SPATIO-TEMPORAL ANALYSIS OF *CHLAMYDIA TRACHOMATIS* IN NEWFOUNDLAND AND LABRADOR AND AN EXPLORATORY ANALYSIS INTO EMPLOYMENT TRAITS AS RISK FACTORS

by

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ABSTRACT

Sexually transmitted infections are an important health concern in Canadian society due to their negative impact on sexual and reproductive health, as well as their social and fiscal ramifications. *Chlamydia trachomatis* is the most common reported sexually transmitted infection in Canada and has been consistently on the rise since 1997. The province of Newfoundland and Labrador routinely publishes case counts of infectious diseases, including chlamydia, but there is minimal examination into age, sex, the regional distributions of cases, the etiology of these infections, or what populations are most at risk. There is also little information on the role of migratory employment in infectious disease risk in Canada. The spatial and temporal distribution of chlamydia in Newfoundland and Labrador between 2007 and 2013 was examined, in addition to an exploration into migratory employment as a contributory cause. Case data were obtained from the Regional Health Authorities and population information from Statistics Canada. Differences in incidence rates for age, sex, and geography were evaluated over time. A linear increase in incidence occurred over the study period. Distinct areas of high incidence were observed and spatial clusters were identified in northern Labrador and St. John's. Using the 2006 Census of Population and 2011 National Household Survey, associations between work-related commuting demographics and chlamydia incidence were found in the province. Understanding the distribution of chlamydia as well as the behaviours of migratory workers can help direct health policy to prevent chlamydial and other infections from occurring, and improve overall sexual health practices of Canadians.

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LIST OF ABBREVIATIONS AND SYMBOLS

CA:	Census Agglomeration
CANSIM:	Canadian Socio-economic Information Management System
CD:	Census Division
CDC:	Centers for Disease Control
CMA:	Census Metropolitan Area
CNDSS:	Canadian Notifiable Disease Surveillance System
CSD:	Census Subdivision
CSDUID:	Census Subdivision Unique Identification Number
ELISA:	Enzyme Linked Immunosorbent Assay
ESRI:	Environmental Systems Research Institute
HIV:	Human Immunodeficiency Virus
LGBTQ:	Lesbian-Gay-Bisexual-Transsexual-Queer
MAUP:	Modifiable Area Unit Problem
MIZ:	Metropolitan Influenced Zone
n:	Number (count)
NAAT:	Nucleic Acid Amplification Test
NAD27:	North American Datum of 1927
NAICSECF:	Labour Market Activities: Industry Sectors (2006 acronym)
NAICS07:	Labour Market Activities: Industry Sectors (2011 acronym)

NHS:	National Household Survey
NL:	Newfoundland and Labrador
p:	Probability
PHAC:	Public Health Agency of Canada
PWCOMMUT:	Place of Work Type of Commuting
PWPR:	Province of Employment
R^2:	Coefficient of Determination
SACTYPE:	Statistical Area Classification
SES:	Socioeconomic Status
SMR:	Standard Morbidity Ratio
STI:	Sexually Transmitted Infection
χ^2:	Chi-squared

CHAPTER 1

INTRODUCTION & PROJECT SUMMARY

General Overview

Infection with sexually transmitted pathogens can cause numerous localized and systemic diseases in both men and women (PHAC, 2008). Infected individuals may have a reduced quality of life through personal anxiety and shame, social stigma, and reduced treatment seeking behaviours (Delva, 1983). Sexually transmitted infections (STIs) increase the burden on the health system due to treatment and complications arising from infection (Goeree & Gully, 1993). The annual costs of treating STIs in Canada are in the millions of dollars (Smylie et al., 2011). These include costs due to drug treatments, primary outpatient care, community monitoring and individual patient out-of-pocket expenditures.

Chalmydia trachomatis is a species of parasitic bacteria that causes infections in humans through sexual contact (Ryan & Ray, 2004). Symptoms of infection include urethral itch, genital discharge, and pelvic pain (McCatchan, 2009). Infection is asymptomatic in more than 60 percent of cases, leaving the potential for major complications for untreated cases as well as increased costs (Peipert, 2003; Tuite et al., 2012). Long term risks of infection can include a variety of sex-specific reproductive and urinary tract diseases and infertility (Macdonald & Wong, 2007). Chlamydial infections are the most commonly reported STI in Canada; accounting for more than 75 percent of reported STI cases (PHAC, 2008). Additionally, the incidence is rising nationally, with an increase of 80 percent between 1998 and 2008 (PHAC, 2010b). This places an increasing burden on the health system due to the direct cost of treatment as well as physiological complications of untreated infections (CDC, 2011; Tuite et al., 2012). There is also a

psychosocial burden on the individual due to the stigma associated with infection (Cunningham et al, 2002).

Rationale of the Study

There is a lack of detailed information in the published literature on rates of STIs in Newfoundland and Labrador (NL). STI incidence, including *Chlamydia* infections, continues to increase in the province with little explanation to etiology or what populations are most at risk (Newfoundland and Labrador Department of Health and Community Services, 2012). Regional Health Authorities (RHAs) release periodic case count information and/or crude incidence on communicable diseases but no further investigation in regional differences or demographic stratification of incidence have been published. The objective of this study is to examine the spatial and temporal distribution of *Chlamydia trachomatis* infections in NL from 2007 to 2013 and examine the role of employment related migration as a potential risk factor for infection. This research gives comprehensive information for policy makers in prioritizing what geographical areas are most in need of chlamydia prevention and intervention, as well as provide new hypotheses for potential risk factors for *Chlamydia trachomatis* infections in the province.

Project Questions

The three questions that this project sought to answer are:

1) What are the incidence rates and temporal trends of *Chlamydia trachomatis* incidence in NL, overall and for subpopulations grouped by age and sex, between January 1st, 2007 and December 31st, 2013? The null hypotheses that are tested include:

a) There are no differences in chlamydia incidence for the overall population in each year of the study period and the incidence does not exhibit seasonal trends.

b) There are no differences in chlamydia incidence with respect to age and sex in each year of the study period and there is no interaction between age and sex.

The unit of analysis for this question is the overall province of NL.

2) What is the spatial distribution of *Chlamydia trachomatis* incidence in NL and does it exhibit spatial clustering? The null hypotheses are as follows:

a) There is no geographical variation in the incidence of chlamydia in NL between the RHAs, Census Divisions (CDs), Census Subdivisions (CSDs), or between urban and rural areas.

b) There are no clusters of incidence of chlamydia in NL and the spatial distribution of cases was random.

The units of analysis for this question are the RHAs of NL, CDs in NL, and CSDs in NL. A CD is a grouping of municipalities, or equivalent area(s) for regional planning based on official designations by Statistics Canada (2011). A CSD is defined as a municipality or equivalent area based on official designations by Statistics Canada (2011).

3) Is work-related migration associated with the incidence of *Chlamydia trachomatis* infections in NL? In addition to commuting, industry sector and Statistical Area Classification (SACTYPE) are included. The null hypothesis that is examined is:

There is no relationship between chlamydia rates and people who commute for work in NL, industry sector, or SACTYPE.

The units of analysis for this question are the province of NL as well as its CSDs.

CHAPTER 2

LITERATURE REVIEW

Pathophysiology and Complications

Chlamydia spp. are bacterial parasites that infect eukaryotic cells (Ryan & Ray, 2004). The primary species of interest in humans is *Chlamydia trachomatis*, which is usually transmitted via contact with infected mucosal surfaces during sexual activity. Transmission primarily occurs via person to person contact, but can also be transmitted vertically from mother to child during childbirth, if the mother has an active infection (PHAC, 2008). Infection primarily affects the cervix and urethra in women and the urethra in men but can also spread to other areas of the reproductive system such as the fallopian tubes or testes, respectively (Berger et al., 1978; Wiesenfeld et al., 2005). While sexual activity constitutes the primary routes of transmission, other mucosal membranes, such as the eyes, can also become infected via non-sexual contact (Kalayoglu, 2002). Communicability exists as long as the individual has *Chlamydia* in their body, regardless of whether or not symptoms are present (Johnson & Ndowa, 2008). Furthermore, individuals are susceptible to infection at any time, as protective immunity has been shown to be only temporary and partial (Batteiger et al., 2010; Vickers et al., 2009).

Symptoms usually present between one and five weeks after initial infection (Furrows & Ridgway, 2006). Non-gender specific complications can include lower abdominal pain, painful intercourse, difficulty urinating, rectal inflammation, infertility, pneumonia, and conjunctivitis (PHAC, 2008). Symptoms specific to women can include abnormal vaginal discharge, vaginal bleeding, cervicitis, endometritis, and pelvic inflammatory disorder (Paavonen & Eggert-Kruse, 1999). For men, prostatitis, urethritis,

epididymitis, testicular pain and abnormal penile discharge can occur (McCatchan, 2009). Lymphogranuloma venereum is a chronic infection that can also occur with some serovars (variations) of *Chlamydia trachomatis* and can result in ulceration and lymphatic complications (Mabey & Peeling, 2002).

Infected persons also show increased physiological vulnerability to other STIs, such as Human Immunodeficiency Virus (HIV), regardless of whether symptoms present (Fleming & Wasserheit, 1999). There is also an increased risk of co-infection with ulcerative STIs such as *Herpes simplex* and *Treponema pallidum* (i.e., syphilis) (PHAC, 2006).

Long term problems such as loss of vision, chronic pelvic pain, reactive arthritis, and chronic lung diseases may also result if the infection is not treated and/or does not clear up on its own (McCatchan, 2009). *Chlamydia trachomatis* is also the leading cause of infectious blindness worldwide, a potential long-term effect of untreated conjunctivitis (Hu et al., 2010; Ryan & Ray, 2004). Chlamydia can cause a variety of prenatal complications such as an increased risk of ectopic pregnancy, spontaneous abortion, and premature delivery (Kadzhaia & Merabishvili, 2005; Rours et al., 2011). Infections of newborns can occur during childbirth and can cause pneumonia and conjunctivitis (Ryan et al., 1990).

In addition to the physical complications of infection, lost or limited work and social activities due to symptomatic discomfort, time for treatment purposes, and psychosocial problems may result (Duncan et al., 2001). Stigmatization, social stress, concerns of reproductive health, interactions with one's partners, and isolation as a result of STI diagnosis can negatively affect mental health for those infected (Holgate & Longman, 1998; Rein et al., 2004).

Diagnosis, Treatment, and Prevention

Diagnosis for chlamydia in a clinical setting involves the collection of a mucosal surface swab or by a less invasive urine sample (CDC, 2010). These tests can be collected, processed and released within a short time frame. Collection of *Chlamydia trachomatis* can be confirmed as one of three possible infections: genital, extra-genital or perinatal (Alberta Health, 2012a). After collection, diagnosis involves isolation and detection of the bacteria through one of three tests.

Three common diagnostic tests for *Chlamydia trachomatis* include cell culturing, enzyme linked immunosorbent assays (ELISAs) and nucleic acid amplification tests (NAATs) (Van Dyck et al., 2001). Cell culturing consists of swabbing a sample with suspected chlamydial cells onto a monolayer of McCoy cells and after 48-72 hours of growth, intra-cytoplasmic inclusions will form in the infected cells, which can then be stained and fluoresced for confirmation (Johnson et al., 2001). Although cell culturing is the slowest diagnostic method, it is the most cost effective and has the benefit of bypassing restrictions of antibiotic resistance; a potential limitation assessment of sensitivity and specificity when using the ELISA or NAAT methods. The simplicity of cell culturing makes it accessible in low resource areas with limited funding or technology, but a lack of sensitivity detracts from practicality in most major health agencies (Van Dyck et al., 2001). Culturing is also recommended for throat specimen collection (PHAC, 2010a). ELISAs detect antigens and specific antibodies that are active during an infection using spectrophotometry (Engvall & Perlman, 1971). In NAATs, sequences of DNA, RNA and plasmids are isolated and amplified for detection using a variety of Food & Drug Administration approved commercial amplification kits (Fredlund et al., 2008).

In Canada, including NL, NAAT testing is used as the gold standard for chlamydial diagnosis (Newfoundland and Labrador Department of Health and Community Services, 2010; PHAC 2016). This is due to its greater sensitivity in comparison to the other two diagnostic methods and its versatility as multiple genomic sequences can be targeted for confirmation with greater accuracy (Van Dyck et al., 2001). NAATs can also use non-invasive methods of specimen collection such as urine samples or mucosal swabs, which makes it more acceptable for the patient than other methods (Serlin et al., 2002).

Chlamydia trachomatis can be treated using a variety of antibiotics. These can include macrolides (e.g., azithromycin) and tetracycline (e.g., doxycycline) products, which are recommended as the preferred treatments (Hillis et al., 1998; Philips, 2013). Treatment is either a single dose of azithromycin, or a seven-day doxycycline regimen. Both have been shown to have a 97% cure rate when patients follow the doctor-prescribed regimen (CDC, 2010). Management may also include a co-treatment of a single dose of cefixime or ceftriaxone for gonorrhoea because patients with chlamydia are often co-infected with gonorrhoea (PHAC, 2013; Sadovsky, 2004). The emergence of antibiotic resistance in STIs is a growing concern for culturing, testing, and treatment protocols which means a need for increased communication and surveillance around select strains (CDC, 2011; CDC, 2010; PHAC, 2014).

There is currently no vaccination against *Chlamydia*, but preventative measures can be taken. Clinical management of STI risk involves both primary screening and secondary prevention strategies as risk varies from person to person (PHAC, 2010a). Primary prevention is the most ideal and involves health education towards preventing exposure. On an individual level, this can include the use of prophylactics such as condoms as well as

routine screening and communication with one's partner(s). Health authorities can provide programs such as sexual health education, prophylactic distribution, diagnostic tests, and surveillance to assess the population for those at the greatest risk of infection. Proactive treatment is often recommended to reduce the incidence of multiple communicable diseases in targeted individuals as many people with one STI often have other infections (Sadovsky, 2004). Secondary prevention, which plays a role in inhibiting the long-term complications associated with infection, involves routine checks by health professionals to identify asymptomatic cases in target populations. Routine screening and safer-sex counselling is recommended, regardless of sexual orientation (PHAC, 2010a). Additionally, the social determinants of health play an interactive role with the behaviours around STI acquisition (Hogben & Leichliter, 2008). In a broader context, addressing disparities such as health care access, racial differences, and socioeconomic status can also help with prevention (Santelli et al., 2000).

Disclosure of infection status to partners remains the prerogative of the patient and many infected individuals are unlikely to disclose their infection status due to fear of repercussions, stigma, and/or a lack of knowledge or access to such services (Balfe & Brugha, 2010; Cunningham et al., 2002). Cunningham et al. (2002) found that many people are discouraged from seeking treatment due to the judgemental nature of health care providers when an STI is expected. People are also often unlikely to share their testing practices with those around them outside of a healthcare setting (Balfe & Brugha, 2010). The negative consequences of testing, self-perceived vulnerability and social norms are some examples of stigmatization that infected individuals face (Barth et al., 2002). Barth et al. (2002) found that this stigmatization results in lack of treatment-seeking behaviour

and/or lead to subsequent risky behaviour. Considering the asymptomatic nature of chlamydial infections and the multiple barriers to prevention and treatment such as cost, stigma, wait times, and lack of knowledge, there is likely a high degree of under-reporting of chlamydia cases (Cunningham, 2009; Tilson et al., 2004). Therefore, more surveillance collaboration and community research were suggested to implement health assessment and promotion programs for high-risk populations that often serve as the primary reservoirs for STIs (Gunn et al., 1998).

Communicable Disease Surveillance in Canada

Disease incidence surveillance in Canada is conducted in a bottom up reporting structure using local, provincial, and national levels. Investigations start in clinics where individuals are checked for the presence of symptoms for *Chlamydia trachomatis* and other infections, diagnostic tests are conducted, and sexual health education materials are provided (PHAC, 2010a). These services can be provided by a variety of primary care sites such as hospitals, walk-in clinics, and sexual health resource centers. Sexual health education materials at these locations can include disease and transmission information, travel health information, individual and community based prevention resources, and decision-making counselling (e.g., how to reduce number of partners and safe sex practices). Risk factors such as contact with infected individuals, previous STIs, and vulnerable population status (e.g., indigenous) are also assessed. It is then recommended that recent sexual partners are located, contacted, and encouraged to be tested using the same protocols and practices as noted above for the primary patient.

Each province has their own unique Public Health Act legislation (e.g., Communicable Diseases Act - RSNL 1990 Chapter C-26 for NL), regulations and

legislation to report information to the Public Health Agency of Canada (PHAC) (Government of Newfoundland and Labrador, 2007a). Identified cases are organized and aggregated as provincial regulatory bodies see fit (Barteluk, 2007). Primary healthcare professionals (i.e., physicians and nurses) are required, by law, to report confirmed cases to the Regional Medical Officer of Health (or designate) within a specified time (Newfoundland and Labrador Department of Health and Community Services, 2010). The notification form includes the patient's medical and contact information, treatment details, and the laboratory findings. Afterwards, the respective RHA can investigate cases further if the need arises.

In NL, health professionals and public health laboratories report notifiable disease cases to RHAs which then determine if further epidemiologic surveillance and further investigation is merited. All individuals that the infected patient had sexual contact with in the last 60 days are contacted by the respective RHA (Newfoundland and Labrador Department of Health and Community Services, 2010). A contact trace may be done to locate the last sexual partner if there had not been any new sexual partners in the last 60 days, even in the absence of symptoms (Newfoundland and Labrador Department of Health and Community Services, 2016). Follow-up testing is also encouraged after six months of treatment. Case management is not routinely performed unless there is a lack of prior treatment success or a history of recurrent infections.

There is variation between provinces for reporting intervals. For example, in NL, incident cases of chlamydia are reported once a week; while health authorities in Alberta are required to report cases every two days to the Regional Medical Officer of Health (Alberta Health, 2012a; Newfoundland and Labrador Department of Health and

Community Services, 2010). Contact tracing is also recommended both within provinces, and between provinces for certain communicable diseases, including chlamydia (PHAC, 2010a; PHAC, 2008). Reports are forwarded to national bodies such as PHAC from RHAs, at the recommendation of the Chief Medical Officer of Health for a given province within a two-month period for subsequent investigation. All provincial case information is aggregated for yearly reports to PHAC and case counts are also released in both the monthly and quarterly Newfoundland Communicable Disease Report(s) (Newfoundland and Labrador Department of Health and Community Services, 2010).

After the surveillance is conducted under provincial/territorial authorities, it is submitted to the Canadian Notifiable Disease Surveillance System (CNDSS) for national tabulation (PHAC, 2010b). The CNDSS is a federal surveillance system designed to capture information regarding Canada's nationally notifiable diseases. Notifiable diseases including *Chlamydia trachomatis* are communicable pathogens which are federally and provincially monitored for control purposes (Carter, 1991; PHAC, 2009a). Chlamydia became a national reportable disease in Canada in 1990 (PHAC, 2008).

Risk Factors

Factors such as poverty, drug use, low education, being incarcerated, and being of a younger age are positively associated with high-risk sexual behaviours and elevated STI rates (Adimora & Schoenbach, 2005; Hogben & Leichliter, 2008). People under the age of 25 often have a greater number of sexual partners and participate in risky sexual behaviours such as intercourse without a condom (Berman & Hein, 1999; Deering et al., 2010). Individuals with multiple partners and those who have casual sexual encounters are more likely to spread *Chlamydia* and concentrate it in subgroups of the population such as those

under 25 (Brunham & Plummer, 1990; Wilson Chialepeh & Sathiyasusuman, 2015). Economic instability has shown to cause instability in relationships – especially in young couples (Hardie & Lucas, 2010). Economic hardship also affects adolescent sexual behaviours such that low socioeconomic status (SES) leads to more high-risk behaviours (Langille et al., 2005). SES has been associated with chlamydia incidence rates, although to a weaker extent than seen with gonorrhea (Winter et al., 2010). The weaker association may be due to a poorly understood interaction with ethnicity, geography, and other factors. For example, chlamydia incidence has not been concretely linked to ethnicity on its own but again may have an interaction with other risk factors (Navarro et al., 2002; Zimmerman et al., 1990). It has been observed that people under the age of 25 of low SES in Canada (i.e., street youth) have up to a tenfold greater risk of infection due to the effects of multiple risk factors such as those noted above (PHAC, 2011).

Compared to the overall population, members of the Lesbian-Gay-Bisexual-Transsexual-Queer (LGBTQ) community are also more likely to have multiple partners, become sexually active at a younger age, and use fewer barrier methods; all of which increase STI exposure risk (Coker et al., 2010; Saewyc, 2011). People in the LGBTQ community also have a higher self-reported incidence of STIs and associated high risk behaviours than heterosexual individuals (Goodenow et al., 2008).

Vulnerable populations such as Aboriginal peoples may make up the greatest portion of new and recurring cases. Rates of infectious diseases in Aboriginal populations are often under-reported due to unavailability of case or population data for incidence assessment (FNIGC, 2012; PHAC, 2009b). Therefore, Aboriginal rates of STIs are often masked within provincial or national estimates. Aboriginal communities are more often

isolated (rural), have a greater proportion of youth, have limited health care access and lower education levels than the general population (Kulig & Williams, 2011).

The highest incidence of STI cases occurs in dense urban centers where individuals often have the greatest culmination of risk factors (CDC, 2011). Chlamydial infections are more prominent in urban communities but seem to be more evenly distributed within the sexually active population rather than clustering in low income areas as is seen in gonorrhea (Blanchard et al., 1998). This can be contrasted with rural locales that may have fewer cases and different risk factors. Rural and remote areas often lack accessibility to primary healthcare providers; lack sexual health education and associated resources such as proper risk assessments; and lack alternatives after having negative interactions with health care providers (Goldenberg et al., 2008b). Rural populations, older populations, and areas of low SES are also affected by issues such as lower levels of education and unstable employment (Nagarajan, 2004).

Economic trends in Canada are pushing individuals from rural and remote areas into more urban areas for work (Rothwell et al., 2002). Migration for employment often occurs when a given locale has limited commercial or industrial opportunities to provide a decent living, resulting in people searching elsewhere for gainful employment (Robinson & Tomes, 1982). This is relevant to NL as more people have migrated for employment in the thriving oil and gas sector following economic decline in the province (Government of Newfoundland and Labrador, 2012).

Workers in the oil and gas sectors often have to migrate substantial distances from their home to their place of work. Migration and related economic empowerment sometimes result in high-risk behaviour such as the patronage of sex workers, increased

number of sexual partners, and injection drug use (Organista & Organista, 1997). Drug and alcohol addictions also play a role in increased risk of infection of STIs, as there is an increase in high-risk behaviours such as reduced condom usage and greater sexual promiscuity (Scott-Sheldon et al., 2009). The exchange of sex for drugs, money or basic amenities results in sex trade workers and their clients having higher incidence of STIs (Windle, 1997). Oil and gas workers often fit the above criteria for drug and alcohol use and are at even greater risk because of local social norms, anxiety due to geographic inaccessibility to family and friends, lower levels of education, and limited access to health information/resources (Goldenberg et al., 2008b; Organista & Organista, 1997).

Epidemiological Trends

The incidence of *Chlamydia trachomatis* infections has been steadily rising since 1997 when it was introduced into the Nationally Notifiable Disease Database and the Sexually Transmitted Disease Registry (PHAC, 2008). Surveillance records from Canada show an incidence rate of 1.38 cases per 1000 in 1999, and 2.49 cases per 1000 in 2009; an increase of over 80 percent in the span of a decade (PHAC, 2009b). There was a decrease in incidence from 1.72 cases per 1000 to 1.13 cases per 1000 between 1991 and 1997 followed by a surge in incidence. This surge may have been due to the introduction of widespread NAAT usage in Canada (Health Canada, 1998). On average, the reported rates equate to a 6.8 percent increase in incidence risk per year (PHAC, 2009b).

Incidence can be further stratified based on various subpopulations such as age, gender and location. Stratifying by age shows the highest incidence rates in women ages 15-19 years and 20-24 years for men (PHAC, 2014). People under the age of 30 dominate the rates of new chlamydial infections in Canada, accounting for over 80 percent of new

cases (PHAC, 2008). The higher rates in people under 30 might be related to the fact that they are more likely to have multiple sexual partners in a 12-month period and have shorter relationships when compared to the overall population (Johnson et al., 2001).

In recent years, the incidence of chlamydia was found to be two to three times higher in females than males (PHAC, 2009b). Men are less likely to be diagnosed because they are tested less often than sexually active women who are routinely checked through pap smear tests, thus resulting in a higher recorded incidence in females (Mckay & Barrett, 2008). As a result of this lack of routine testing, particularly in asymptomatic males, may result in an underrepresentation of males in surveillance registries while furthering transmission. While women have an overall higher incidence of chlamydia, men beyond 40 years of age have a greater rate (PHAC, 2009b). Previous studies have found an interaction between age and sex but no known studies have assessed this in a Canadian population (Datta et al., 2007).

The greatest issue in controlling the spread of *Chlamydia trachomatis* is that asymptomatic individuals are estimated to comprise between 50 and 70 percent of infections for men and women respectively (Weir, 2004). They make up a large and difficult to track reservoir of infection for new and recurring infections. The asymptomatic nature of many chlamydial infections, or delay in onset of symptoms likely contributes to a lack of accurate incidence estimates of this pathogen (Farley et al., 2003).

Geographical Distribution and Spatial Mapping

Understanding the spatial heterogeneity of disease prevalence or incidence facilitates the understanding of both prevention and intervention (Nyarango et al., 2006). One method of evaluating the spatial distribution of disease is through the use of geo-

visualization. Geo-visualization uses cartographic tools and functions to explore, simplify and portray spatial data in a variety of ways for better dissemination (Boulos, 2003). In infectious disease epidemiology, geo-visualization allows for an examination of disease rates and trends on a variety of spatial levels. By examining maps, we can employ more targeted, hence more effective, interventions than are typically used (Riley, 2007).

Plotting data can be conducted through the use of points and polygons. Data points are single observations for a given measurement for a given point in space. Point data serve as the base level for plotting data that vary continuously over a geographical area (e.g., rainfall). Point data can be aggregated into larger spatial partitions called areal units (polygons) which can be more practical for spatial trend analysis (Shepard, 1968).

Both point data and areal data can be assessed for spatial autocorrelation to see whether there is evidence of a locational relationship (Griffith, 1987). Spatial autocorrelation is an assessment of the degree to which similar spatial data and/or features are clustered or dispersed. Local spatial autocorrelation can be used in the identification of clusters, while global spatial correlation can be used for clustering across the entire study area. Inferences can then be made and hypotheses generated as to the prevalence/incidence of a disease to see if they are randomly distributed or if there are localized clusters of infection.

Mapping and identifying spatial clusters (or hotspots) of disease rates can be important for contact tracing, understanding etiology, and effective implementation of interventions (Jennings et al., 2005). A cluster is a spatial and/or temporal set of health events that may be related (Jacquez, 2008). Some methods allow for the estimation of relative risk for clusters in a given study area (Kulldorff, 1997). The relative risk gives the

strength of a relationship for a given outcome to a particular exposure factor (Aschengrau & Seage, 2008). The spatial scan statistic is one such method which can be used for detection of the presence and the location of localized clusters and subsequent evaluation of relative risk (Kulldorff, 1997). A further explanation of the spatial scan statistic can be found in the methodology section below.

Spatial Distribution of STIs

Clustering often occurs with STIs, including infections caused by *Chlamydia trachomatis* (Schleihauf et al., 2009). Chlamydia has a more diffuse spatial distribution than what is seen in other STIs (Zimmerman et al., 1990). Furthermore, high incidence STIs such as chlamydia have larger areal clusters which results in greater spatial variability of infections (Law et al., 2004). This potentially means that chlamydial infections are often spread over a much larger area. The analysis of chlamydia incidence for spatial clusters is warranted because it allows both the provincial government and its RHAs to plan for targeted screening and treatment. Identification of clusters is important as there often limited resources for infectious disease investigations; especially in geographical areas as large as the RHAs in Newfoundland and Labrador.

Certain geographical areas, such as inner cities, rural areas, and communities with a low SES are prone to re-infection (Ellen et al., 1997). Spatial mapping of STIs based on regionality often shows high infection areas in urban locales but a poor understanding of the spatial distribution in rural areas is due to the limited availability of health education, services, and research (Elliot et al., 2002). This is a concern to NL as 41 percent of its population is considered rural and a lot of travel exists between rural and metropolitan areas (Statistics Canada, 2011a). Furthermore, more than 70 percent of communities in the

province have fewer than 500 people living in them and almost half of all workers have to leave their home community for their occupation (Government of Newfoundland and Labrador, 2011). Transmission of infectious diseases such as STIs are often attributed to the connectivity of rural and urban areas as opposed to simply having isolated core areas of infection (Gesink et al., 2013). Common examples of this connectivity are shown through commuting between urban and rural areas, intra-provincially, and interprovincially.

Employment Migration and STIs

As there is often a lack of job opportunities in Canadian rural areas, many people will commute substantial distances to work (Green & Meyer, 1997). Migratory patterns exist across provincial borders and are frequently influenced by economic changes (Finnie, 1999). The importance of interprovincial employment in the past decade was demonstrated by the high percentage of total salaries/benefits from those who participated in interprovincial employment, as well as increase in Atlantic province unemployment following the economic recession (Morissette & Qiu, 2015). Due to a global recession as well as provincial economic decline, workers in NL have turned to employment opportunities outside of the province for extended periods of time (MacDonald et al., 2012). In general, commuting can often be more appealing than permanent migration due to the elevated price of housing in urban centers (Turcotte & Vezina, 2010). An estimated 20 percent of residents claim to work out of province and there has been a 30 percent increase in yearly migration to and from the province in the past decade (Government of Newfoundland and Labrador, 2012). Interprovincial migration across the country increased by roughly 60 percent between 2004 and 2009 and the number of people going to Alberta almost doubled during the same period (Laporte et al., 2013). Furthermore, Laporte et al.

(2013) reported that just under 40 percent of interprovincial employees working in Alberta were from the Atlantic provinces; with the largest proportion coming from NL. According to the Work Activity Survey (2010), 47 percent of NL migratory workers were travelling to and from Alberta; the majority of which were for seasonal work (Government of Newfoundland and Labrador, 2011).

Travel both within, as well as to and from the province may be increasing disease transmission and may be generating novel disease clusters. Migratory employment could lead to increased connectivity of sexual networks. From the perspective of a transmission model, a sexually active individual in a high-risk area with high STI rates, such as Northern Alberta, would have a greater impact upon returning to a lower risk area (Alberta Health, 2012b; Koopman & Lynch, 1999). Alberta had more than an 80 percent increase in chlamydia incidence rates in the decade leading up to 2009 (PHAC, 2008). Numerous studies have looked at individual factors of STI determinants such as sexual behaviours in Canada but few have looked at population determinants in the general population, such as the influence of migratory employment (Rotermann, 2012).

Overall, there were no known geographical studies in the province of NL regarding the incidence of *Chlamydia trachomatis* infections. Considering the ongoing increase in incidence in Canada, identifying clusters of disease incidence is becoming increasingly important in planning interventions on known clusters of infected individuals and potential high-risk populations (Law et al., 2004; PHAC, 2011). Furthermore, the temporal distribution of chlamydia cases has not been extensively studied in NL outside of the monthly case counts and yearly crude incidence released regularly by the NL Department of Health and Community Services on behalf of the RHAs. Beyond this, the RHAs only

publicly reported the counts, so it cannot be determined which demographic groups are the most affected.

CHAPTER 3

RESEARCH METHODS

Study Design and Population

This project was a descriptive study that used a cross-sectional design to examine the temporal distribution of chlamydia incidence in NL. An ecological design was used for both the spatial distribution of chlamydia incidence, and for the exploration into migratory employment as a risk factor. The inclusion criteria for the study population for temporal and spatial analyses were the laboratory confirmed chlamydia cases recorded between January 1st, 2007 and December 31st, 2013 in patients over the age of 15. Both non-NL residents that were diagnosed in the province and NL residents who were diagnosed outside of the province were excluded from the analysis. A case was defined as a positive NAAT for chlamydia as performed by the NL Public Health Laboratory. NAAT testing has been shown to have a sensitivity above 90% and specificity greater than 99% (Johnson et al., 2002). The total sample size of NAAT diagnosed chlamydia infections across the study period was 4368 cases. The analysis of the migratory behaviours and chlamydia examined NL residents who filled out the 2006 Census of Population or 2011 National Household Survey linked to the chlamydial data described above.

Data Sources and Cleaning

Chlamydia Case Data and Population Denominators

The number of laboratory confirmed chlamydia cases was obtained from the four provincial RHAs (Eastern, Central, Western, and Labrador-Grenfell). The data from RHAs have unique de-identified patient codes, date of diagnosis, age at diagnosis, sex, and community of residence. Community of residence represents the name of the town or city

identified as the primary home by the patient. Incomplete or incorrectly entered records (e.g., patient age of 200 years or date of diagnosis in January 2014) were removed from the data sets. Additionally, many communities in NL share the same name (e.g., six places named Riverhead) and if the case information could not be reasonably matched (through postal code or other noted specification), the cases were dropped. Community names were standardized before combining the datasets to match up during the aggregation process discussed below (e.g., "Saint Johns" and "St Johns" would both be renamed as "St. John's"). Similarly, variable names were standardized in all four RHA datasets which were then appended together into a single list in a case file. A new variable was created to represent the health region a given case had originated from. The final sample size after cleaning and compiling was 4308 cases (i.e., exclusion of 60 cases). A flowchart of the data cleaning is shown in Figure 3.1 below.

Age and sex population estimates for the province for each year from 2007 to 2013 were downloaded from the Comprehensive Census Profile page (CANSIM) in the Census of Population (Statistics Canada, 2011b; Statistics Canada, 2013a). The population estimates were taken from July 1st of a given year and the assumption was made that the population remained constant for that year of study. Variable names were also recoded to match up with those in the case and geographical files. National chlamydia incidence rates, stratified by age and sex, were obtained from the "2011 Report on Sexually Transmitted Infections in Canada" (PHAC, 2014).

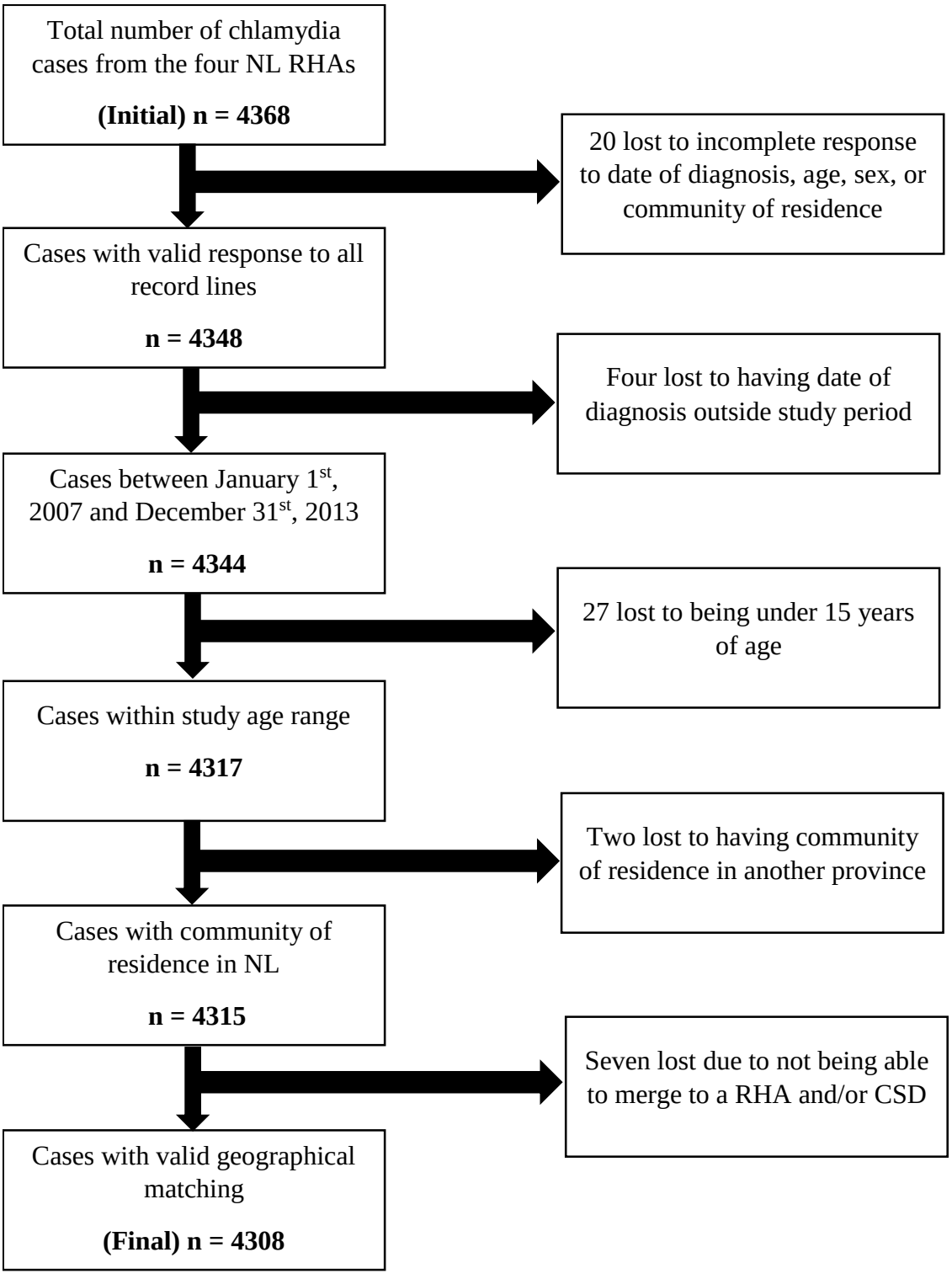

Figure 3.1. Derivation of final chlamydia case sample

Case Data Study Variables

"Season of Diagnosis" and "Year of Diagnosis" were derived from "Date of Diagnosis" to allow for multiple levels of temporal assessment. Seasons were defined by their respective calendar dates as winter, spring, summer, and autumn (e.g., March 21st to June 20th constituted spring) to examine trends. To match up with age categorization standards used by PHAC for STIs, "Age at Diagnosis" was recoded for both the case datasets, and all supporting datasets listed below, to the categories of 15-19, 20-24, 25-29, 30-39, 40-59 and 60+ years. "Patient code" was used as a placeholder variable to represent one case. The study variables and their respective coding are outlined in Table 3.1 below.

Table 3.1

Summary of study variables from the four RHAs in NL.

Study Variables	Definition	Coding (if applicable)
Patient Code	De-identified patient code number	No additional coding was required.
Community of Residence	Name of town/city identified as primary residence by patient	No additional coding was required.
Sex	Sex of the case	Coded as 0 for male and 1 for female.
Date at Diagnosis	Date patient tested positive for chlamydia	For season of diagnosis, dates were coded as 1 for winter, 2 for spring, 3 for summer, and 4 for autumn. For year of diagnosis, dates were coded as 1 for 2007, 2 for 2008 (etc.) up to 7 for 2013.
Age at Diagnosis	Age of patient when tested positive for chlamydia	Coded as 0 for 15-19 years, 1 for 20-24 years, 2 for 25-29 years, 3 for 30-39 years, 4 for 40-59 years, and 5 for 60+ years as per PHAC age subcategories.

Spatial Data

Digital cartographic boundary files of Canadian CSD and CD areas were downloaded from the Statistics Canada's Census catalogues and contained 376 and 11 CSDs and CDs, respectively in NL based on 2011 Census Data (Statistics Canada, 2011c). Information on Statistical Area Classification (SACTYPE) was also downloaded from the Statistics Canada online catalogue (Statistics Canada, 2011d). A coordinate file containing the latitude and longitude for all NL communities was obtained from the NL Statistics Agency.

Age and sex population estimates for each CSD and CD were taken from the 2011 Census of Population. Sex and age stratified populations for each of the four RHAs were similarly taken from the 2011 Census of Population and intercensal estimates (Statistics Canada, 2011b; Statistics Canada, 2013a). Age categories were constructed to the same groupings as noted in the temporal assessment. No other cleaning was required.

Spatial Data Aggregation

Community of residence was aggregated up to the geographical levels of CSD, CD and health region for spatial analysis, as well as for privacy purposes. Aggregation of data for spatial assessment requires the merging of several datasets at different scales. Spatial and relational joining involves combining two spatial layers, or tables using Environmental System Research Institute's (ESRI) ArcGIS software (Version 10.2). For example, a point to polygon spatial join function was used to connect points that represent communities in NL to the province's CDs and CSDs that were represented by polygons in a boundary file of the province. The result were communities that were associated with a specific Census Subdivision Unique Identification Number (CSDUID) and Census Division Unique

Identification Number (CDUID). This process allows for geographical analysis such that if the community was located within the boundary of a given CSD, it would be joined to that CSD. This information was then merged (relationally joined) to case data in an ArcGIS spreadsheet. Population data were then merged with this combination using the same procedure. This geography file was then exported as a table to STATA® for incidence rate calculations at the CD and CSD level (StataCorp, 2015). The calculated rates were finally imported back into ArcGIS for visualization (ESRI, 2013).

Spatial Data Study Variables

CSDs represent municipal areas and were classified based on their integration with urban cores using SACTYPE, a stratification of metropolitan influence (Statistics Canada, 2012). A stratified listing of SACTYPE is included below in Table 3.2. Census Agglomerations (CAs) and Census Metropolitan Areas (CMAs) are urbanized geographical regions with populations greater than 10,000 persons. Rural CSDs have a population of less than 10,000 and were stratified into four categories of Metropolitan Influenced Zones (MIZ). These categories are strong, moderate, weak, and non-influenced MIZs that reflect the percentage of persons commuting to a neighbouring urban core for employment purposes. Incidence rates were calculated for each SACTYPE and each urban/rural categorized CSD to help make inferences on the role of travel on incidence rates by comparing MIZs to nearby CAs/CMAs. Analysis of MIZs allows for a more detailed assessment of the distribution of disease and other health factors in rural areas than simply comparing urban and rural areas alone. (Ostry, 2009; Pearl et al., 2009; Shields & Tjepkema, 2006).

Table 3.2

SACTYPE classifications for CSDs used in the Canada Census of Population (2011).

Classification	Description
Census Metropolitan Area (CMA)	Region in an urban core with a population greater than 100,000.
Census Agglomeration (CA)	Region in an urban core with a population between 10,000 and 99,999.
Strong Metropolitan Influenced Zone (MIZ)	Region with an employment migration greater than 30% to a neighbouring urban core, CA or CMA.
Moderate Metropolitan Influenced Zone (MIZ)	Region with an employment migration between 5% and 30% to a neighbouring urban core, CA or CMA.
Weak Metropolitan Influenced Zone (MIZ)	Region with an employment migration between 0% and 5% to a neighbouring urban core, CA or CMA.
Non-influenced Metropolitan Influenced Zone (MIZ)	Region with no employment migration or lack of information.

A new variable, “Location Type”, was constructed based on the SACTYPE of a given CSD (Statistics Canada, 2011b). CSDs were classified as urban or rural, where “rural” constituted CSDs that are classified as one of the four MIZs and “urban” constituted CSDs classified as CA or CMA. SACTYPE was chosen as opposed to population density to define urban and rural areas to align with the CSD aggregation for the employment analysis (discussed below). “CSDUID” and “CDUID” were used as geographical identifiers for later mapping. A breakdown of the variables and their respective coding are included in Table 3.3.

Table 3.3.

Summary of spatial study variables.

Study Variables	Definition	Coding (if applicable)
Location Type	Urban or rural CSDs (more or less than 10,000 people in a CSD, respectively). CAs and CMAs were grouped for urban CSDs while all four MIZs were grouped for rural CSDs.	Coded as 1 for CA, 2 & 3 for CMA, 4 for Strong MIZ, 5 for Moderate MIZ, 6 for Weak MIZ, and 7 for non-influenced MIZ. 1 to 3 were coded as urban and 4 to 7 were rural.
Health Region	Aggregation of communities to one of four RHA jurisdictions in NL.	Coded in case file as 1 for Labrador-Grenfell, 2 for Western, 3 for Central and 4 for Eastern Health.
Census Subdivision Unique Identification (CSDUID)	Seven-digit code for grouping of communities into municipal areas as defined by Statistics Canada.	No additional coding was required – Spatially joined to Community of Residence
Census Division Unique Identification (CDUID)	Four-digit code for grouping of CSDs into larger aggregates as defined by Statistics Canada.	No additional coding was required – Spatially joined during community to CSD merge.

Employment Data

Data on employment trends was extracted from the 2006 Census of Population and the 2011 National Household Survey (NHS) at the CSD level, CD level, and provincial level from the confidential master microdata files at the Statistics Canada Research Data Center of Memorial University of Newfoundland (Statistics Canada, 2011e; Statistics Canada, 2006). The NHS is a cross-sectional self-reported survey that was introduced in 2011 as a voluntary alternative to the long-form census. Both the Census of Population and

NHS contain demographic and socioeconomic questions, including those relating to employment migration in relation to where individuals live (PWCOMMUT), industry sector (NAICSECF/NAICS07), and location of employment (PWPR). Individuals who fell under the unavailable category in any of the above datasets, or were unemployed/retired were not included in the analysis. No other data cleaning was necessary for either of these datasets. Data on chlamydia cases from the RHAs were also brought in for this question (discussed below).

Employment Data Study Variables

Place of work type of commuting (PWCOMMUT) represents the distance people travel for their job. PWCOMMUT was broken down into those who work and live in their CSD, those who work in a different CSD, those who work in a different CD, and those who work in a different province – the latter two being considered migratory. Industry sector categories were added for comparison with commuting to see what employment sectors were more likely to see migratory employment. To simplify the industry comparison, industries typically not directly related to primary and secondary industries (e.g., the extraction of raw materials, such as mining for the former; and the manufacturing of products from these materials, such as ore smelting for the latter) were grouped under a miscellaneous category (Fisher, 1939). This was done by looking at the most commonly reported professions for mobile workers from NL and industries with high rates of interprovincial employment (Government of Newfoundland and Labrador, 2011; Laporte et al., 2013). A full listing of these sectors and the miscellaneous grouping based off the North American Industry Classification System (2007) can be found in Table 7.1 of Appendix A. All variables used in the employment migration analyses are included in Table 3.4 below.

Table 3.4.

Summary of employment and migration study variables from the 2006 Census of Population and 2011 NHS.

Study Variables	Definition	Coding (if applicable)
Census Subdivision Type	Urban core influence (SACTYPE)	Coded as 1 for CA, 2 & 3 for CMA, 4 for Strong MIZ, 5 for Moderate MIZ, 6 for Weak MIZ, and 7 for non-influenced MIZ.
Commuting Type	Place of work type in comparison to place of residence (PWCOMMUT)	Coded as 1 for working in CSD of residence, 2 for working in different CSD within the province, 3 for working in a different CD and 4 for working in a different province.
Industry Sector	Labour market activity categorization (NAICS)	Coded as per the predefined guidelines in the NHS (see Table 7.1 of the appendices) with the exception of the grouping of miscellaneous industries (all coded as 01).
Province of Work	Employment province if different from home province (PWPR)	Yukon, Nunavut and Northwest Territories were recoded (11-13) into 'Northern' (14) territories due to population aggregation requirements. No other coding was required for other provinces.

Incidence Rate Calculations

Incidence rates were calculated for both the spatial and temporal analyses and defined using the formula in Figure 3.2 below (Schoenbach & Rosamond, 1999). Population estimates were based on the 2011 Canada Census of Population or the intercensal estimates for the time periods of 2007-2010 and 2012-2013 for NL (Statistics Canada, 2011b; Statistics Canada, 2013a) depending on the year of diagnosis for the cases. It was assumed that the population remained stable for each respective year and was based on the estimate on July 1st of a given year (Statistics Canada, 2011d). The length of time-

period is dependent on the analysis being performed and ranges from a three-month season, to the full seven years of the study period.

$$Incidence\ rate = \frac{number\ of\ cases\ in\ observed\ population}{population\ at\ risk * length\ of\ time\ period}$$

Figure 3.2. Formula for Crude Incidence Rate Calculation

For the temporal analysis, crude incidence rates for each year in the study period were first estimated for the overall province. Crude incidence rates were calculated as the number of cases divided by the total population estimate for that year and then multiplied by 1,000. Rates were then calculated for the strata of age and sex. In this case, the number of cases and population at risk represent the respective values for each year of the study in each stratum. For example, in sex-stratified incidence rates, the number of cases in men during a given year was divided by the estimated number of men in the population during that year. This calculation was repeated each year of the study and then for women.

In the spatial analysis, the incidence rate calculation represents the geographical area of interest. The total number of cases for a RHA was determined by adding up all the cases in that area for each year while CSDs and CDs were determined by adding up the case counts for all the communities in the respective area over all seven years. The population at risk and length of time-period was the full seven years of the study at the CD and CSD level as stratified populations at lower levels of geography during intercensal years were unavailable. Due to this restriction, the population at risk estimates were taken from the 2011 Canada Census of Population, which included age and sex estimates for each respective CSD/CD that were multiplied by seven to compensate for the seven years of

case data (Statistics Canada, 2011b & Statistics Canada, no date). For age and sex stratification, the age or sex-specific counts and populations were used for that area. For example, incidence rates in a selected CD were calculated by dividing the number of cases in a CD by the 2011 population estimate (multiplied by seven).

Standardization

Comparing crude rates of chlamydia incidence would be misleading due to potential confounding caused by heterogeneous, varying sized sub-population distributions such as age and sex (Jager et al., 2008). Indirect standardization estimates a comparable rate for a study population that would be expected if the study population was the same as the standard population (Adams, 2008). For example, to age standardize sex-specific infection rates, the incidence rates from the standard population (e.g., the Canadian national rates for each age group) were multiplied by the population distribution from our study population (i.e., the sex specific population of NL) for that age group. The overall incidence rates for chlamydia in Canada, obtained from the "Report on Sexually Transmitted Infections in Canada: 2011" were used as the standard (PHAC, 2014). In addition to the overall rates, they were stratified by age and sex for each province in Canada. The standardized rates were originally expressed as the incidence per 100,000 person-years but were converted to incidence per 1,000 person-years for ease of interpretation. Incidence rates were indirectly standardized due to the small population size of many of the CSDs in the province. Calculations in small or unstable populations can result in unstable rate estimates, (i.e., rural NL CSDs) making them unsuitable for direct standardization (Breslow & Day, 1975). Indirectly standardized incidence rates were calculated using the formulae in Figure 3.3 for a given age, sex, or age-sex stratum (Armitage et al., 2002). Standard Morbidity Ratios

(SMR) intervals and 95% confidence intervals were estimated using the indirect standardization command in STATA® (StataCorp, 2015). The SMRs were in comparison to the national rate for that specific population group.

$$SMR = \frac{number\ of\ cases\ in\ observed\ population}{rate\ in\ reference\ population * number\ of\ people\ in\ observed\ population}$$

$$Standardized\ rate = SMR *\ crude\ rate\ of\ reference\ population\ (per\ 1{,}000)$$

Figure 3.3. Formulae for indirectly standardized incidence rate calculations (Armitage et al., 2002)

Temporal Incidence Rates

The outcome measures for the temporal assessment were the annual crude and age-sex standardized incidence rates of chlamydia for the overall population, sex-adjusted incidence rates for age, age-adjusted incidence rates for sex across the study period. A seasonal analysis (e.g., December 21st through March 20th for winter) was also conducted for all seven years combined to compare the overall difference in incidence between each of the seasons.

Incidence rates were indirectly standardized to examine overall trends as well as age and sex specific rates for each year of the study. To examine age differences, sex-standardized rates were estimated. Likewise, age-standardized rates were estimated to examine differences between sexes. Age-sex standardized rates were similarly calculated at a seasonal level for the overall population. The denominator in estimating the incidence rate for each season was based on the annual population estimated mid-year for that year. Graphs were generated to visually show chlamydia incidence rates in NL over time.

Spatial Incidence Rates

The outcome measures for the spatial assessment were chlamydia rates stratified at several geographical levels. The age-sex adjusted incidence rates of chlamydia for each CSD as well as each CD were calculated. To examine differences between urban and rural populations, age-sex standardized rates for the province were estimated. To examine the rates in each RHA, age-sex standardized rates for all four health regions were estimated based on community of residence for each case for each year. Stratum specific rates for urban-rural and health region were similarly age-sex standardized as noted above in the temporal analysis.

Analysis of Temporal Data

To examine if there was a secular trend, negative binomial regression was conducted with case counts as the dependent variable, and population at risk used as an offset in the model. Negative binomial regression was chosen rather than Poisson regression to correct for over-dispersion caused by the low case counts and a lack of model fit. This method is appropriate for count data such as the chlamydia cases in this study (Dohoo et al, 2009). Age and sex were included in the model as categorical covariates to adjust for cofounding while time (year of diagnosis) was included as a continuous variable. The interaction between age and sex was also assessed in this model. A significance level of $p<0.05$ was used for this analysis. A graph showing the predictive margins and associated confidence intervals of an age-sex interaction was also produced following the regression model to visually assess changes between these strata.

Analysis of Spatial Data

Geospatial Visualization

Choropleth maps were generated to examine the spatial distribution of chlamydia incidence based on the rates in the CDs and CSDs across the province for the full study period. Choropleth maps are maps of regional areas (e.g., CDs) that allow for colour or shading of the areas based on a range of values for a variable of interest. Maps were generated and geo-referenced using the NAD27 datum and a 3^{o} Modified Transverse Mercator projection, as per community mapping standards by the Government of NL (Government of Newfoundland and Labrador, 2013). This projection conserves scale and shape, which are appropriate for the accuracy of provincial maps.

Several maps were constructed at the CD level to compare the spatial distribution of sex and age specific rates (standardized as described above). Breakpoints for categorizing the rates as shown in the legend(s) were based off the default natural breaks (jenks) in ArcGIS which maximize the difference between value groupings to best visually portray a given dataset (Jenks, 1977). Jenks were chosen to stratify the incidence on the choropleth maps to better visually distinguish incidence rate differences. Percentiles (i.e., 5^{th}, 25^{th}, 75^{th} and 95^{th}) were originally chosen but the large deviance between the incidence in Labrador CDs made the Newfoundland CDs indistinguishable from one another using this system.

Global Spatial Clustering of Incidence Rates

Moran's *I* is a statistic used to examine the spatial autocorrelation of areal units and tests the null hypothesis that there is no spatial autocorrelation in disease incidence among areas of interest (Jensen & Jensen, 2013). Moran's *I* was used to evaluate global spatial autocorrelation among the incidence rates of chlamydia in NL CDs and CSDs (Pfeiffer et

al., 2008). Moran's *I* ranges from -1.0 to +1.0 where negative values indicate that areas are located near areas with different values, and positive values indicate areas are located near areas with similar values (Griffith, 1987). For example, a high, positive Moran's *I* gives an indication that disease rates may be clustered and positively autocorrelated. A high, negative Moran's *I* gives an indication that there is uniform dispersion and negative autocorrelation. Finally, a Moran's I near 0 shows little to no relationship (i.e., random distribution).

Local Spatial Clustering of Incidence Rates

Scan statistics are statistical methods that detect the location of events (i.e., disease clusters) in space, time, or space and time (Naus, 1965). SaTScan (Version 9.3) is specialized software that was used to examine for spatial clustering with the spatial scan statistic (Kulldorff, 1997). The spatial scan statistic was used to evaluate for spatial clusters of high incidence and estimate the relative risk for significant clusters (Kulldorff & Nagarwalla, 1995). The spatial scan statistic generates an infinitely expanding circle from a selected point (e.g., CSD centroid) representing a candidate cluster of a given location and size. Using a likelihood ratio statistical comparison of expected and observed events (i.e., cases) inside and outside the circle, the likelihood of clustering is automatically calculated and candidate clusters are reported once the circle reaches a certain threshold size (Kulldorff, 2014). The spatial scan statistic calculates the expected number of cases based on the total observations, current size of the circle and the overall size of the study area. Circles with high likelihood ratio values were denoted as potential clusters. A p-value is subsequently computed for each potential cluster using Monte Carlo simulation testing to determine statistical significance of the geographical distribution and occurs when the log

likelihood ratio is greater than the critical value (Kulldorff, 1997). This maximum geographical cluster size was set to the default 50% of the population size to most suitably detect both small and large clusters (Kulldorff, 2014). The aggregated case counts, population estimates for each CSD, and coordinate information were imported into SaTScan for these calculations. Identified clusters were then visualized on a map to show their location, size and associated relative risk of being inside the cluster.

Centroid locations were calculated for each CSD using ArcGIS and then imported to SaTScan. These were used as the grid point(s) for cluster detection. SaTScan has proven effective in spatial cluster detection for its high sensitivity and its ability to assess clusters for their relative risk levels (Aamodt et al., 2006). A discrete Poisson distribution model was chosen for the estimations that automatically adjusts for the population at risk in the calculations (Kulldorff, 2014). Monte Carlo simulations were set to 9999 iterations. Spatial clusters and their statistical significance were subsequently estimated and evaluated to determine whether clustering of chlamydial cases exists in NL.

Employment Migration and Chlamydia

The NL chlamydia age-sex standardized incidence rates at the CSD level were first merged by CSDUID to the NHS data. Linear regression was used to examine the relationship between age-sex standardized rates of chlamydia incidence at the CSD level with the proportion of people who commute different distances for work, the proportion of people in a CSD in a specific industry of work, and SACTYPE from the 2011 NHS. Age-sex standardized chlamydia rates were transformed using a natural logarithm to preserve the model assumption of homoskedacicity. The percentage of respondents in each CSD for each category in the variables PWCOMMUT and NAICSECF were logarithmically

transformed as well. The six levels of SACTYPE were included in the model as a categorical variable (Statistics Canada, 2011d). An overall multivariate model was produced as well as univariate models comparing chlamydia incidence to each individual employment variable noted above. A significance level of $p<0.05$ was used and residual analysis was conducted after to determine if modelling assumptions were met. Base five rounding was also used on all tabulations (i.e., all raw counts of a given category had to be rounded to the nearest 5 or 0) prior to release due to Statistics Canada privacy guidelines.

Ethics and Data Management

Ethics approvals were obtained from the Health Research Ethics Authority of NL (reference number: 2015004) as well as from each RHA. Institutional approval was acquired from the Research Proposals Approval Committee. Research Data Center access at Memorial University of Newfoundland was acquired from Statistics Canada. The four chlamydia case datasets were de-identified by the RHAs prior to analysis, minimizing privacy and confidentiality concerns, and only aggregated data were presented in the results. CSDs with less than five cases were omitted to further protect privacy. Data from RHAs were electronically stored on an encrypted hard drive with access only to the primary researchers. The data will be destroyed five years after the final publication of this project. The ethical and privacy requirements as set by Statistics Canada and Memorial University of Newfoundland were incorporated and followed.

Project Software

STATA® (Version 14.1 for Windows) software was used for data cleaning and coding (StataCorp, 2015). Microsoft Excel 2013 was used to reorganize the population data and national rate data, prior to importing into STATA® for cleaning and analysis. ESRI's

ArcGIS (Version 10.2) was used to perform spatial joins and produce the maps for analysis. Moran's *I* was also calculated using ArcGIS (ESRI, Version 10.2). SaTScan (Version 9.3) was used to produce the spatial scan statistic for the chlamydial cases at the CSD level.

CHAPTER 4

RESULTS

Chlamydia Temporal Trends

For the seven years of the study period, 2496 (58%), 202 (5%), 455 (10%) and 1215 (28%) cases were provided from Eastern Health, Central Health, Western Health, and Labrador-Grenfell Health, respectively. Summary statistics of the study population are shown in Table 4.1 below. Younger age categories and women had a much greater percentage of cases.

Table 4.1

Summary of the study population and the substrata of age and sex in NL between 2007 and 2013 (n = 4308).

Mean (standard deviation) of age at diagnosis	23.33 (±6.40) years old
Percent of cases by age group	
15 to 19 years old	26.28
20 to 24 years old	44.29
25 to 29 years old	17.04
30 to 39 years old	9.35
40 to 59 years old	2.88
60+ years old	0.16
Percent of cases by sex	
Male	27.74
Female	72.26
Percent of cases by year	
2007	9.80
2008	12.37
2009	11.54
2010	13.63
2011	15.51
2012	19.41
2013	17.76

Figure 4.1 shows the percent of cases by age and sex. A noticeable difference between men and women was found in younger age groupings but became more equal in older age groupings. Women had a higher percentage in younger ages up until the 40-59 years old category where men overtook women in having more cases.

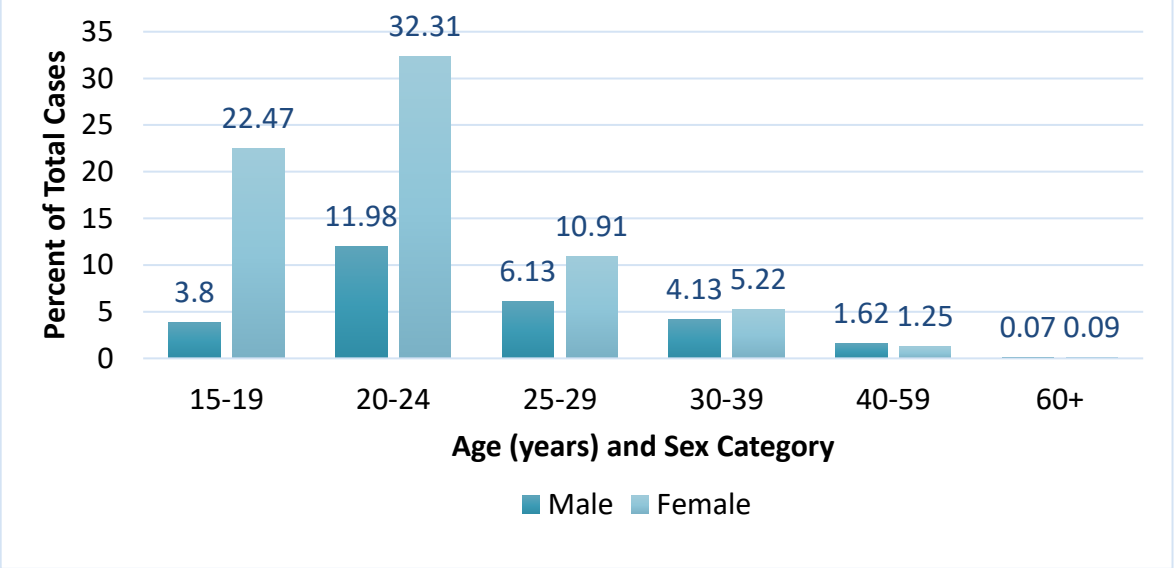

Figure 4.1. Percent of age-sex stratified *Chlamydia trachomatis* cases in NL for the study period of 2007 to 2013 (n = 4308).

Crude and Overall Incidence in NL

Summary statistics (mean, range, and SMR) for the overall *Chlamydia trachomatis* infection rates across the province are presented in Table 4.2. Over the study period, there were 1.303 cases per 1,000 person-years.

Table 4.2

Summary statistics for overall Chlamydia trachomatis infections in NL for the overall period of January 2007 to December 2013.

Population Strata	Mean Incidence Rate[1] (standard deviation)	95% Confidence Interval[1]	SMR[2]	95% SMR Interval[2]
Overall (Crude)	1.381 (±0.32)			
Overall (Standardized)	1.303 (±0.35)	1.255 – 1.332	0.447	0.414 – 0.485

[1] Incidence rate shown per 1,000 person-years
[2] In relation to standardized rate seen in Canadian population

Yearly crude incidence rates and age-sex standardized incidence rates are shown in Figure 4.2 and show an upward trend with peak rates of chlamydial infections in 2012 for the study period. The overall yearly incidence of chlamydia in 2013 was over double what it was in 2007.

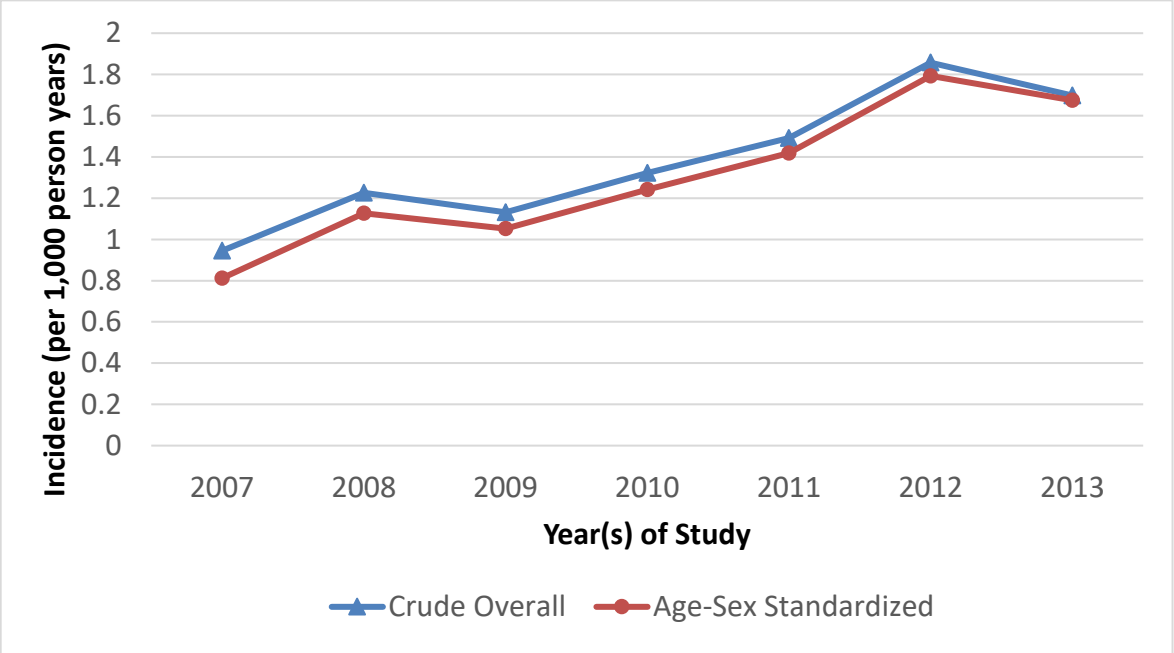

Figure 4.2. Crude and age-sex standardized incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

Seasonality of Incidence

A summary table with the incidence rates by season are presented in Table 4.3. Summer was found to have the highest incidence rate, though it was only 10 percent greater than spring which had the lowest rate of any season. Seasonality was not found to be significant as all four seasons had overlapping confidence intervals. Changes in incidence across each season of the study period are shown in Figure 4.3. As with the yearly incidence of chlamydia, seasonal incidence increased over time but with greater variance.

Table 4.3

Summary statistics of incidence of Chlamydia trachomatis in each of Winter, Spring, Summer and Autumn in NL between 2007 and 2013.

Season	Mean Incidence Rate[1] (standard deviation)	95% Confidence Interval[1]	SMR[2]	95% SMR Interval[2]
Winter	0.329 (±0.08)	0.308 – 0.347	0.453	0.385 – 0.529
Spring	0.308 (±0.10)	0.287 – 0.325	0.424	0.359 – 0.498
Summer	0.340 (±0.11)	0.317 – 0.357	0.468	0.399 – 0.545
Autumn	0.326 (±0.08)	0.305 – 0.344	0.450	0.382 – 0.526

[1] Incidence rate shown per 1,000 person-years
[2] In relation to standardized rate seen in Canadian population

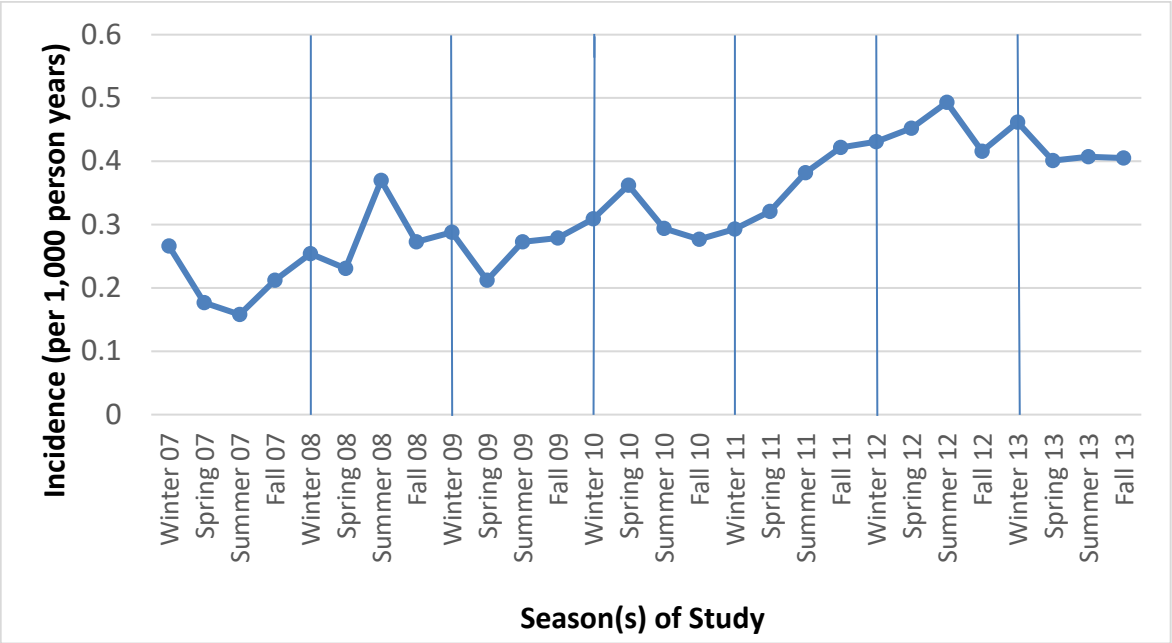

Figure 4.3. Seasonal age-sex standardized incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

Age- and Sex-Specific Incidence

Summary statistics for the age stratified and sex stratified rates are included in Table 4.4 below. The incidence of chlamydia in women was 2.5 times greater than in men over the study period. The age categories above 40 years of age had SMRs less than a quarter of the national average. The 20 to 24 years old category had roughly six times the overall age-sex standardized rate of 1.303 cases per 1,000 person-years. Age standardized incidence rates for each year for men and women are presented in Figure 4.4. Women had a higher reported incidence in all seven years of the study but both sexes showed increased rates over time. Sex standardized incidence for each year is shown in Figure 4.5 for the different age categories. Except for the 60+ year old age category, all other groupings saw a general increase across the study period. The highest rates were consistently found in the 15 to 19 and 20 to 24 years old categories. The largest relative increase was seen in the 25 to

29 years old category which was more than triple the incidence when comparing the start and end of the study period and the only age category that continued to increase in 2013.

Table 4.4

Summary statistics for age and sex for *Chlamydia trachomatis* infections in NL for the overall period of January 2007 to December 2013.

Population Strata	Mean Incidence Rate[1] (standard deviation)	95% Confidence Interval[1]	SMR[2]	95% SMR Interval[2]
Age Stratified				
15-19 year olds	5.209 (±0.73)	4.883 – 5.491	0.454	0.387 – 0.529
20-24 year olds	8.478 (±2.32)	8.114 – 8.881	0.545	0.482 – 0.613
25-29 year olds	3.324 (±1.44)	2.977 – 3.445	0.443	0.364 – 0.534
30-39 year olds	0.873 (±0.35)	0.786 – 0.958	0.311	0.238 – 0.402
40-59 year olds	0.107 (±0.02)	0.089 – 0.127	0.203	0.120 – 0.321
60+ year olds	0.009 (±0.01)	0.003 – 0.018	0.199	0.031 – 0.664
Sex Stratified				
Men	0.648 (±0.30)	0.699 – 0.784	0.370	0.318 – 0.430
Women	1.614 (±0.40)	1.765 – 1.894	0.488	0.443 – 0.535

[1] Incidence rate age-standardized for sex and sex standardized for age and is shown per 1,000 person-years

[2] In relation to standardized rate seen in Canadian population

Figure 4.4. Sex-stratified age-adjusted incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

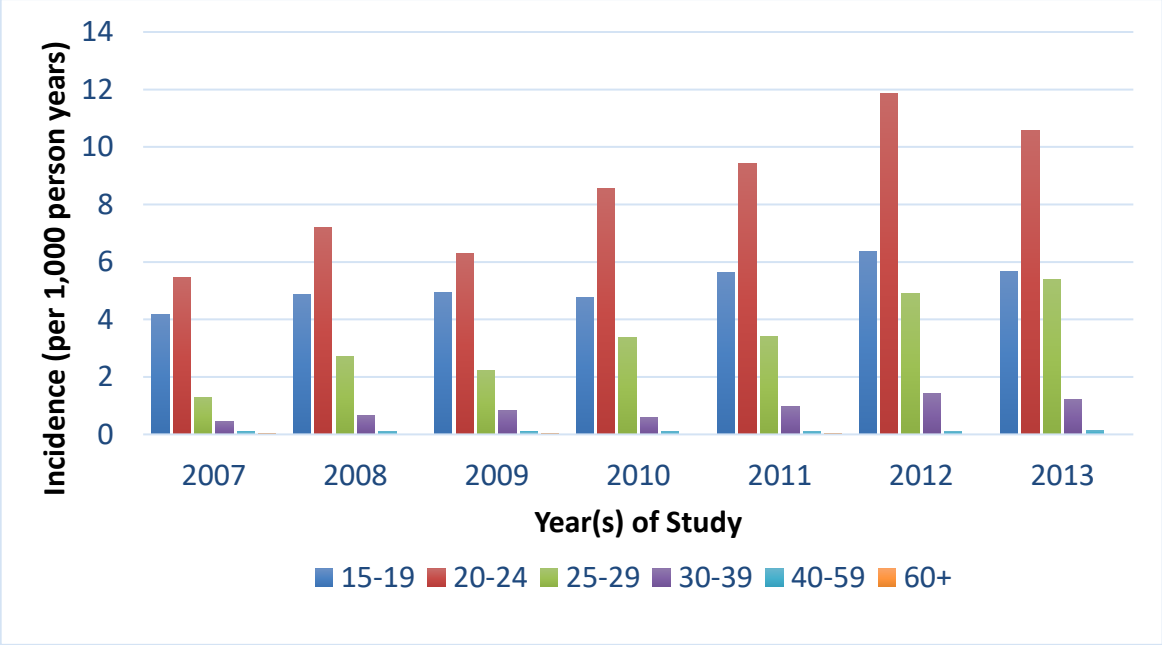

Figure 4.5. Age-stratified sex-adjusted incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

Negative binomial regression was conducted with year as a continuous variable. The results of the model are in Table 7.2 in Appendix B. A linear increase in incidence for the overall rates, while controlling for age and sex was observed. There was a statistically significant increase in chlamydia incidence rates (β=0.135; IRR=1.14; $p<0.01$) for each year of the study period. This means for each year, the rates of chlamydia increased by 14%. Age and sex were found to have a significant interaction in this model. The predictive number of cases for males and females by age, based on the above model is shown in Figure 4.6. An interaction between age and sex can be observed as the difference between the predicted number of cases for males and females became less as age increased. A table of these values is included in Appendix C for reference.

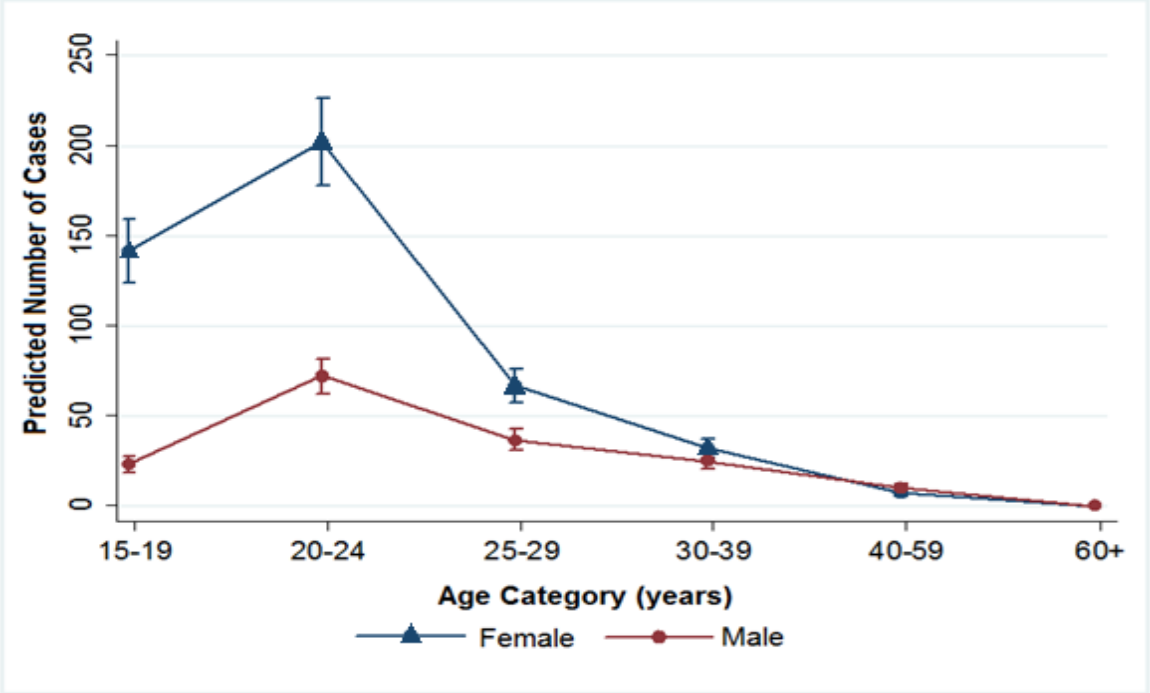

Figure 4.6. Predictive margins with 95% confidence intervals of *Chlamydia trachomatis* infections by age and sex in NL from 2007 to 2013.

Chlamydia Spatial Distribution

Urban and Rural Stratified Incidence

Table 4.5 displays the summary statistics for the urban versus rural rates in NL. Rural areas had a higher mean incidence rate for the overall study period. The age-sex standardized urban and rural incidence rates are shown in Figure 4.7. The incidence rate in rural designated areas was higher from 2007 to 2011, compared to urban areas, but urban incidence rates were higher in the final two years of the study period. Urban rates of chlamydia were roughly two thirds of rural rates at the beginning of the study period but gradually caught up with the rural rates and were roughly five percent higher in 2013. The locations of the urban and rural CSDs can be found in Figure 7.1 of Appendix D. As SACTYPE was used to define the urban/rural grouping, a proportional breakdown of the SACTYPE stratified cases for the full study period is in included in Figure 7.2 of Appendix E. This figure shows the clustering of CAs/CMAs around the capital city of St. John's, as well as around Corner Brook on the west coast.

Table 4.5

Summary statistics for urban-rural strata for *Chlamydia trachomatis* infections in NL for the overall period of January 2007 to December 2013.

Location stratification	Mean Incidence Rate[1] (standard deviation)	95% Confidence Interval[1]	SMR[2]	95% SMR Interval[2]
Urban	1.239 (±0.41)	1.182 – 1.280	0.427	0.383 – 0.473
Rural	1.397 (±0.26)	1.331 – 1.457	0.481	0.425 – 0.542

[1] Incidence rate is age-sex standardized and shown per 1,000 person-years
[2] In relation to standardized rate seen in Canadian population

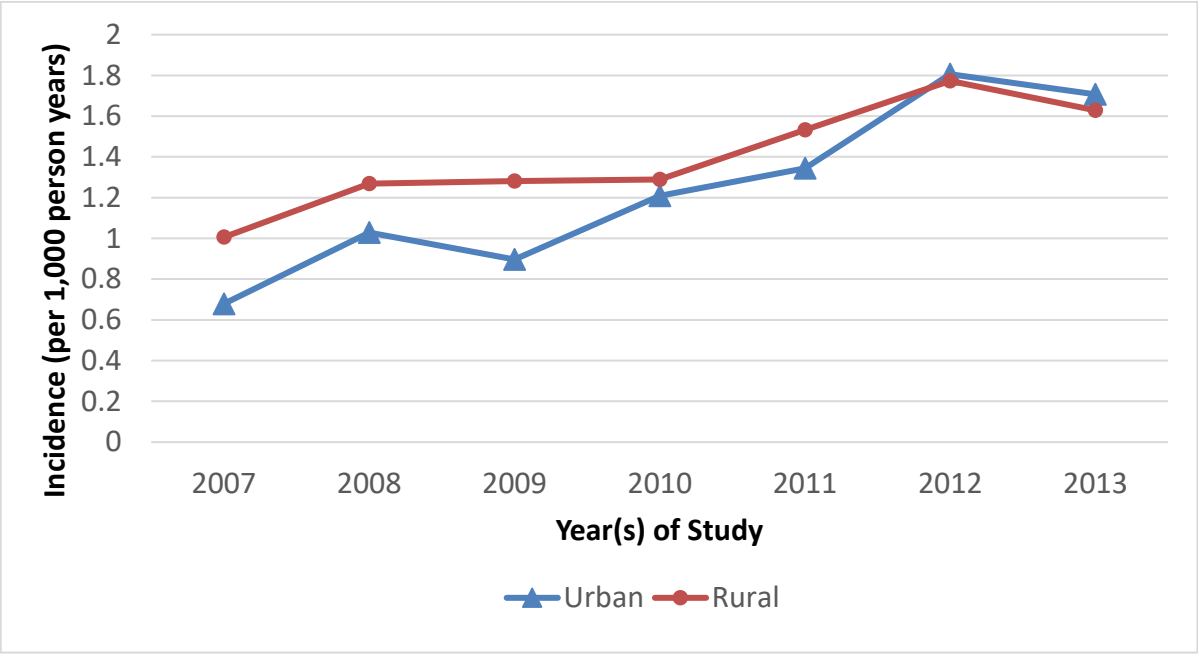

Figure 4.7. Urban-rural stratified age-sex adjusted incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

Incidence in NL Regional Health Authorities

Summary statistics for each RHA including the age-sex stratified rates are shown in Table 4.6 and Figure 4.8 shows the age-sex standardized yearly incidence for each of the RHAs. Table 4.6 shows Labrador-Grenfell having the highest rate for the overall time period of 4.55 cases per 1,000 person-years with an SMR of 1.567 while the others all had less than the provincial average. Incidence rates in the Central Health RHA were the lowest overall and increased by just over 30 percent. This region had a much smaller deviation than any other RHA. By the end of the study period, rates in the Eastern Health and Western Health regions had approximately doubled and tripled their respective rates found at the beginning of the study period. The most notable finding from assessing the RHAs was the high incidence in Labrador-Grenfell, which until 2013, had roughly four times the

incidence rates of the next highest RHA. It also did not follow the general upward trends of the other RHAs.

Table 4.6

Summary statistics for Chlamydia trachomatis infections in each RHA in NL for the overall period of January 2007 to December 2013.

Health Authority	Mean Incidence Rate[1] (standard deviation)	95% Confidence Interval[1]	SMR[2]	95% SMR Interval[2]
Eastern Health	1.189 (±0.37)	1.143 – 1.237	0.410	0.368 – 0.454
Central Health	0.391 (±0.08)	0.336 – 0.448	0.134	0.089 – 0.195
Western Health	1.182 (±0.55)	1.066 – 1.285	0.423	0.277 – 0.436
Labrador-Grenfell Health	4.549 (±0.48)	4.297 – 4.819	1.567	1.340 – 1.821

[1] Incidence rate is age-sex standardized and shown per 1,000 person-years
[2] In relation to standardized rate seen in Canadian population

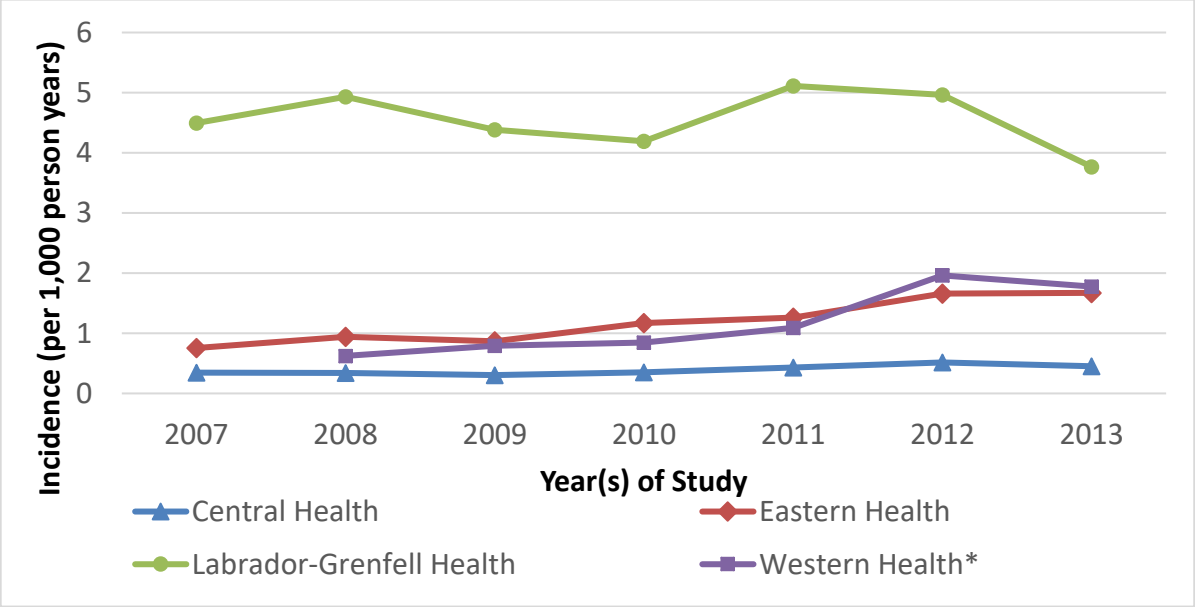

Figure 4.8. Health Region stratified age-sex adjusted incidence rates of *Chlamydia trachomatis* in NL from 2007 to 2013.

Incidence in CDs and CSDs

Figure 4.9 shows the overall age-sex standardized incidence of chlamydial infections. The rates were the highest in Labrador, with CD 1011 having the highest with an SMR of 5.30. The lowest rates were in Central Newfoundland. Figures 4.10 and 4.11 show the patterns of age standardized chlamydial incidence in men and women, respectively. Rates were highest in Labrador, but on the island of Newfoundland, the geographical distribution of the rates was more homogenous in women. Figures 4.12 through to 4.16 show the sex standardized incidence of individuals in the age brackets (years) of 15-19, 20-24, 25-29, 30-39 and 40-59. No choropleth map was produced for the 60+ age category due to an overall lack of cases in this demographic during the study period. Labrador CDs 1011 and 1010 had the highest and second highest incidence rates, respectively, in all age categories except for the 40-59 years old category. On the island of Newfoundland, higher incidence rates were consistently observed on the west coast (CDs 1004, 1005, and 1009) as well as CD 1001 on the east coast. Age-sex standardized rates at the CSD level are shown in Figure 4.17. This map shows a differentiation from the CD incidence rates in there being many areas without cases. Some of the highest rates were seen in the small northern Labrador CSDs of Nain, Natuashish, Makkovik, and Hopedale. A full listing of the CDs in NL with their respective geographical descriptions and populations can be found in Table 7.4 of Appendix F. A CSD incidence map is included in Figure 7.3 of Appendix G.

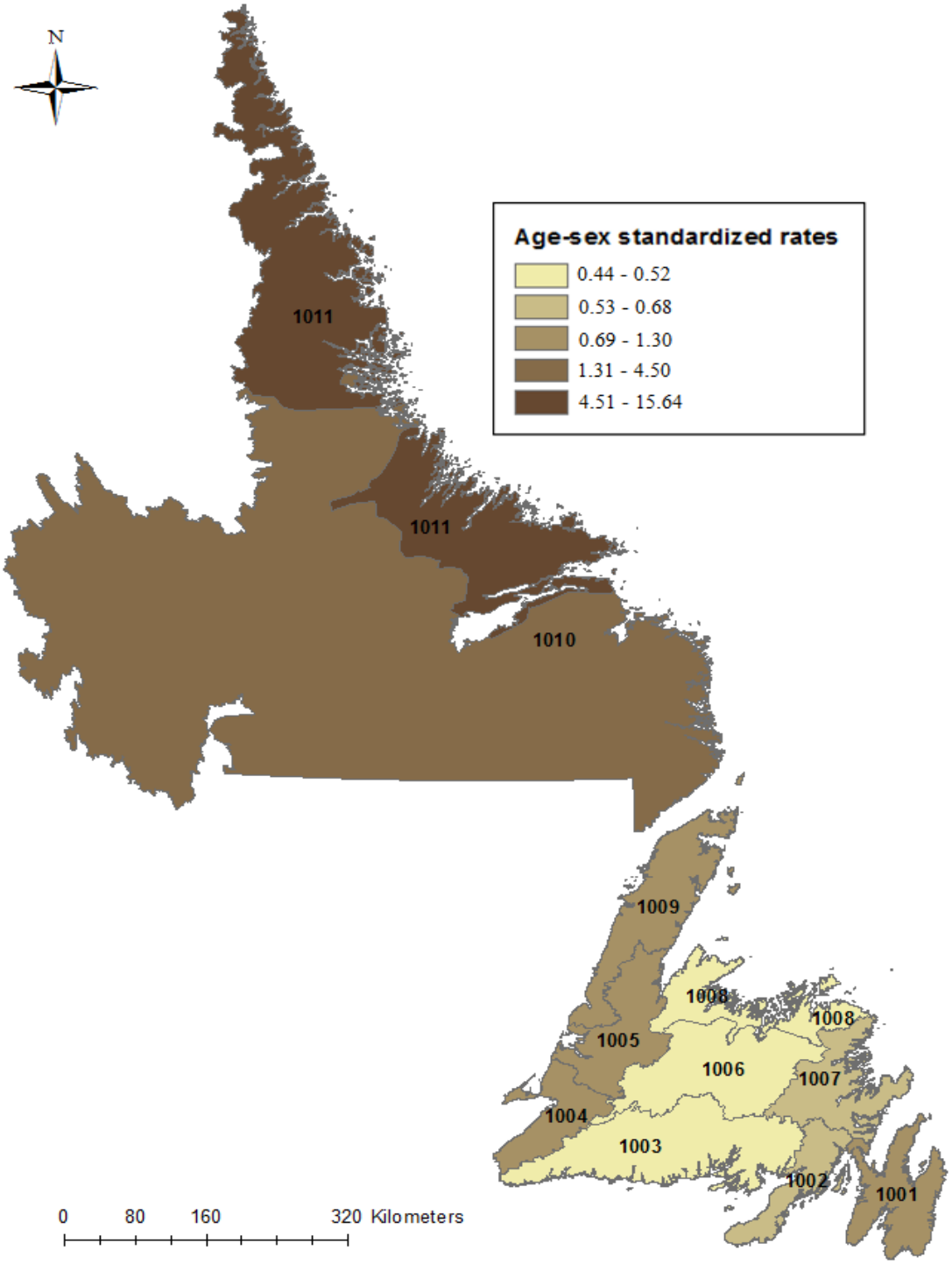

Figure 4.9. Overall age-sex standardized incidence per 1,000 person-years for chlamydial infections between 2007 and 2013 in NL – separated by CD.

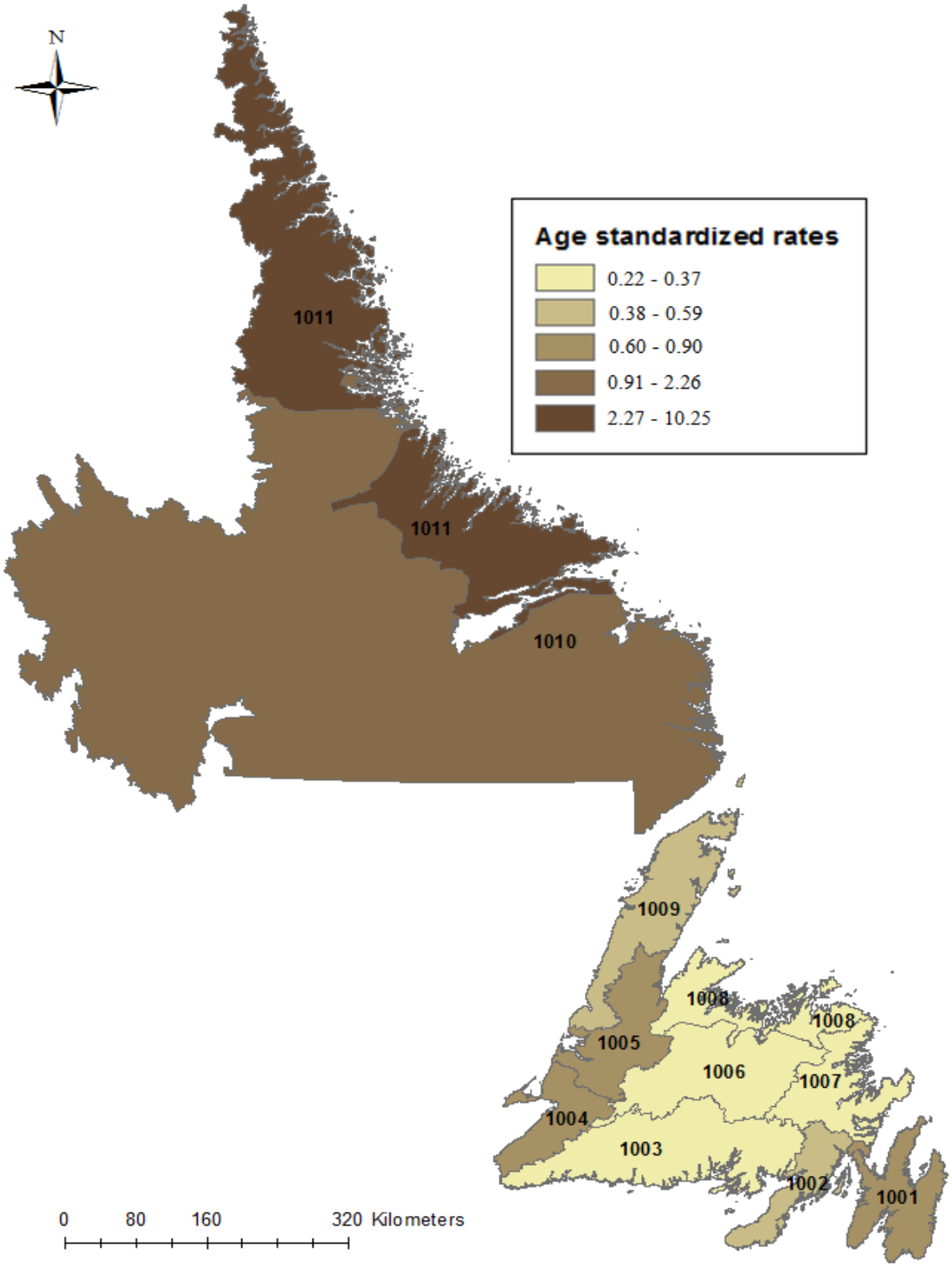

Figure 4.10. Age-standardized incidence per 1,000 person-years of chlamydial infections in men between 2007 and 2013 in NL – separated by CD.

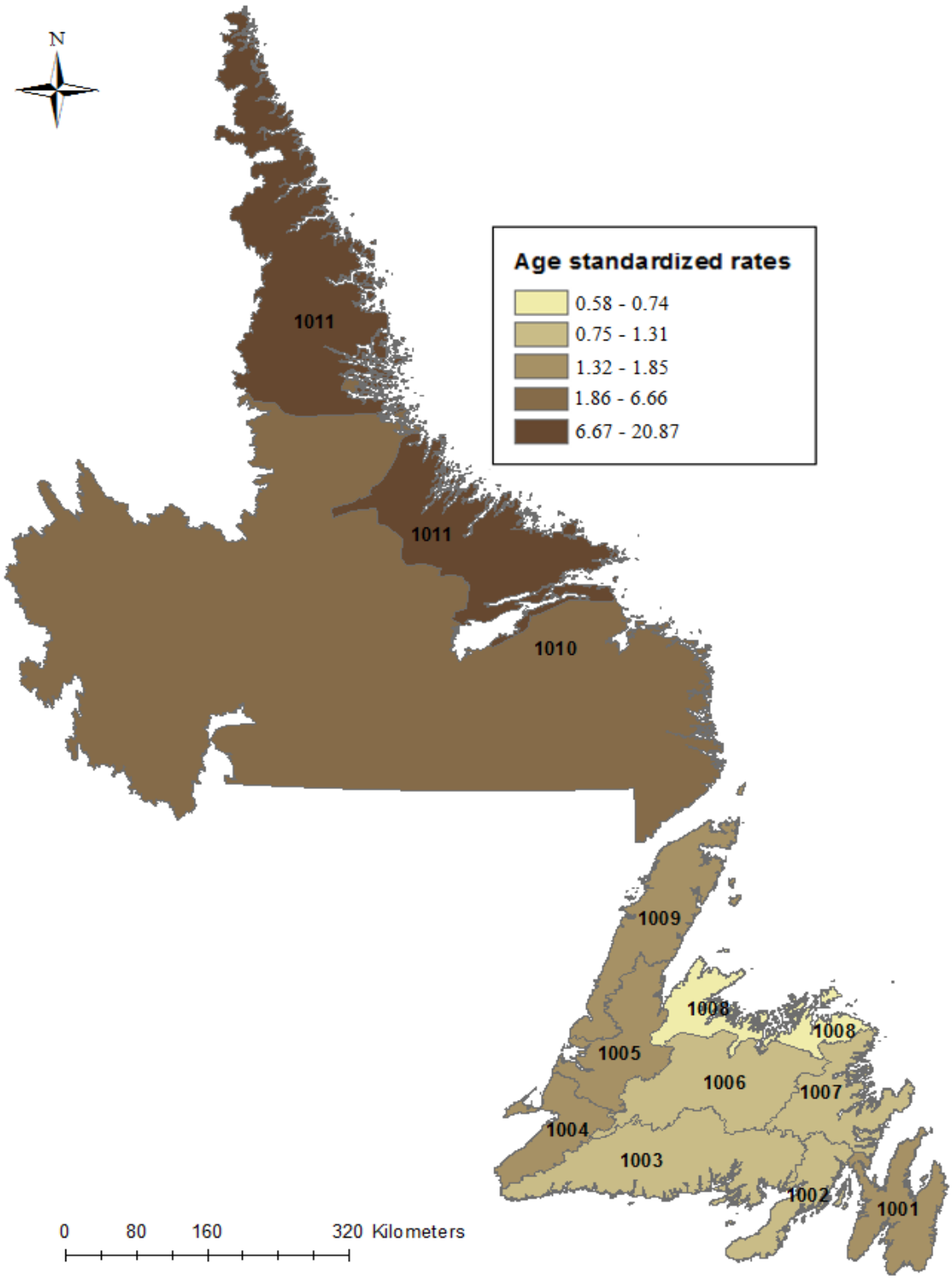

Figure 4.11. – Age-standardized incidence per 1,000 person-years of chlamydial infections in women between 2007 and 2013 in NL – separated by CD.

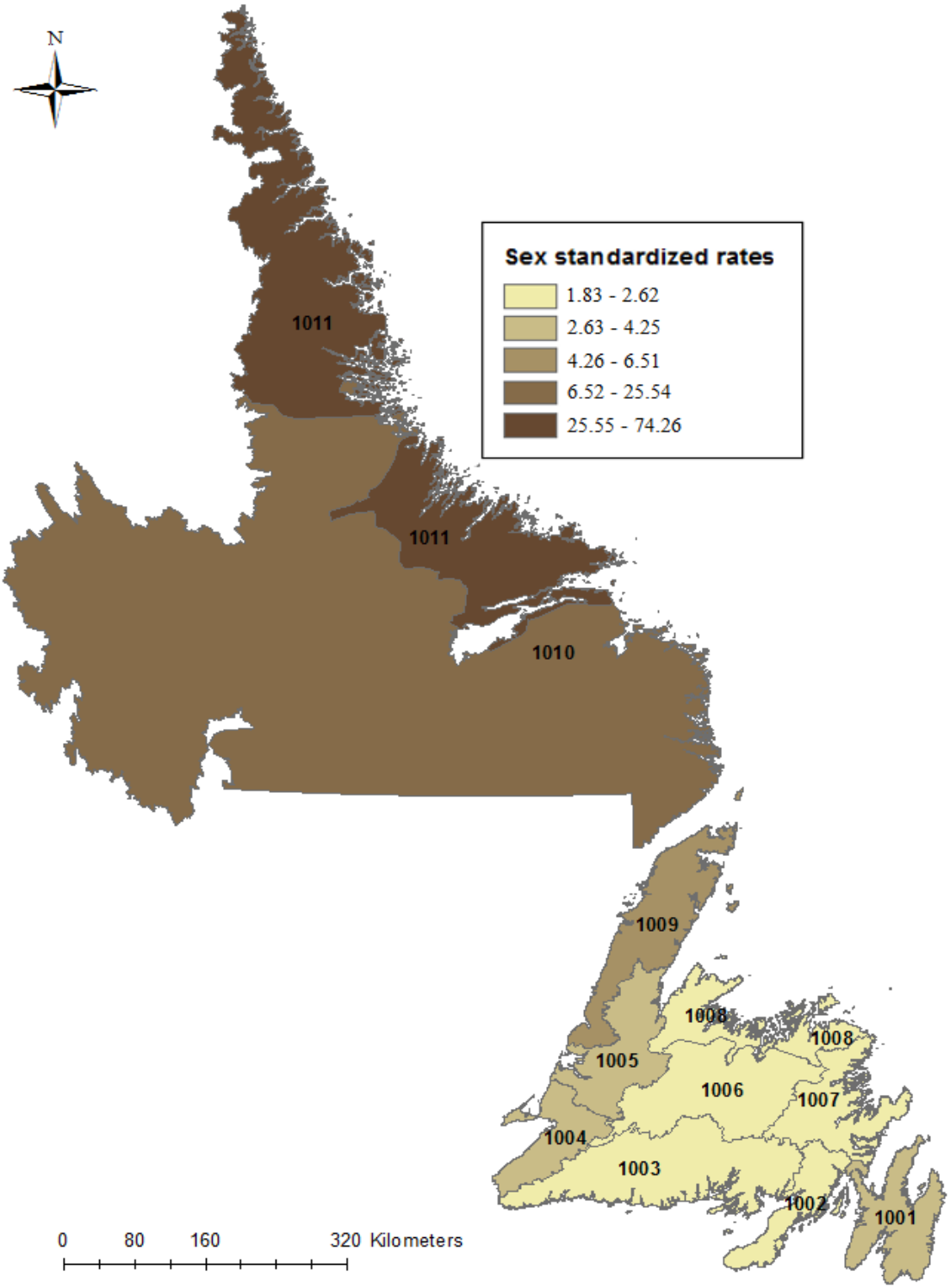

Figure 4.12. Sex-standardized incidence of chlamydial infections per 1,000 person-years in individuals 15 to 19 years of age between 2007 and 2013 in NL – separated by CD.

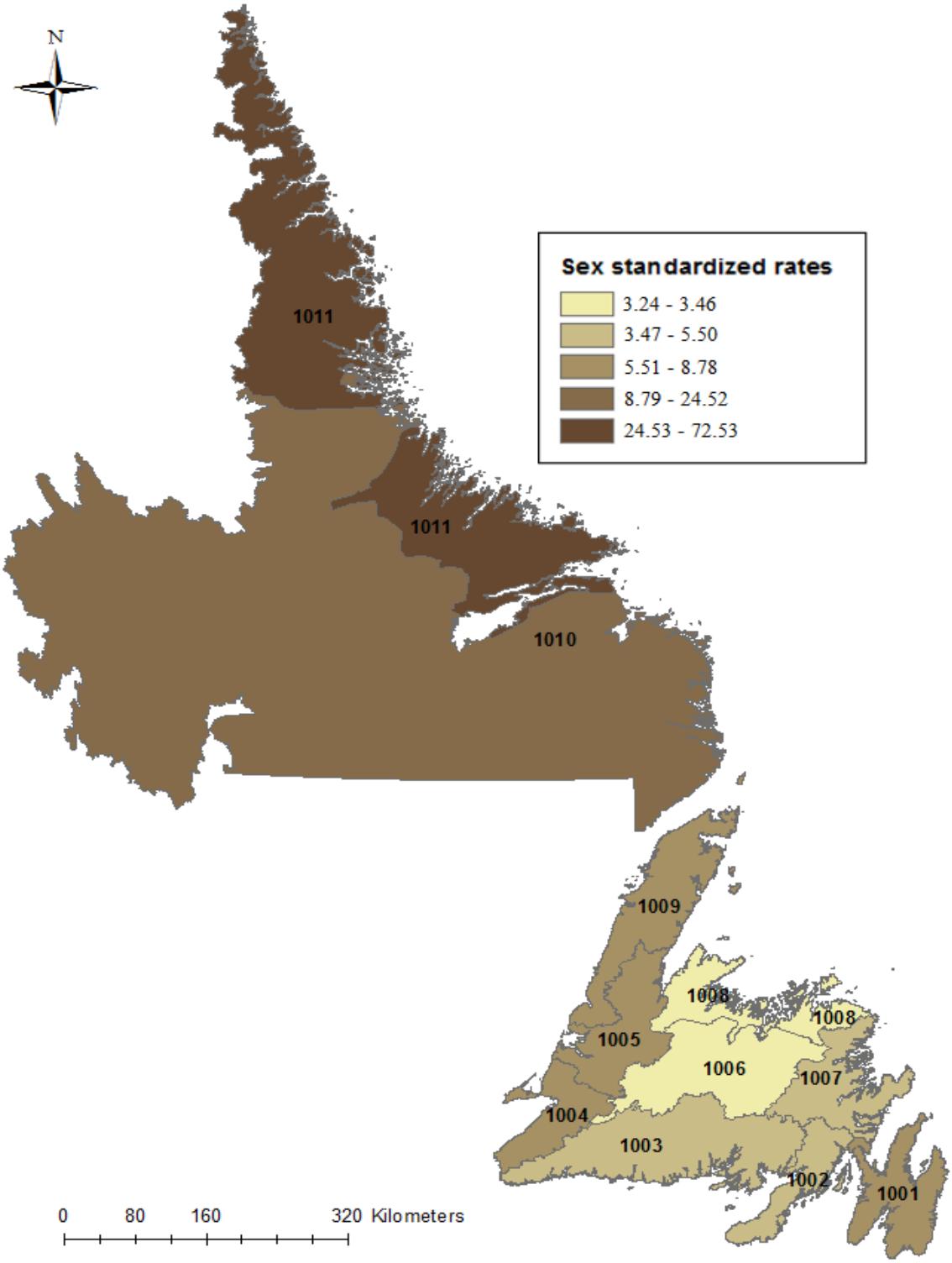

Figure 4.13. Sex-standardized incidence of chlamydial infections per 1,000 person-years in individuals 20 to 24 years of age between 2007 and 2013 in NL – separated by CD.

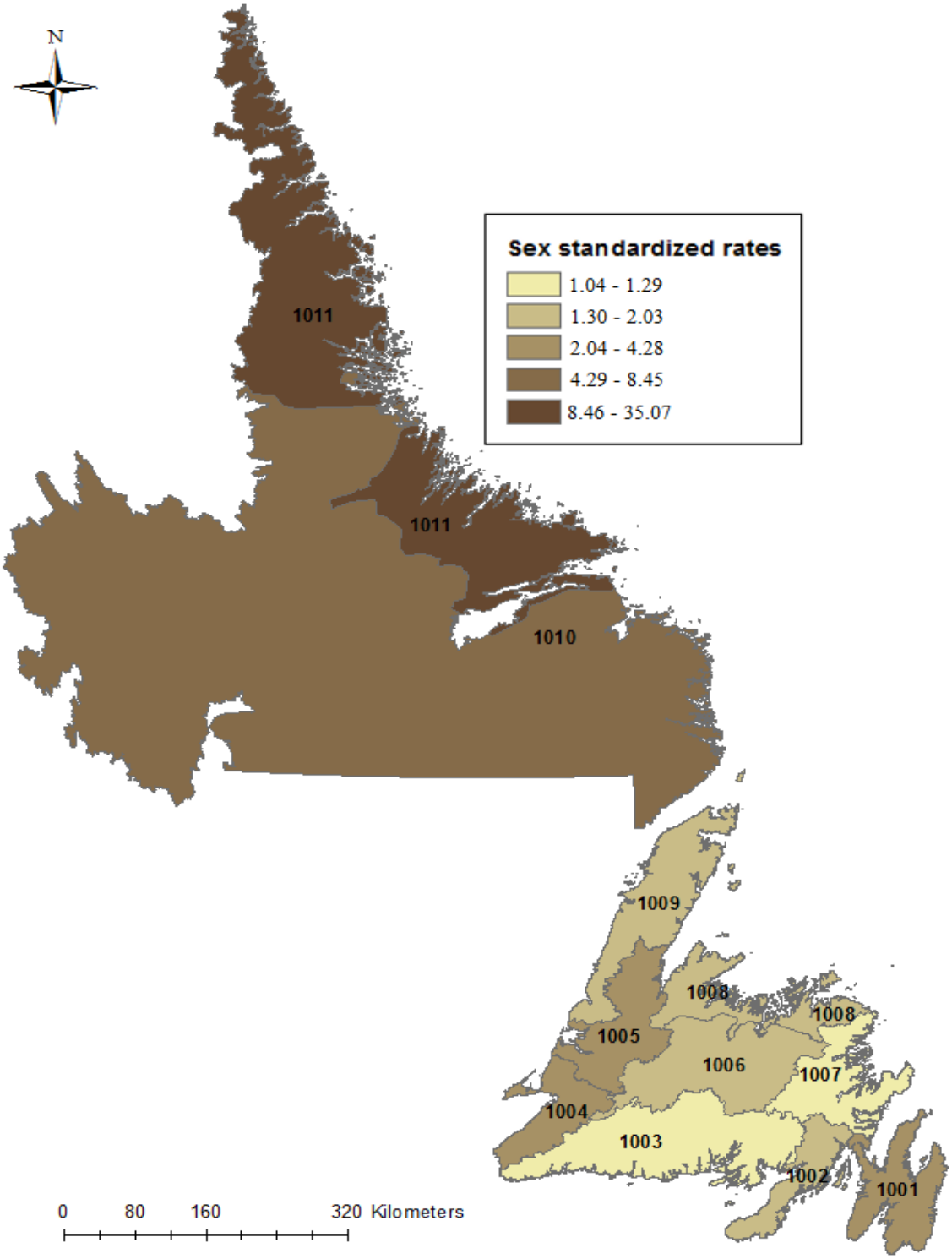

Figure 4.14. Sex-standardized incidence of chlamydial infections per 1,000 person-years in individuals 25 to 29 years of age between 2007 and 2013 in NL – separated by CD.

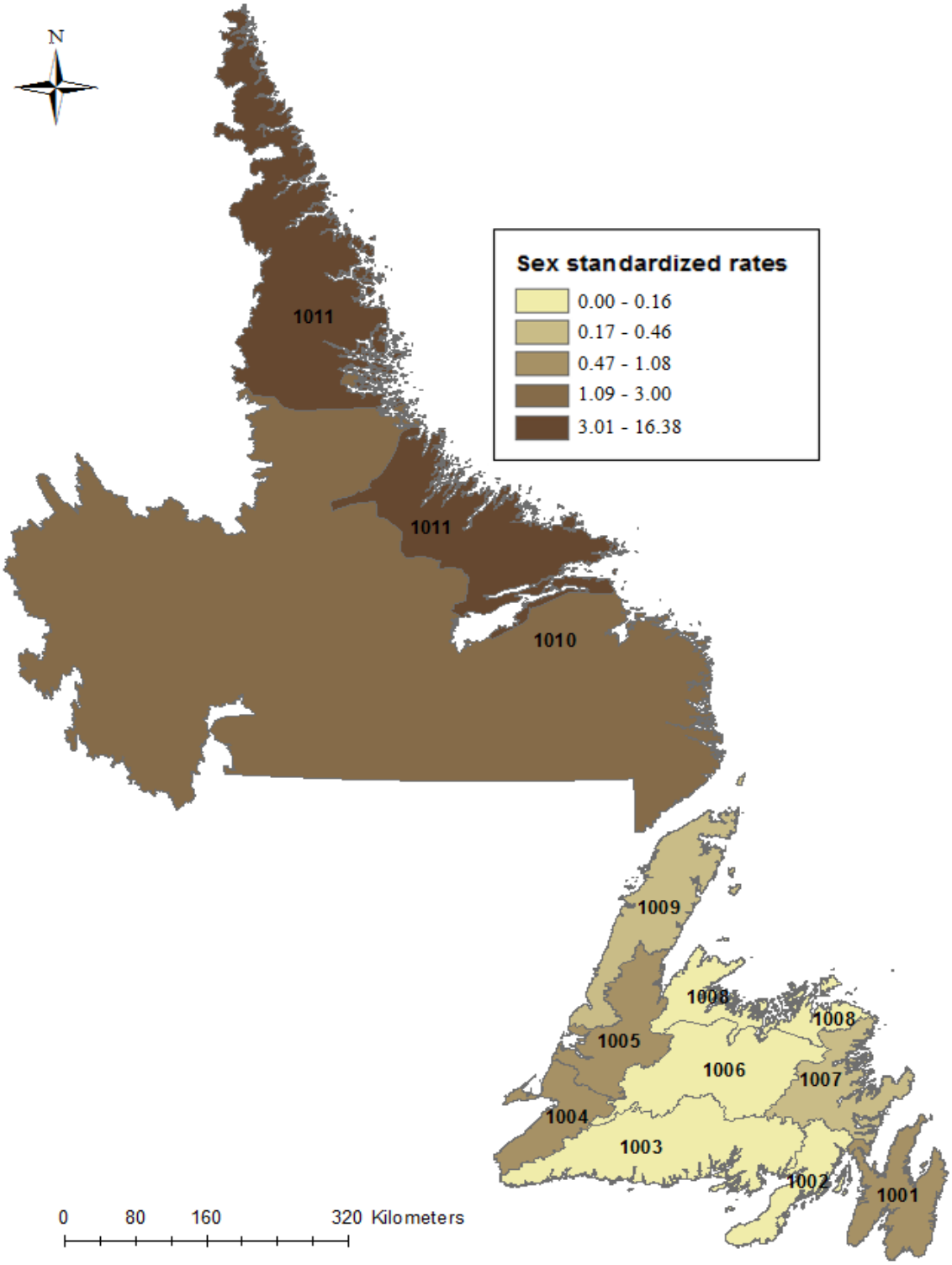

Figure 4.15. Sex-standardized incidence of chlamydial infections per 1,000 person-years in individuals 30 to 39 years of age between 2007 and 2013 in NL – separated by CD.

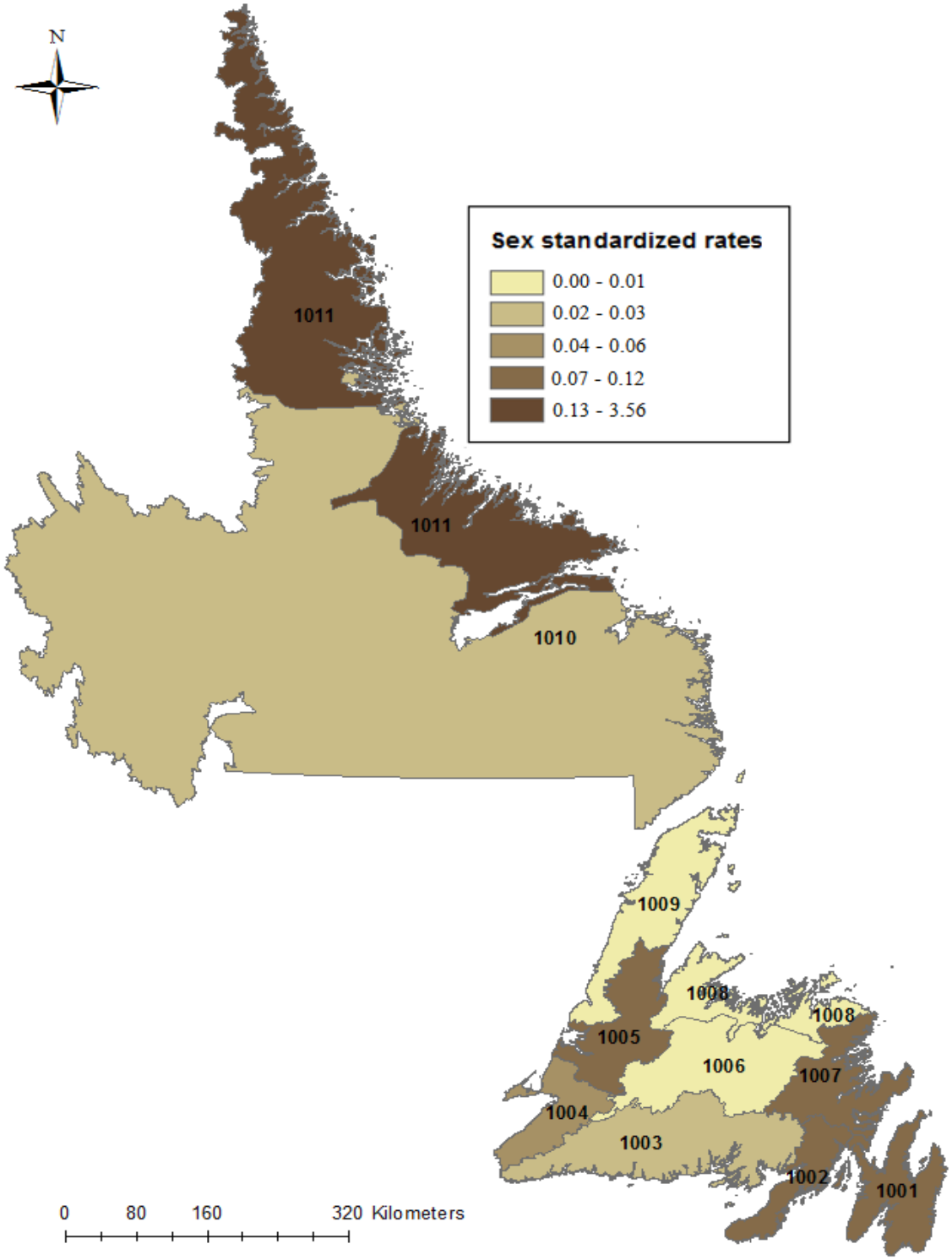

Figure 4.16. Sex-standardized incidence per 1,000 person-years of chlamydial infections in individuals 40 to 59 years of age between 2007 and 2013 in NL – separated by CD.

Global and Local Spatial Clustering

Moran's *I* and associated p-values are shown in Table 4.7. Weak positive spatial autocorrelation was observed for all age categories, except the 40-59 year old category, and the overall incidence rate. The 40-59 years old category was the only one that was found to be non-significant. The detected clusters from the Spatial Scan Statistic and their respective relative risk and p-values are shown in Table 4.8. The most likely cluster (relative risk of 6.98) was found to be in a sizable area of Labrador (CDs 1010 and 1011), while a secondary cluster (relative risk of 2.05) was found on the Avalon peninsula (CD 1001). The third cluster (relative risk of 61.03) on the Northern Peninsula (CD 1009) was significant, but had a small and unstable population. A map of the affected CSDs and the expected significant clusters from SaTScan are shown in Figure 4.17 below.

Table 4.7

Moran's I values for Chlamydia trachomatis infections for different age or sex groups between 2007 and 2013 in NL.

Population Strata	Moran's *I*	Significance (p-value)
Overall (Census Division)	0.183	0.004
Age Stratified		
15-19 year olds	0.204	0.001
20-24 year olds	0.197	0.002
25-29 year olds	0.160	0.008
30-39 year olds	0.149	0.011
40-59 year olds	0.082	0.065
Sex Stratified		
Men	0.158	0.008
Women	0.194	0.002
Overall (Census Subdivision)	0.050	0.001

Table 4.8

SaTScan spatial clusters of overall chlamydia incidence and associated relative risk between 2007 and 2013 in NL.

SaTScan Cluster	Affected CSDs	Significance	Relative Risk
1	1011015, 1011005, 1011020, 1011030, 1011010, 1010801, 1010022, 1010802, 1010042, 1010025, 1011035	p<0.001	6.98
2	1001519	p<0.001	2.05
3	1009047	p=0.018	61.07
4	1008063	p=0.115	15.09
5	1009004, 1009007	p=0.242	2.42

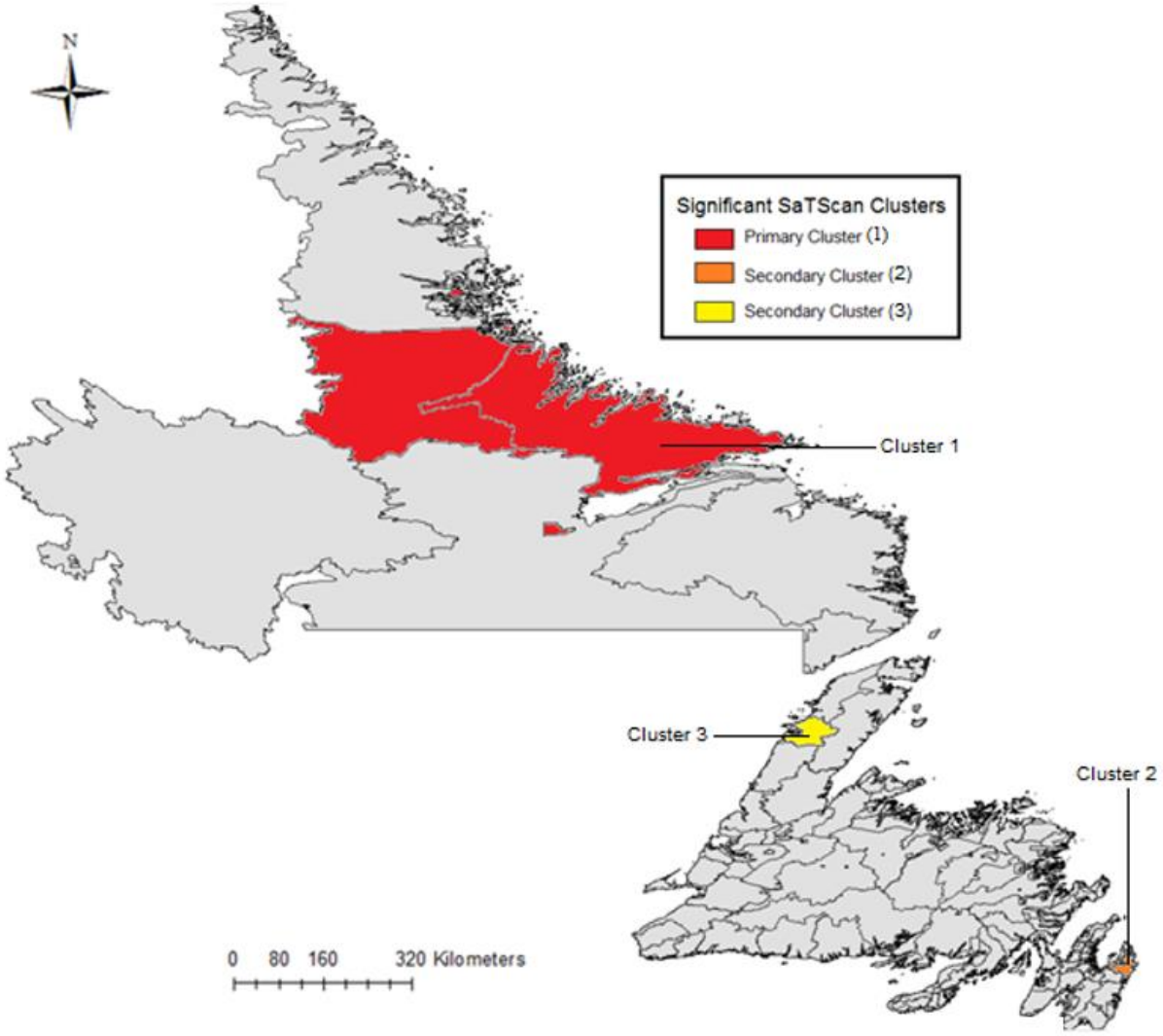

Figure 4.17. SaTScan spatial clusters of overall chlamydia incidence between 2007 and 2013 in NL – separated by CSD.

Employment Migration and Chlamydia Incidence

Descriptive statistics and associated chi-squared values for the employment information are included in Appendix H for both the 2006 Census of Population and the 2011 NHS. The results of the multivariate linear regression examining the association between chlamydia rates and employment factors are shown in Table 4.9. The percent of people in a CSD who commute to other provinces for work was negatively associated with the incidence of chlamydia in a CSD. This means that as the percent of people in a CSD who travelled outside the province for work increased, the number of people with chlamydial infections would decrease. This effect is multiplicative such that the higher the percent, the greater the effect. The percent of people in a CSD who work in the mining, oil & gas, and quarrying sector and percent of people who live in non-metropolitan influenced zones were significantly associated with the rate of chlamydia in a CSD and demonstrated a positive association (i.e., the higher the proportion of people, the greater the incidence rate of chlamydia, again with a multiplicative effect). The coefficient of determination (R^2) was 0.370 and indicates moderate influence, but also suggests that there were other unaccounted-for factors that are affecting the rates. For reference, the results of the univariate models for chlamydia with commuting, industry of work, and SACTYPE are included in Table 7.13 of Appendix I.

Table 4.9

Multivariate relationship between logarithmically transformed age-sex standardized chlamydial rates and logarithmically transformed employment factors for NL as determined by linear regression.

Variable (Percent of population that…)	β coefficient	95% Confidence Interval	p-value
Work in same CSD	-0.123	-0.514 – 0.268	0.532
Work in different CSD	-0.234	-0.598 – 0.131	0.205
Work in different CD	-0.125	-0.387 – 0.138	0.347
Work in different province	-0.370	-0.709 – -0.031	0.033
Industry A*	-0.012	-0.247 – 0.222	0.918
Industry B*	0.332	0.037 – 0.626	0.028
Industry C*	0.135	-0.310 – 0.580	0.547
Industry D*	-0.100	-0.432 – 0.231	0.547
Industry E*	-0.194	-0.543 – 0.156	0.273
Industry F*	0.362	-0.081 – 0.804	0.108
Other Industries*	0.385	-0.823 – 1.594	0.527
CA	0.242	-0.932 – 1.418	0.682
Strong-MIZ	0.625	-0.517 – 1.768	0.279
Moderate-MIZ	0.324	-0.704 – 1.352	0.532
Weak-MIZ	0.425	-0.615 – 1.465	0.418
Non-MIZ	1.888	0.645 – 3.132	0.003
Intercept (β0)	-7.874	-11.728 – -4.022	0.000

*****Industry A is agriculture, forestry, fishing, and hunting. B is mining, quarrying, and oil & gas extraction. C is construction. D is transportation and warehousing. E is professional, scientific, and technical services. F is administrative and support, waste management and remediation services. “Other” includes all miscellaneous industries noted in the appendices.

CHAPTER 5

DISCUSSION

Chlamydia Temporal Trends

Crude and Overall Incidence in NL

This study examined temporal trends in chlamydia incidence for the overall population in NL by year and season. The null hypothesis that yearly chlamydia incidence was constant over the study period was rejected. A significant increase in age-sex standardized incidence rates was observed from 2007 to 2013 and was supported by the negative binomial model meaning that the age and sex distribution of chlamydia rates were significantly different, and increased over time. Canada saw a similar rate of increase over time compared to NL during this time (Totten et al., 2015). Overall, the finding of this study was consistent with the literature as Canada wide rates of chlamydial infections were roughly double the rates seen in NL over the study period. One notable difference was that Canada saw a constant increase over the study period whereas NL had a small decrease in 2009.

Given the asymptomatic nature of chlamydial infections, it is likely that the estimated rates presented here were underestimations of the true number of cases that exist within the province. The assumption of underestimations in chlamydia incidence has been previously demonstrated (Weir, 2004). Attitudes towards sex have been changing for the past few decades and millennials (individuals born between 1982 and 1999) were shown to be more likely to participate in behaviours such as nonmarital sex, same-sex sexual activities, and sex at younger ages (Twenge et al., 2015). Twenge et al (2015) also showed that these behaviours, as well as the total number of sexual partners, have been steadily

increasing overall as recent as 2012 in millennials. Changing attitudes towards sex suggests increased promiscuity and the subsequent risk of exposure may be increasing the number of STIs transmissions observed.

Seasonality of Incidence

Our study confirmed the null hypothesis regarding seasonality. It was found that the incidence of chlamydia did not exhibit seasonal trends. This finding was contrary to the literature. Seasonal variation in human behaviour affects the transmission and growth of many pathogens (Grassly & Fraser, 2006). Seasonality of infections is also suggested to play a role in STI incidence rates as peaks are often seen in the summer and autumn, often due to increased opportunity for interaction (Cornelisse et al., 2016; Schroeder et al., 2001). In general, difficulty of transportation in the winter and spring months also leads to differing social behaviours such as lowered promiscuity and reduced healthcare accessibility (Wright & Judson, 1978). The timing of increased chlamydial infections in university populations have been associated to seasonality (Herold et al., 1993). Since the current study did not find such an increase during the school year (i.e., September to April), it could be suggested that the universities and colleges are not substantial reservoir for infection. Our findings suggest that seasonal behaviour noted in the literature elsewhere may not contribute to chlamydial infection rates in NL and that localized etiological factors should be examined in future studies in this province.

Age- and Sex-Specific Incidence

The study also examined the differences in incidence between men and women, as well as various age groupings. Hypotheses were made that no differences in these demographic strata existed in NL and that there were no interactions between age and sex.

Both hypotheses were rejected as incidence rates of chlamydia were higher in women, compared to men, and higher in the 25-29 years old age groupings and those younger than this. An interaction was also observed between age and sex which is discussed below. This trend was consistently observed over the study period as both sexes and most age groups saw a general increase in incidence rates.

These demographic differences in rates were similar to what was seen at the national level (PHAC, 2014). People under 30 years of age in both sexes represent a disproportionate amount of the chlamydial cases both at a national and provincial level. The 20-24 years old age category saw the most cases in both sexes in the study. Incidence rates at the national level in women were roughly double the rates in males while the findings in this study had women with rates closer to three times more likely than men to get chlamydia. While women had greater incidence rates compared to men, the actual incidence rates may be much closer because of the asymptomatic nature of chlamydia, better sexual health maintenance practices in women, or that men's health care utilization increases in older populations (Forward, 2010; Haworth-Brockman & Isfeld, 2009; PHAC, 2007). This difference decreases in the older age categories and men overtake women in both Canada and NL in those aged 40 years and above. Unprotected sex and having multiple partners is a common risk factor seen in young people (Rotermann, 2008). Overall, these risk factors may not be contributing substantially to the rise of chlamydia rates as their respective proportions of chlamydia in various subpopulations remained relatively unchanged in NL between 2003 and 2009/2010 (Rotermann, 2012).

Chlamydia Spatial Distribution

Urban and Rural Stratified Incidence

This study also assessed the geographic variation between urban and rural areas in NL. Rates were found to be initially higher in rural NL but became gradually equal to urban areas towards the end of the study period. Similar studies show that urban areas often have higher rates of STIs than rural areas (Raychowdhury et al., 2008). Rural NL has seen a shift in the demographic towards older populations which were shown to have lower rates of infection in both our study, and nationally (PHAC, 2014). Rural areas also have a greater migration to urban areas as well as other provinces. There has been a lower birth rate in rural locales as well as steady outmigration of young people to urban centers and other provinces (Simms & Greenwood, 2015). These factors may be contributing to urban rates overtaking rural rates, and a reflection of national trends as people under 30 years of age were shown to have higher rates of infection.

As many communities in rural NL are so small and isolated, it is difficult for clusters to form, possibly suggesting that sexual networks are linked to urban centers (Gesink et al., 2013; Thomas & Tucker, 1996). Urban areas would allow the greatest opportunity to expand sexual contact webs due to the highest risk of exposure as there are more sociocultural, economic, and geographical factors that could result in a higher risk of infection. For reference, Figure 7.1 in Appendix D shows the location of urban and rural CSDs in the province where the former includes CAs and CMAs with a population of greater than 10,000 person(s), while the latter includes MIZs with less than 10,000 persons. A similar pattern can be seen visually in the CSD map (Appendix G) with a greater number of cases around the urban centers of St. John’s and Corner Brook.

Statistical Area Classification was reclassified into urban and rural due to a lack of population data for the study period at the CSD level to accurately estimate age-sex standardized rates. The 2006 and 2011 Censuses show the rural population at 42 and 41 percent respectively while the Canadian average was 20 and 19 percent for these two years (Statistics Canada, 2011a). While NL effectively has double the rural population as the national average, the urban-rural divide was instead defined using the SACTYPE to examine the role of metropolitan influenced zones. Urban-rural status was also defined using SACTYPE to ensure congruence with the other research questions, allow for easy alignment with population information, and to minimize the error due to lack of precision in the case geography (i.e., postal codes not known for some case data). Given the small case count and population size over large areas for some CSDs, other methods of urban-rural assessment, such as through population density, were not feasible due to privacy reasons.

Incidence in NL Regional Health Authorities

The study found a difference in the incidence of chlamydia between the four RHAs in NL across the study period and the hypothesis that they had equal rates was rejected. Central Health had the lowest incidence rate while Labrador-Grenfell had a highest incidence rate during all years of the study period. Labrador-Grenfell is unique as it has the smallest population, the largest area, no urban centers, and the greatest number of indigenous communities. The rates observed in Labrador-Grenfell were driven by cases in Aboriginal communities which often have higher rates of infectious diseases including STIs (FNIGC, 2012). Labrador only has two communities with over 5,000 people (i.e., Happy Valley-Goose Bay and Labrador City), both located in the southern part of Labrador.

Northern communities have limited healthcare access as demonstrated in other studies (Wong & Regan, 2009). There may be an isolation aspect that inhibits access to health promotion, disease prevention, and education services. Additionally, there may be smaller social networks where core areas may be forming due to the distance required to find new partners (Gesink et al., 2013). There is also the potential that rates may be higher than presented here. Overall, the high rates were supported by the primary cluster that was found with the spatial scan statistic in northern Labrador.

All RHAs except for Labrador-Grenfell had peaks in 2012 that were consistent with the other incidence rate breakdowns (PHAC, 2015). Unlike the other RHAs or national trends, Central Health was both substantially lower in its rates as well as consistent in its yearly rates. The lower rates observed could be due to the region having an older population. This pattern may suggest that sexual networking remains small or rates may be related to migratory workers getting tested out of province which is feasible as two of the three CDs in the Central RHA had higher migratory populations (see Appendix H). Such testing in migratory workers may follow high risk behaviour as a result of changes in cultural norms (Goldenberg et al., 2008b; Organista & Organista, 1997). Lastly, a possible explanation is that sexual health education is better in this RHA which has been demonstrated to influence sexual behaviour (Kirby et al., 2007). Additional choropleth maps and tables are included in the appendices J and H respectively, which show the layout of the RHAs as well as the demographic distribution on different scales.

Incidence in CDs and CSDs

The spatial distribution of chlamydia incidence was assessed and contrary to the hypothesis, geographical variation of chlamydia incidence was found at both the CD and

CSD scales. The areas with the highest rates, CDs 1010 and 1011, were both in Labrador-Grenfell RHA. Census Divisions 1001, 1005 and 1006 contained the CAs and CMAs for the province. While the incidence in 1001 and 1005 were consistently higher, rates in 1006 (which includes the cities of Gander and Grand Falls – Windsor) were lower than average in all geographical comparisons. This may be due to the overall population demographic being skewed toward older ages and a lack of migration of young people to the area (Government of Newfoundland and Labrador, 2007b). Such demographic distributions may explain why there were fewer cases in most rural areas in NL.

Global and Local Spatial Clustering

The hypothesis that there were no clusters of incidence was rejected as the study also found both global and local clustering (i.e. – not a random spatial distribution). Global clustering, as measured by Moran's *I*, was found at both the CD and CSD levels. Significant clustering was also found for different age groups and sexes. In all cases, Moran's *I* found a weak positive autocorrelation. This finding should be interpreted cautiously because of the low number of CDs and missing information at the CSD level.

Local clustering was also observed at the CSD level for three areas in the province. The spatial scan statistic found the most likely cluster to be between CSDs in northern Labrador. This cluster may have been the result of high rates in the indigenous communities of Labrador which are predominantly in that part of the province. A secondary cluster found in the St. John's CSD which is a hub for younger populations due to being home to the university, colleges, and most of the province's commercial and recreational presence. The inflation in the relative risk in the third significant cluster in western Newfoundland was likely due an unstable estimate of disease incidence due to a

low population denominator in that CSD. Clustering of STIs, including chlamydia, has been demonstrated elsewhere but had not been extensively studied in Canada (Law et al., 2004; Schleihauf et al., 2009).

Employment Migration and Chlamydia Incidence

The study hypothesis that there was no relationship between chlamydia rates and people who commute for work, industry sector, and SACTYPE was rejected. A negative relationship between chlamydia rates and the proportion of people in NL who commute for work was found. As the percent of people in a CSD who travelled outside the province for work increased, the number of people with chlamydia infections decreased. Labrador CDs (1010 and 1011) had the highest rates of chlamydia overall and in almost every age and sex substrata but also had the lowest percentage of interprovincial workers in both 2006 and 2011 with less than two percent of the population migrating for work (see Appendix H). It can be concluded that employment related travel has a minimal influence on STI incidence in Labrador. There may be an influence of intraprovincial travel from workers travelling to Labrador for work (e.g. – Muskrat Falls) but the employment data does not show the destination CD. As a result, the relationships found in the multivariate model may not adequately explain the clustering of incidence when comparing different areas (i.e. – Labrador versus St. John's).

Other variables that were unavailable in the chlamydia case data may be playing a greater role in explaining the incidence, such as education level, ethnicity, or SES. When comparing chlamydia rates to CDs with high migratory employment percentages within the province, CDs 1007 and 1008 most often had lower than average rates of chlamydia in almost all categories which could show a limited influence of employment migration or

could be explained by other factors such as an older population residing there. Despite this finding and an overall decrease in interprovincial commuting between 2006 and 2011, the proportion of migratory workers who travelled to Alberta, Manitoba, Saskatchewan, and the territories all increased during this period (see Appendix H). These provinces/territories collectively comprise the top six spots for the highest chlamydia rates in Canada (PHAC, 2012).

Interprovincial commuter demographics have changed over the past several decades when the peak age used to be in the 30 to 49 years old range and with a more even split of men and women (Green & Meyer, 1997). The current study found more men than women commute between provinces as well as a more homogenized age distribution (see Appendix H). Commuting demographics have also changed between 2006 and 2011. Other current studies have found high rates of long distance commuting in young men, people from rural areas, and from industries such as mining, oil & gas and construction in NL (Haan et al., 2014; MacDonald et al., 2012; Morissette & Qiu, 2015). Young men as well as those commuting to work in the oil & gas industries in Canada have been shown to be at higher risk for STIs (Goldenberg et al., 2008b). Therefore, an increase in the number of people commuting and in these industries could explain increased rates of chlamydia.

Mining, quarrying, and oil & gas extraction industries were found to be a significant predictor of chlamydia incidence. Working in these industries may contribute to increased high risk behaviours; especially in younger people (Langille et al., 2005). Unlike oil & gas extraction, the relationship between mining and STIs has been noted in other countries but has not been extensively studied in Canada (Desmond et al., 2005; Palmer et al., 2002). Wabush and Labrador City have economies reliant on iron ore mining (Thistle,

2016). Both of these communities were located in an area that had a high incidence of chlamydia (i.e. – CD 1010). A more thorough investigation is needed to see if people are migrating in province to and from here and to see if a link exists.

SACTYPE was shown to be a significant positive predictor in the model for chlamydia incidence. People living in a non-MIZ CSD was associated with an increased risk of chlamydial infection. Weak MIZs and non-MIZs are where less than 5% of people travel to neighbouring urban centers for work, and made up 80% of the cases from rural areas (see Appendix E). This association may be due to limited health promotion programs such as sexual health education in rural, isolated areas (Goldenberg et al., 2008a; Nagarajan, 2004). However, it may also be due to health inequities such as poverty, substance abuse, or cultural norms, that limit the effectiveness of sex education and health promotion programs (O'Reilly & Piot, 1996).

The lack of significance of many of the NHS employment variables in explaining chlamydia incidence rates suggest that a different methodological approach (i.e. – not an ecological design) to examine the rate of employment migration in chlamydia incidence rates is required. A low coefficient of correlation between incidence rates and employment suggests that there are other covariates that require consideration. Demographic differences in sexual health education, health care access, ethnicity, or changing attitudes on sexual behaviour may be viable alternative explanations (Goldenberg et al., 2008a; Nagarajan, 2004; Twenge et al., 2015).

Limitations

Data Source(s) Limitations

Validity and generalizability of this study were dependent on the quality of the case information received from the RHAs as well as the population information. The NL Public Health Lab noted that the location of the case information may not be consistent with respect to whether the diagnostic address was chosen or their home address when referring to the community of residence variable (L. Gilbert, personal communication, November 2015). This could result in ambiguity on where the individual contracted the disease if they travelled to a metropolitan center for their diagnosis and/or treatment which could skew the geographical distribution. Overall, this limited or misclassified information could result in a misclassification bias, leading to underestimations of the number of cases in certain populations and/or areas.

Unreported cases from the population may bias the findings, especially in rural locations where the demographics are smaller and often skewed. Cases from NL residents who were tested outside of the province (such as potential migratory employees who were away for work when diagnosed) were not included in the analysis. Despite that this only applied to two cases in the datasets, there are likely many more that were not communicated back to RHAs in NL. No case data in 2007 from Western Health was provided so the overall estimation and change in incidence rates in this region may be underestimated. Similarly, the 60 cases that were dropped during the initial cleaning may have affected the rates if the cases were in smaller communities. Cases in the 10-14 years old age range were also not included, while they were included in national estimates of chlamydia incidence. Overall, observations dropped from analysis due to missing and

erroneous data could result in an underestimation of the actual number of individuals infected, resulting in a conservative estimate of the chlamydia rates.

The population used in the population at risk may be slightly skewed from year to year as the population for a given area was estimated for intercensal years, apart from 2011 population estimates which were based on the census for that year (Statistics Canada, 2011a). Many people travel to and from the province seasonally and since the estimate was only taken once at the middle of the year, the result may vary depending on whether such subpopulations are present. The population information from Statistics Canada on CD/CSD breakdowns of age and sex were rounded to a final digit of '5' or '0' which may cause substantial skewing in areas with very small and/or unstable populations. This is more noticeable in smaller rural areas where such circumstances could result in an underestimation or overestimation of the actual chlamydial incidence rate. Similarly, some CSDs had to be discarded as rates in these CSDs could not be age-sex standardized due to the case count being greater than the stratified population estimates. Between this barrier and the ethical restriction of only being able to show the rates of CSDs with five or more cases, only 90 percent of cases were allowed to be shown on the choropleth map.

Temporal Methodology Limitations

Considering that only the variables of age, sex, time, and location were provided, there may be other confounding variables that were not being accounted for with this project such as racial disparities, socioeconomic conditions, and screening programs in certain areas or populations (e.g., pregnant women). The NL population has one of the lowest levels of education in the country with roughly 35% of working age people having a high school education or less as of 2010 (Government of Newfoundland and Labrador,

2011). At the individual level, education may be a contributing factor in the possibility of transmitting an STI with higher levels of education being protective against contracting an STI (Annang et al., 2010). Improving educational attainment may have a positive impact in lowering chlamydia rates in the province. Sexual health education targeting areas with low levels of education may also prove beneficial. STI incidence rates have also been shown to differ by ethnicity which has been shown to be a contributing factor elsewhere but was not examined in the current study (Annang et al., 2010). While not available in the case data of the current study, controlling for these variables may have allowed for a better estimation of the relationship between employment migration variables and chlamydia incidence.

Spatial Methodology Limitations

The interpretation of the spatial analysis may be influenced by the modifiable area unit problem (MAUP) which can happen based on the level of aggregation used and pre-defined boundaries (Openshaw & Taylor, 1979). MAUP is a bias that can occur after data aggregation from one geographical scale to another that can reduce the representativeness of the results produced. This could have occurred in the study when combining the case data with the NHS variables at the provincial level when both were originally at the community level. The impact of this aggregation could be that generalizations are incorrectly made for the province when they are only relevant to certain areas.

A visual bias of map interpretation may result as larger areas are given more weight, visually, due to their size relative to smaller, more populous areas. Large geographical areas with small populations may also falsely show chlamydial infections as being a greater or lesser issue than they may actually be. An example of this could be with CD 1011 where most of the area is uninhabited but the shading of the results can mislead the reader into

believing that there was a high rate of infections over the entire geographical area. An example of this problem were the northern Labrador indigenous communities which were barely noticeable when looking at the map of CSDs but account for most of CD 1011's high incidence. As a result, larger areas with little to no population dominate the visual interpretation of the chlamydia rates on the map.

Only one map was created at the CSD level due to low case counts and/or population estimates which made the calculations infeasible in many locations. Some CSDs had more cases than population or cases in a location with no population estimate was available. This scenario would occur when the rounding of population estimates by Statistics Canada (to the nearest 5 or 0) of an age-sex category in a low population area was conducted to protect privacy. The result would falsely show that the number of people there in that category was zero, when in fact there may have been a greater than zero population estimate for that area. There were 180 CSDs (48%) with zero cases or an unstable population estimate which made mapping the rate not possible in that CSD. There were 129 CSDs (34%) that had between one and four cases and did not meet the ethics requirement to display. Overall, this meant that only 67 CSDs (18%) out of the 376 in the province could be properly displayed for visual assessment. Additionally, while the CSD level allows for better precision, these complications made it more difficult to assess, and as such, it was decided to display stratified geographical data at the CD level.

Estimates of Moran's *I* may not be reliable due to the small sample size at the CD level (i.e., 11). The spatial scan statistic is limited by missing and/or incomplete case or population data (Kulldorff et al, 2005; Kulldorff, 1997). Misclassified geographical location of cases may result in identified spatial clusters being missed or identified in a

different spatial location or imprecisely sized. Similarly, given the sparse data, some CSDs were included in the primary cluster (Northern Labrador) but had an incidence rate of zero or undefined (i.e., due to a population estimate of zero).

Employment Migration Limitations

The NHS was voluntary in 2011 and had a 68.9% response rate compared to a 93.8% response rate on the 2006 long-form census (Statistics Canada, 2013b). There may be some biases in estimates of employment migration variables that resulted due to some demographic groups having a lower response rate than others. For example. Low SES individuals were less likely to respond (Lorant et al., 2007). This may result in underestimations of the selected NHS variables in these groups. Furthermore, considering that the Census of Population and NHS are cross-sectional surveys, all answers collected with respect to one's dwelling or place of work were in relation to the week of May 1st to 7th of 2011. The limited time-period may bias employment rates in seasonal work because many of these workers may have been unemployed at the time of assessment, or working away from home. Given the fluctuations in the economy and migratory employment during the study period, there may be unaccounted variation across in these questions when generalizing to the 2011 snapshot (Laporte et al., 2013). Limited information is available on interprovincial employment as the self-reporting of working outside the province varies and was much lower in the NHS than what was seen in the 2010 provincial Work Activity Survey which shows eight percent of the workforce travels to and from the province compared to 3.66 percent in the 2011 NHS (Government of Newfoundland and Labrador, 2011). This discrepancy is important regarding the representativeness of the geographical information relating to employment.

There is a possible selection bias for the variables that were selected from the NHS such that other questions may have shown a relationship with chlamydia rates at the CSD level. For example, the negative relationship between chlamydia rates and interprovincial travel, there is the possibility that this conclusion is biased by individuals getting tested and treated in their work community outside of NL, which would lower the number of cases in this category. The elevated risk for people in the mining, quarrying and oil & gas sector may be due to another factor such as education or certain demographics being more likely to work in this industry, which were not controlled for inn this analysis. Lastly, the ecological design of the study links two datasets at the CSD level and concludes relationships between chlamydia rates and employment variables where they may not exist. Furthermore, ecological fallacies are a common problem with the interpretation of aggregated (areal) data and the conclusion(s) may be misleading in the deduction of conclusions on group-level data in this study (Greenland & Morgenstern, 1989; Openshaw, 1984).

Conclusions

Project Summary

Chlamydial infections are an ongoing health concern and is on the rise in NL. This project adds a descriptive and temporal perspective to infections caused by *Chlamydia trachomatis* in NL by showing the overall incidence rates, as well as rates stratified by age and sex between 2007 and 2013. Yearly rates significantly increased during the study period but seasonal trends were not observed. A breakdown by age showed individuals under the age of 25 as having the highest incidence rates, while women were found to have higher incidence rates than men. The rates of chlamydia were found to decrease as age

increased in both men and women. An interaction between age and sex was also observed. Understanding what demographics were affected will help with future prevention efforts in high risk demographics.

The spatial distribution of *Chlamydia trachomatis* in NL was assessed on several geographical levels. Urban areas had lower incidence rates than rural areas at the beginning of the study period but more at the end of the study period. For the RHAs, Labrador-Grenfell had the highest incidence rate while Central had the lowest. A breakdown by CD showed Northern Labrador with the highest rates of chlamydia in most demographic stratifications. Elevated rates were also seen on the east and west coast of Newfoundland but with lower incidence than seen in Labrador. Analysis at the CSD level provided a finer perspective on the incidence rate distribution, but the impact of low case counts and unstable populations on estimates limited the interpretation of the analysis at this spatial scale. Weak positive global clustering was observed on both the CD and CSD maps. Several local spatial clusters were found with notable locations in St. John's and Northern Labrador. Geographical visualization and subsequent analysis of chlamydia incidence in the province provides support for prioritizing the geographical areas most in need of STI prevention and intervention.

Commuting, industry of employment, and metropolitan influence were all found to be associated with chlamydial infections in NL. Interprovincial commuting was found to have a negative association with chlamydia incidence. This finding may imply that chlamydia infections are being predominantly spread by within province factors. However, a positive association was found with the mining, quarrying, and oil & gas industries as well as those people living in non-MIZ CSDs. These findings demonstrate that rural areas

and these industries may have unique sexual health risk factors compared to urban areas and other industries.

Policy Recommendations and Future Research

Treating chlamydial infections and their complications carries a growing financial burden in Canada that needs to be better addressed (Smylie et al., 2011; Tuite et al., 2012). Given that sexual networks typically form among people with similar demographic attributes, it can be assumed that the majority of the transmission is occurring within similar strata of the population (Laumann et al, 1994). Health promotion and education in the province should therefore be emphasized on younger people of both sexes as this is where most of the cases were found. Considering the difficulty with community interventions and the role of social determinants of health, some subpopulations may need a tailored message or additional supports for health promotion strategies to be effective (Marmot, 2005; O'reilly & Piot, 1996).

More comprehensive information on populations at risk of STIs is needed to allow for site specific prevention programs in NL. This gap can be addressed through an examination of which demographic groups are getting tested the most and least frequently. The results could help design better sexual education programs for groups that are less engaged with their sexual health. To potentially deal with the unknown number of undiagnosed cases in NL, the RHAs should adopt a similar screening model to Manitoba where all individuals under 25 that seek assistance from a health professional are encouraged to have STI testing done (Moses et al., 2002).

Examining if rural sexual health needs such as accessibility to physicians and testing are being adequately met could similarly be studied as there has shown to be a

disparity in health care access on the urban-rural continuum (Sibley & Weiner, 2011). Many areas of high incidence were found in Labrador and more efforts should be made to intervene in isolated communities on the north coast. Several areas of high incidence in Labrador were notably where some Innu communities are located. Aboriginal peoples in Canada have been shown to have elevated rates of infectious diseases including STIs (Adelson, 2005; Beaudoin et al., 2005). Future studies could look at ethnic or racial differences in chlamydial incidence in NL including the impact it has on indigenous communities.

Sexual health issues in the Atlantic Provinces stem from broad issues including unstable economies, chronic unemployment, and low education; all of which limit individuals' coping with factors that influence safe sexual practices (PHAC, 2006). The Census of Population is useful as a starting point for assessing migratory employment trends but longitudinal and qualitative research would be needed to get a better picture of how this relates more directly to their sexual health. Overall, this evidence can help the province and its RHAs to design better public policy to support and maintain positive and safe sexual practices through the improvement of both individual and community capacities around sexual health.

Overall, while chlamydia rates were lower than the national average, the stratifications by age and sex were shown to be similar. This project adds a new perspective that there is a possible link between chlamydia and the mining, quarrying, oil & gas industries in NL. Further investigation is needed on the role of commuting and testing in other provinces. As many provinces only use case counts and crude rates for reporting

STIs, the framework of this study could also be used to better stratify and understand who is at risk.

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APPENDIX A

A breakdown of the NAICS categories are included in Table 7.1 with the grouping into miscellaneous if they lacked a relationship to migratory employment in Canada.

Table 7.1

Summary of 2007 NAICS sectors and miscellaneous industry grouping.

Industry Sector	Original Code (2006 / 2011)	Grouping Code
Agriculture, forestry, fishing and hunting	02 / 11	N/A
Mining, quarrying, and oil and gas extraction	03 / 21	N/A
Utilities	04 / 22	Miscellaneous (01)
Construction	05 / 23	N/A
Manufacturing	06 / 31	Miscellaneous (01)
Wholesale trade	07 / 41	Miscellaneous (01)
Retail trade	08 / 44	Miscellaneous (01)
Transportation and warehousing	09 / 48	N/A
Information and cultural industries	10 / 51	Miscellaneous (01)
Finance and insurance / management of companies and enterprises	11 / 52	Miscellaneous (01)
Real estate and rental and leasing	12 / 53	Miscellaneous (01)
Professional, scientific, and technical services	13 / 54	N/A
Management of companies and enterprises	14 / N/A	Miscellaneous (01)
Administrative and support, waste management and remediation services	15 / 56	N/A
Educational services	16 / 61	Miscellaneous (01)
Health care and social assistance	17 / 62	Miscellaneous (01)
Arts, entertainment, and recreation	18 / 71	Miscellaneous (01)
Accommodation and food services	19 / 72	Miscellaneous (01)
Other services (except public administration)	20 / 81	Miscellaneous (01)
Public administration	21 / 91	Miscellaneous (01)
Not available	01 / 88	Miscellaneous (01)
Not applicable	01 / 99	Miscellaneous (01)

APPENDIX B

Table 7.2 below shows the age and sex stratification of the negative binomial regression model of chlamydia cases. A statistically significant increase over the study period. The 15-19 year old females were used as the reference group(s) and therefore combinations using these two groups cannot be individually calculated in the model.

Table 7.2

Negative binomial regression model of chlamydia case count offset by the population for time (years) while examining the interaction between age and sex between 2007 and 2013 in NL.

Variable	β coefficient	95% Confidence Interval	p-value
Year of diagnosis	0.135	0.110 – 0.160	< 0.001
Females*	-	-	-
Males	-1.850	-2.073 – -1.626	< 0.001
15-19 years old*	-	-	-
20-24 years old	0.307	0.137 – 0.477	< 0.001
25-29 years old	-0.848	-1.034 – -0.662	< 0.001
30-39 years old	-2.296	-2.505 – -2.087	< 0.001
40-59 years old	-4.631	-4.944 – -4.318	< 0.001
60+ years old	-6.947	-7.941 – -5.953	< 0.001
20-24 year old males	0.790	0.503 – 1.077	< 0.001
25-29 year old males	1.337	1.029 – 1.646	< 0.001
30-39 year old males	1.658	1.324 – 1.991	< 0.001
40-59 year old males	2.134	1.688 – 2.580	< 0.001
60+ year old males	1.681	0.159 – 3.202	0.030
Intercept (β0)	-276.194	-326.940 – -225.447	< 0.001

Alpha parameter = 0.020; Likelihood ratio test of alpha = 36.49, p <0.001
*Reference group

APPENDIX C

The predicted number of events (i.e., margins) for the above negative binomial model are shown in Table 7.3 below and demonstrates the interaction between age and sex for the chlamydia cases.

Table 7.3

Predictive margins of chlamydia case count offset by the population for the categories of age and sex between 2007 and 2013 in NL.

Grouping (age and sex)	Margin	Standard Error	95% Confidence Interval	z-score	p-value
15-19 females	143.39	9.23	125.30 – 161.49	15.53	< 0.001
15-19 males	23.52	2.26	19.10 – 27.95	10.42	< 0.001
20-24 females	201.32	12.37	177.08 – 225.56	16.28	< 0.001
20-24 males	72.17	5.10	62.17 – 82.16	14.15	< 0.001
25-29 females	66.68	4.81	57.26 – 76.10	13.88	< 0.001
25-29 males	36.90	3.06	30.90 – 42.89	12.05	< 0.001
30-39 females	32.21	2.80	26.72 – 37.69	11.52	< 0.001
30-39 males	25.05	2.34	20.46 – 29.64	10.71	< 0.001
40-59 females	7.73	1.14	5.50 – 9.97	6.80	< 0.001
40-59 males	10.06	1.33	7.46 – 12.66	7.58	< 0.001
60+ females	0.57	0.29	0.008 – 1.14	1.99	0.047
60+ males	0.43	0.25	-0.058 – 0.92	1.72	0.085

APPENDIX D

Figure 7.1 below shows the distribution of urban and rural areas in the province using the SACTYPE classification system for CSDs. CAs and CMAs have populations greater than 10,000 people and are predominantly centralized around St. John's and Corner Brook.

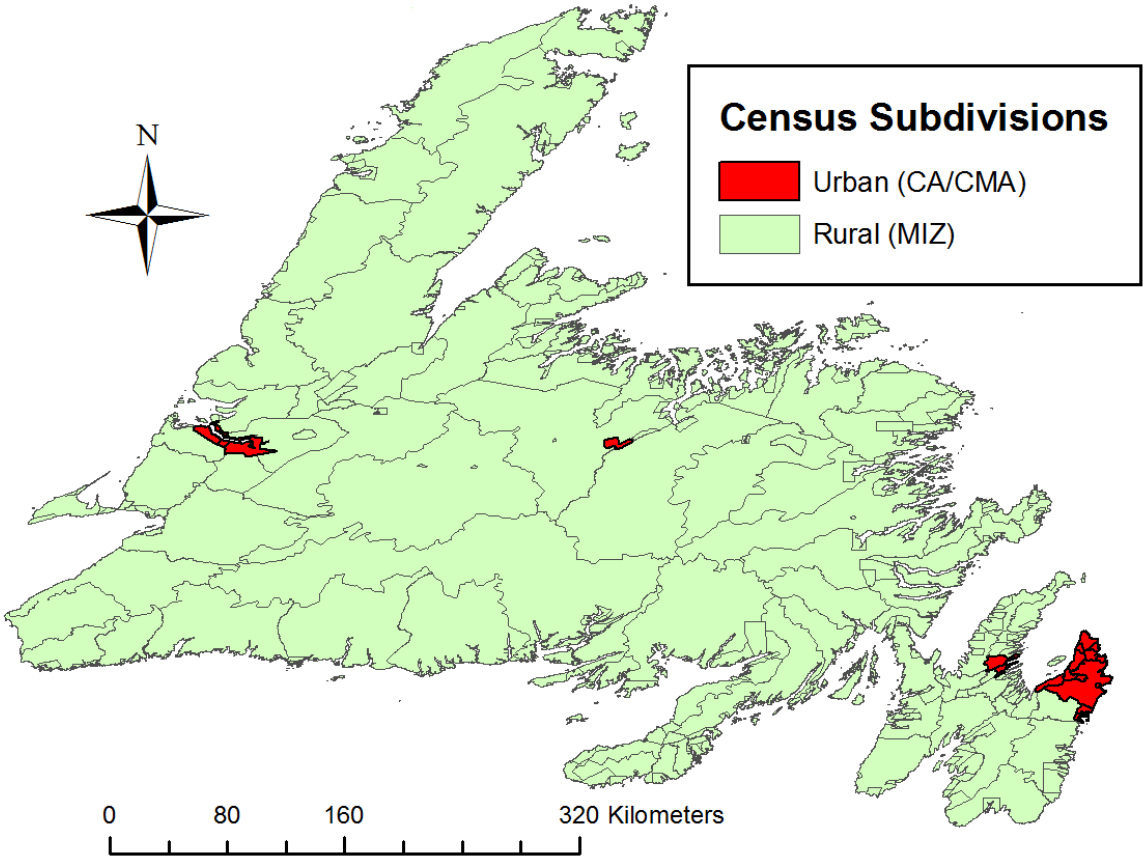

Figure 7.1. CSDs of Newfoundland separated by SACTYPE into 'Urban' (CAs and CMAs) and 'Rural' (MIZs). Note: Labrador not included as all CSDs are classified as MIZs (light green).

APPENDIX E

A breakdown of the percent of cases by SACTYPE is included in Figure 7.2 below. A breakdown of rates by SACTYPE was not included in the main analysis due to stratified CSD population information only being available in 2011 of the study period, and many CSDs having unusable populations for rate calculations.

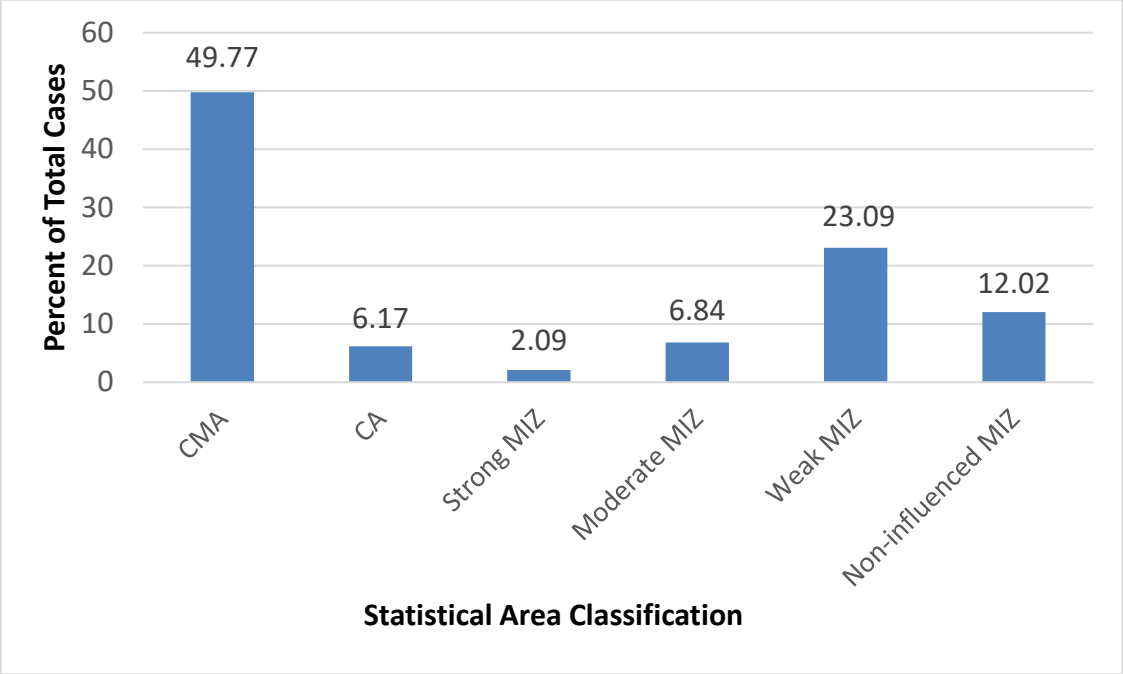

Figure 7.2. Percent of *Chlamydia trachomatis* cases in NL CSDs based on SACTYPE for the period of 2007 to 2013 (n = 4308).

APPENDIX F

Table 7.4 shows a stratification of the population by CD as well as their respective descriptions. The largest CD (1001) is the Avalon Peninsula on the east coast of the island and includes almost half of the province's population around the capital of St. John's.

Table 7.4

Descriptions of Census Divisions in NL from the 2011 Canadian Census of Population.

Census Division Code	Census Division Name	Population 15+ years old
1001	Avalon Peninsula – St. Johns	222,325
1002	Burin Peninsula – Marystown	18,375
1003	South Coast – Channel-Port aux Basques	14,135
1004	St. George's – Stephenville	18,025
1005	Humber District – Corner Brook	35,035
1006	Central Newfoundland – Grand Falls-Windsor	31,495
1007	Bonavista/Trinity – Clarenville	30,090
1008	Notre Dame Bay – Lewisporte	32,375
1009	Northern Peninsula – St. Anthony	14,640
1010	Labrador – Happy Valley-Goose Bay	19,400
1011	Nunatsiavut – Nain	2,005

APPENDIX G

One choropleth map was produced for age-sex standardized rates for all CSDs in NL in Figure 7.3. CSDs with less than five cases and/or those with zero population at risk for a given age-sex strata were not included in the analysis and were included in a separate "insufficient" category on the choropleth map.

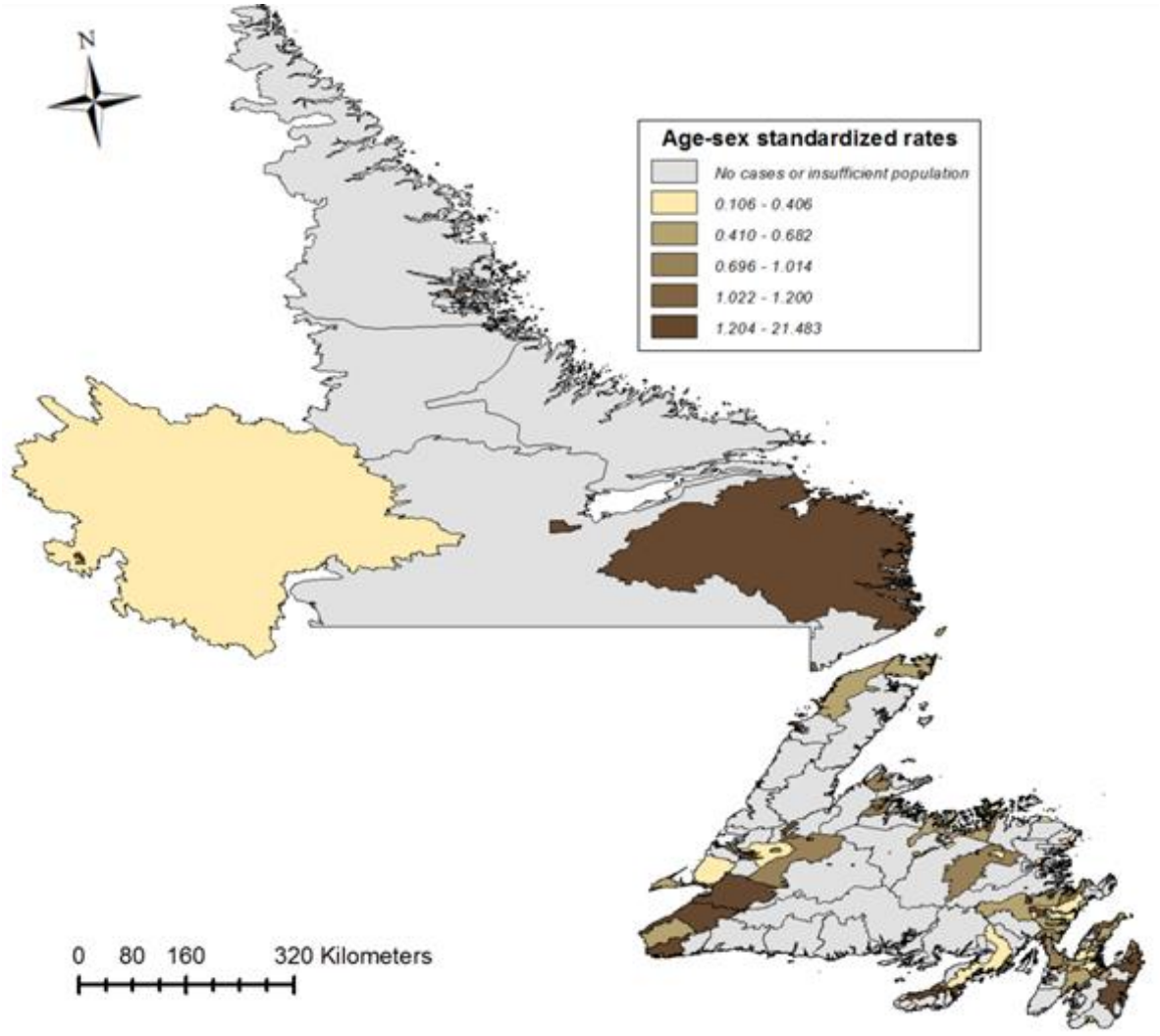

Figure 7.3. Age-sex standardized incidence per 1,000 person-years of chlamydial infections between 2007 and 2013 in NL – separated by CSD.

APPENDIX H

To assess how far people travelled for work, comparisons were made using simple proportions for work related commuting (PWCOMMUT) that compared NL to the Canadian averages using both the 2006 Census of Population and 2011 NHS. Work related commuters were subsequently stratified by the type of CSDs they were from (SACTYPE), age group, sex, urban-rural status, and industry sector (NAICSECF / NAICS07). The associated chi-squared statistic (χ^2) and p-value are shown below each table for 2006 and 2011, respectively.

While comparisons were made at the provincial level, an additional estimation of the proportion of the people who commuted different distances as defined by the PWCOMMUT variable was made at the CD level. A proportion estimation was also made for the province of destination for inter-provincial workers from NL in 2006 and 2011. Frequency weighting was employed to account for the sampling design and to obtain appropriate estimates of the variance. Various tables which break down PWCOMMUT by the factors noted above are included on the subsequent page(s).

A comparison of NL to Canada for work-related commuting is shown in Table 7.5. NL had more interprovincial commuting in both 2006 and 2011 than Canada, but less people commuting between CDs. NL was found to have a decrease in inter-provincial commuting in 2011 compared to 2006 while people who worked in different CDs remained relatively the same.

Table 7.5

Percent of people who commute to work in NL versus Canada overall for the 2006 Census of Population and the 2011 NHS.

Commuting Type	2006 Census		2011 NHS	
	Newfoundland and Labrador	Canada (overall)	Newfoundland and Labrador	Canada (overall)
Work & live in same CSD	57.02	63.12	55.64	62.09
Work in different CSD	33.89	18.71	36.25	18.99
Work in different CD	4.43	16.92	4.45	17.61
Work in different province	4.66	1.24	3.66	1.30

A breakdown of commuting by Census Division is included in Table 7.6 for workers who travel outside of their CD and/or the province. In both 2006 and 2011, the highest rates of commuting in were seen in CDs 1007 and 1008 (Bonavista/Trinity & Notre Dame Bay) for working in another Census Division, while CDs 1003 and 1004 (South Coast & St. George's) had the greatest proportion of workers in another province.

Table 7.6

Percent of people in each CD in NL who commute to work in a different CD or province for the 2006 Census of Population and the 2011 NHS.

Census Division Code	2006 Census		2011 NHS	
	Work in different CD	Work in different province	Work in different CD	Work in different province
1001	1.40	2.86	1.22	2.21
1002	7.94	7.42	9.08	9.21
1003	8.43	11.68	9.05	9.46
1004	5.63	12.02	10.03	12.22
1005	3.15	3.47	3.97	3.32
1006	4.78	4.41	5.27	3.38
1007	13.69	7.33	13.53	4.99
1008	15.17	10.55	16.81	8.00
1009	6.43	7.24	8.52	5.58
1010 & 1011 *	4.43	2.00	3.23	1.08

*****Merged to meet Statistics Canada minimum population requirement for release.

Tables 7.7 through to 7.10 show the percentages of different types of commuting for NL residents stratified by the categorical variables that the chlamydia incidence was stratified by for both Census years, including sex, age, and urban/rural status. People in rural CSDs had a greater proportion of commuters to both other provinces, and other CDs, in 2006 and 2011 than people in urban CSDs as noted in Table 7.7.

Table 7.7

Percent of people in NL who commute to work based on urban/rural classification for the 2006 Census of Population and the 2011 NHS

Commuting Type	2006 Census		2011 NHS	
	Urban	Rural	Urban	Rural
Work & live in same CSD	60.96	53.08	58.19	52.65
Work in different CSD	35.43	32.35	38.82	33.21
Work in different CD	1.32	7.55	1.12	8.37
Work in different province	2.29	7.02	1.86	5.77
2006: $\chi^2 = 8000$ and $p < 0.01$		2011: $\chi^2 = 9400$ and $p < 0.01$		

Work related commuting for the different sexes is shown in Table 7.8. Men had higher rates of commuting to other CDs and other provinces in both years.

Table 7.8

Percent of people in NL who commute to work based on sex for the 2006 Census of Population and the 2011 NHS.

Commuting Type	2006 Census		2011 NHS	
	Male	Female	Male	Female
Work & live in same CSD	53.30	60.39	52.42	58.51
Work in different CSD	33.99	33.79	35.99	36.48
Work in different CD	5.81	3.19	5.88	3.18
Work in different province	6.90	2.62	5.72	1.83

2006: $\chi^2 = 3400$ and $p < 0.01$ 2011: $\chi^2 = 3500$ and $p < 0.01$

An examination of work related commuting, broken down by age category, is shown in Table 7.9. The highest rates of commuting to other CDs and other provinces were in the 20-24 years old age category in 2006 but that there was a substantial decline in interprovincial commuting when compared with 2011 – especially in people under 30.

Table 7.9

Percent of people in NL who commute to work based on age grouping (years) for the 2006 Census of Population and the 2011 NHS.

Commuting Type	Age Group					
	15-19	20-24	25-29	30-39	40-59	60+
2006 Census of Population						
Work & live in same CSD	63.22	54.42	54.70	53.87	57.80	62.93
Work in different CSD	28.47	28.84	36.32	38.20	34.17	27.10
Work in different CD	3.40	7.03	3.68	3.95	4.25	5.50
Work in different province	4.92	9.71	5.30	3.97	3.79	4.46
2011 NHS						
Work & live in same CSD	62.06	56.84	59.77	53.28	54.26	58.46
Work in different CSD	31.13	33.17	32.49	39.77	37.84	30.91
Work in different CD	4.71	6.30	4.43	3.84	4.20	4.96
Work in different province	2.09	3.68	3.31	3.11	3.70	5.67

2006: $\chi^2 = 2900$ and $p < 0.01$ 2011: $\chi^2 = 1500$ and $p < 0.01$

The proportion of people involved in different levels of commuting for work for each SACTYPE are shown in Table 7.10. The highest rates of commuting to other CDs were in non-MIZs while the highest rates of commuting to other provinces was found in moderate MIZs.

Table 7.10

Percent of people in NL who commute to work based on SACTYPE for the 2006 Census of Population and the 2011 NHS.

Commuting Type	SACTYPE					
	CMA	CA	Strong MIZ	Moderate MIZ	Weak MIZ	Non MIZ
2006 Census of Population						
Work & live in same CSD	58.70	69.97	26.51	47.20	62.57	51.43
Work in different CSD	38.34	23.84	63.91	35.30	24.57	31.53
Work in different CD	0.97	2.69	3.65	8.47	7.14	9.39
Work in different province	1.99	3.50	5.94	9.03	5.72	7.66
2011 NHS						
Work & live in same CSD	56.31	66.98	22.98	42.52	65.50	47.49
Work in different CSD	41.40	26.79	67.82	40.36	22.51	34.12
Work in different CD	0.71	3.06	4.81	9.15	7.43	12.29
Work in different province	1.58	3.18	4.40	7.97	4.56	6.11

2006: $\chi^2 = 17000$ and $p < 0.01$ 2011: $\chi^2 = 21000$ and $p < 0.01$

Table 7.11 shows work related commuting by industry sectors – separated by year. The industries with the greatest commuting were found to be industry B (mining, quarrying and oil & gas extraction) and industry C (construction). Comparing 2006 and 2011, all sectors saw decreases in commuting to different CDs and different provinces except for industry A (agriculture, forestry, fishing, and hunting) and industry B (mining, quarrying and oil & gas extraction).

Table 7.11

Percent of people in NL who commute to work based on industry of employment using the 2006 Census of Population and the 2011 NHS.

Commuting Type	Industry of Employment*						
	A	B	C	D	E	F	Other
2006 Census of Population							
Work & live in same CSD	63.16	21.44	37.32	52.14	60.39	56.56	59.26
Work in different CSD	24.50	49.92	30.86	33.16	30.79	32.49	34.21
Work in different CD	6.67	11.87	10.07	6.17	3.81	4.65	3.65
Work in different province	5.67	16.78	21.76	8.52	5.01	6.30	2.89
2011 NHS							
Work & live in same CSD	56.35	42.40	37.52	55.17	56.17	55.41	57.27
Work in different CSD	28.05	27.84	34.57	33.62	38.21	36.49	36.96
Work in different CD	8.18	11.02	10.60	3.63	2.35	3.51	3.81
Work in different province	7.42	18.74	17.31	6.34	3.27	3.24	1.95

2006: $\chi^2 = 14000$ and $p < 0.01$ 2011: $\chi^2 = 14000$ and $p < 0.01$

*****A is agriculture, forestry, fishing, and hunting. B is mining, quarrying, and oil & gas extraction. C is construction. D is transportation and warehousing. E is professional, scientific, and technical services. F is administrative and support, waste management and remediation services. “Other” includes all miscellaneous industries noted in the methods.

Table 7.12 gives a proportional breakdown of the province of employment for migratory workers who travelled outside of NL in 2006 and 2011. In both years, the largest group of migratory workers travelled to Alberta. Notable changes between the years include a greater increase to Alberta and decreases in Ontario – both more than 10 percentage points.

Table 7.12

Proportional breakdown of the destination province(s) of interprovincial workers from NL for the 2006 Census of Population and the 2011 NHS.

Province of Employment	Percentage (2006)	Percentage (2011)
British Columbia	3.82	2.19
Alberta	39.50	51.78
Saskatchewan	0.70	1.69
Manitoba	1.06	1.94
Ontario	25.63	15.45
Quebec	2.06	2.44
New Brunswick	4.77	3.69
Nova Scotia	11.56	8.69
Prince Edward Island	4.22	4.19
Northern (Yukon / Northwest Territories / Nunavut) *	6.68	7.94

*Merged to meet Statistics Canada minimum population requirement for release.

APPENDIX I

The univariate model results of the linear regression are shown in Table 7.13 and individually compare each of the selected employment variables with the chlamydia rates at the CSD level. Positive relationships were found in those working in the same CSD, administration, support, waste management and remediation industry, and the non-MIZs.

Table 7.13

Univariate relationships between logarithmically transformed age-sex standardized chlamydial rates and each logarithmically transformed employment factor for NL as determined by linear regression.

Variable (Percent of population that…)	β coefficient	95% Confidence Interval	p-value
Employment Commuting			
Work in same CSD	0.232	0.079 – 0.386	0.003
Work in different CSD	-0.154	-0.313 – 0.005	0.058
Work in different CD	0.013	-0.138 – 0.165	0.861
Work in different province	-0.072	-0.238 – 0.094	0.392
Industry of Employment			
Industry A [a]	0.025	-0.098 – 0.147	0.693
Industry B [a]	0.140	-0.032 – 0.313	0.110
Industry C [a]	-0.159	-0.395 – 0.077	0.186
Industry D [a]	-0.069	-0.284 – 0.147	0.531
Industry E [a]	-0.099	-0.325 – 0.127	0.390
Industry F [a]	0.283	0.048 – 0.517	0.018
Other Industries [a]	0.238	-0.242 – 0.718	0.329
SACTYPE [b]			
CA	-0.085	-0.885 – 0.714	0.833
Strong-MIZ	-0.051	-0.664 – 0.563	0.871
Moderate-MIZ	0.115	-0.410 – 0.640	0.665
Weak-MIZ	0.340	-0.189 – 0.869	0.206
Non-MIZ	0.867	0.335 – 1.399	0.002

[a] Industry A is agriculture, forestry, fishing, and hunting. B is mining, quarrying, and oil & gas extraction. C is construction. D is transportation and warehousing. E is professional, scientific, and technical services. F is administrative and support, waste management and remediation services. “Other” includes all miscellaneous industries noted in the appendices.
[b] CMAs were used as the reference group for SACTYPE as it was a categorical variable.

APPENDIX J

A map distinguishing the boundaries of each of the RHAs in NL is included in Figure 7.4 below. The four RHAs did not change in their jurisdictive parameters during the duration of the study period.

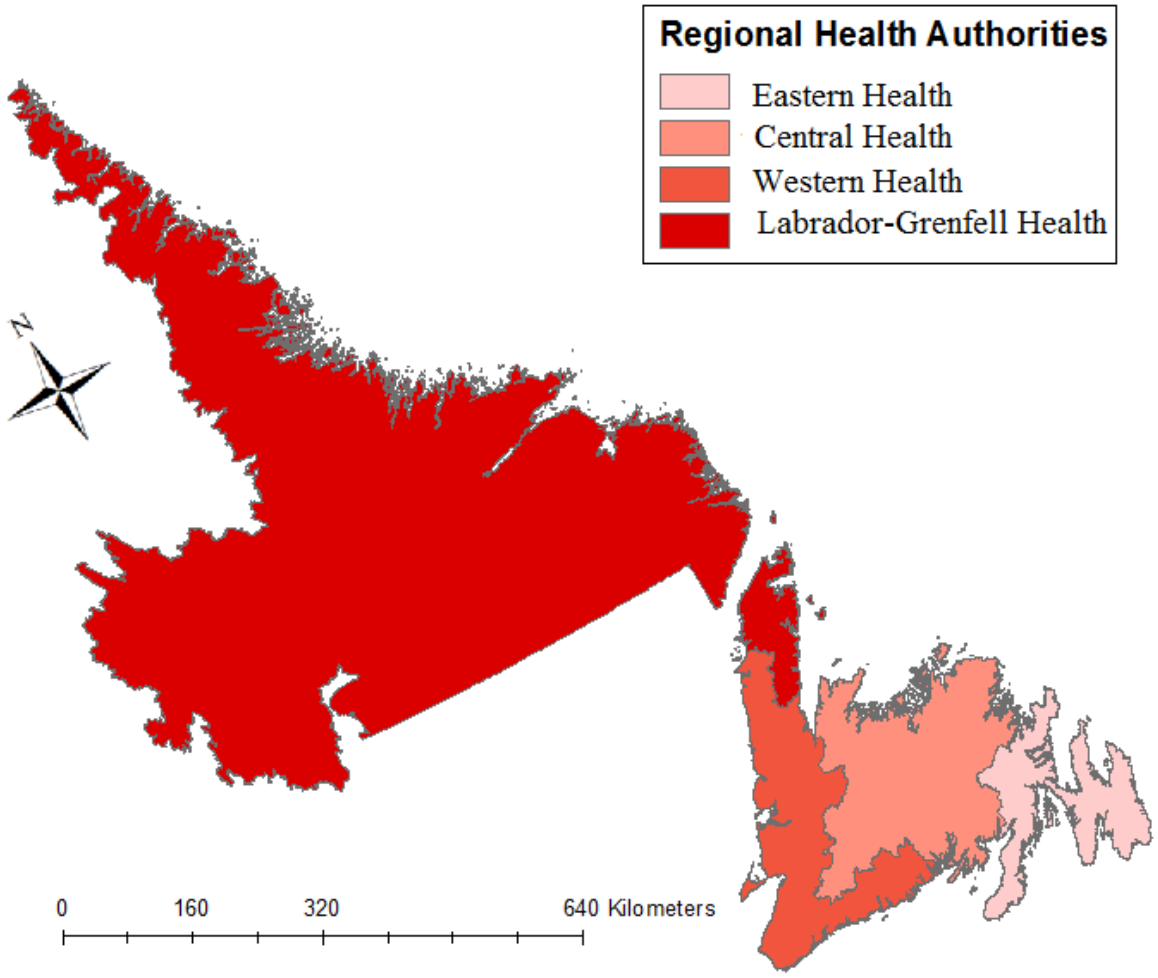

Figure 7.4. Jurisdictions of the four Regional Health Authorities of NL (2011).