chef d'administration de programmes du Service régional Info-Santé Info-Social

Centre Christ-Roi
675, rue Saint-Jean-Baptiste
Nicolet (Québec) J3T 1S4
www.csssbny.qc.ca

Téléphone : 819 293-2071
Télécopieur : 819 293-6160
infocsssbny@ssss.gouv.qc.ca

Centre de santé et de services sociaux
de Bécancour–Nicolet-Yamaska

Le 7 janvier 2013

Madame Francine Courchesne
Directrice de la santé physique et des services diagnostiques
CSSS de Bécancour–Nicolet-Yamaska
Service régional Info-Santé Info-Social
625, avenue Godefroy, bureau 200
Bécancour (Secteur Saint-Grégoire) G9H 1S3

Objet : Demande d'autorisation

Madame,

Par la présente, j'autorise une prolongation de l'accès aux bases de données d'Info-Santé de SOGIQUE dans le cadre du projet de recherche universitaire de Mme Michèle Shemilt, étudiante à la maîtrise au Centre de recherche du CHUQ.

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Nous vous prions d'accepter, Madame, nos salutations les meilleures.

[redacted]
Docteur Dominique Tardif
Directeur des services professionnels

c.c. Mme Annie Saint-Cyr, conseillère cadre à la Direction de la santé physique et des services diagnostiques

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Téléphone : 819 293-2071
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Centre de santé et de services sociaux
de Bécancour–Nicolet-Yamaska

Le 24 octobre 2013

Madame Francine Courchesne
Directrice de la santé physique et des services diagnostiques
CSSS de Bécancour–Nicolet-Yamaska
Service régional Info-Santé Info-Social
625, avenue Godefroy, bureau 200
Bécancour (Secteur Saint-Grégoire) G9H 1S3

Objet : Demande d'autorisation

Madame,

Par la présente, j'autorise une prolongation de l'accès aux bases de données d'Info-Santé de SOGIQUE dans le cadre du projet de recherche universitaire de Mme Michèle Shemilt, étudiante à la maîtrise au Centre de recherche du CHUQ.

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De plus, cette autorisation doit être limitée dans le temps. Dans ce contexte, la présente autorisation prendra fin le 31 décembre 2014.

Nous vous prions d'accepter, Madame, nos salutations les meilleures.

[redacted]

Docteur Dominique Tardif
Directeur des services professionnels

c.c. M. Patrick Lebel, chef d'administration de programme Service régional info-santé et info-social

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