Rural-Urban Differences in Prevalence of Diagnosed Dyslipidemia in Newfoundland: Findings from the Eastern Health Eastern Health Laboratory Information System

By

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A thesis submitted to the School of Graduate Studies in partial fulfillment of the requirements of the requirements for the degree of Master of Science

Faculty of Medicine

Memorial University of Newfoundland

Spring 2017

Abstract

Background

Newfoundland and Labrador has a higher level of cardiovascular disease (CVD) mortality than any other Canadian province. This may be partially explained by the lipid profile of this province. Anecdotal evidence suggests that Newfoundlanders have lower levels of high-density lipoproteins (HDL) and higher levels of low-density lipoproteins (LDL) than other Canadians. It is unclear if lipid profiles differ between rural and urban locations within Newfoundland. This study aims to assess rural-urban differences in prevalence of diagnosed dyslipidemia in NL

Methods

This is a cross-sectional study design using a secondary data analysis of laboratory data from the Eastern Health Authority. It includes 94,612 patients aged 20+ with a complete lipid profile (HDL, LDL, Triglyceride (TG), Total Cholesterol) from the period of January 1, 2009 to December 31, 2010. Primary outcome measures were low HDL (<1.0 for men and <1.3 for women), high LDL (≥3.4), high TG (≥1.7), high Total Cholesterol (≥5.2). Rural and urban area were identified using three digit postal code and geo-referenced for visualization using ArcMap-GIS 10.2.

Results

Rural residents had a significantly higher prevalence of low HDL (48% vs 44%, p <0.001), high TG (35% vs 29%, p <0.001), and high Total Cholesterol/HDL ratio (26% vs 23%, p <0.001). Urban inhabitants had a significantly higher prevalence of high Total Cholesterol (38% vs 37%, p= 0.035).

Conclusions

The analysis suggests that patterns of dyslipidemia differ between rural and urban regions with rural having a more adverse dyslipidemia lipid profile. The results of this study will help guide future research about dyslipidemia as well as other risk factors for CVD in NL. Further investigation is required using data from all health authorities in NL to better represent the differences.

Acknowledgments

First and foremost, I would like to thank my supervisor, Dr. Shabnam Asghari. Without her encouragement this project would never have been completed. I am truly thankful for her friendship and continual support.

Thanks to Dr. Aubrey and Dr. Godwin for their numerous suggestions and edits. Thank you to Andrea and Adam Pike for being there each step of the way and showing me what Newfoundland is all about. You two made my experience at the PHRU a great one. Thanks to Ricky Cullen and Oliver Hurley for your help with understanding postal-codes and using GIS. I would also like to thank David Mercer for his patience, interest, time and invaluable assistance with the geographical aspect of the project.

Thank you to my parents for their unwavering support throughout this extended degree and thank you wonderful wife, Patricia MacDonald, for keeping me on going and helping me out every step of the way.

Finally, I would like to thank Emily Eaton for being a fantastic cube-mate. Thanks for all your help along the way and perpetual constructive criticism on both my project and my singing.

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Table 1 Abbreviation	
Analysis of Variance	ANOVA
Apolipoprotein	Apo
Blood Pressure	BP
Body Mass Index	BMI
Canadian Heart Health Surveys	CHHS
Canadian Institute for Health Information	CIHI
Cardiovascular Disease	CVD
Coronary Artery Disease	CAD
Diacylglycerol	DAG
Dyslipidemia International Study	DYSIS
Forward Sortation Area	FSA
High-density Lipid	HDL
Low-density Lipid	LDL
Myocardial Infarction	MI
National Cholesterol Education Program-Adult Treatment Panel II	NCEP-ATP
National Health and Nutrition Examination Survey	NHANES III
Organization of Economic Co-operation and Development	OECD
Protein kinase-C	PKC
Retinol-binding Protein 4	RBP4
Sex-hormone Binding Globulin	SHBG
Single Nucleotide Polymorphism	SNP
Socioeconomic Status	SES
Triglyceride	TG
Very-low-density Lipids	VLDLs
Years of Life Saved	YOLS
Eastern Health Laboratory Information System	EHL
Rural and Small Town	RST
Census Metropolitan Area	CMA
Census Agglomerations	CA
Metropolitan Influenced Zone	MIZ
Modifiable Areal Unit Problem	MAUP
Canadian Primary Care Sentinel Surveillance Network	CPCSSN
Postal Code Conversion File	PCCF

Chapter 1 Introduction

1.1 Cardiovascular Disease in Canada

Cardiovascular disease (CVD) is a chronic disease that is developed by the interplay of genetic predisposition, lifestyle and environment [1]. Medical advances have produced a reduction in the number of CVD related events as well as improved the quality of life of those living with CVD[1]. With increased understanding of CVD there has been a shift towards preventative medicine such as smoking cessation, regular exercise, nutrition and proper management of hypertension, diabetes and dyslipidemia [1]. Even though we possess this information, one in three Canadians die due to CVD [1].

According to the Canadian Public Health Agency 1,322,500 Canadians suffered from CVD in 2007 [1]. Men accounted for approximately 55% of these cases. In 2005, CVD accounted for 2,466,842 hospitalizations and 226,584 deaths [1]. Indirect costs of CVD includes anxiety, depression and a decreased quality of life as people are often less able to take part in daily activities [1].

These direct and indirect impacts of CVD result in a massive economic burden on the healthcare system, costing Canada $22.2 billion in 2000 [1] (the most up-to-date from public health agency of Canada at the time of this study). This made CVD the second most expensive in all diagnostic categories [1].

In deciding whether or not it is cost-effective to target risk factors for CVD it is important to note that lipid lowering therapy provides twice the benefit of blood pressure (BP) therapy over a life span [2]. Between 27 and 102 person years of treatment of dyslipidemia is required to save one year of life, while hypertension requires 53-157 person years of treatment[2]. On average the cost-effectiveness

ratio for lipid lowering therapy has been found to be $16,700 per year of life saved (YOLS), and antihypertensive therapy to be $37,100/YOLS [2].

Lee et al [3] examined risk factor trends for CVD among Canadians and took temporal, socio-demographic and geographic factors into consideration. The researchers used data from 1994-2005 collected by the National Population Health Survey and the Canadian Community Health Survey.

The results of the study showed that the prevalence of heart disease for males was 3.6% and 2.8% for females in 1994 and these values increased to 4.3% and 2.9% in 2005. This was an increase of 19% for men and 2% for women. There was also an increase in early onset of heart disease (<age 55 for males and <65 for females). It was estimated that over this time period there was an increase of 380,000 Canadians with heart disease [3]. Patients of lower socio-economic status (SES) had a higher prevalence of heart disease compared to those of higher SES. It was observed that higher levels of income had smaller rises in disease prevalence over time [3].

Geographic variations of CVD risk factors were found across the provinces, with the Atlantic Provinces having a higher prevalence of all risk factors. Newfoundland and Labrador had the 3rd highest prevalence of hypertension [3], and the highest prevalence of diabetes and obesity. Newfoundland and Labrador also experienced the greatest increase in obesity across the time period at 50% [3].

1.2 Dyslipidemia

One significant modifiable risk factor for CVD, and the focus of this paper, is dyslipidemia. This is defined as abnormal lipid profiles and consists of several different components: low high-density lipoprotein (HDL) <1.0 [4], high low-density lipoprotein (LDL) ≥3.4, high triglyceride (TG) ≥1.7, and high Total-Cholesterol ≥5.2[4]. A paper by Joffres et. Al. [5] in 2012, reported that 36% of Canadian adults

were classified as having dyslipidemia. The prevalence of disease increased with age and was significantly higher in men (43%) than women (29%) [5]. Nearly 36% of Canadian adults had high levels of LDL, and 30% have low levels of HDL [6].

When the use of lipid lowering therapy was added to the definition, the prevalence of dyslipidemia increased to 45% [5]. There is a positive correlation between age and cholesterol level: 27% of adults age 20-39 have high cholesterol, 47% of adults age 40-59, and 54% of adults age 60-79 [6].

The Canadian Cardiovascular Society generates guidelines for lipid target levels, which are revised every three years with a goal of lowering the prevalence of CVD. The primary target for dyslipidemia therapy is LDL [7], and the primary therapeutic agent is an HMG-CoA reductase inhibitor[8].

The Framingham study [9], which was a large longitudinal study that focused on cardiovascular disease and risk factors, found that 6 of 10 participants developed borderline-high LDL (3.4-4.0mmol/L) levels and 4 of 10 participants developed high LDL levels over the 30-year study period. Two of 10 women and 4 of 10 men developed low HDL levels [9]. After adjustments for baseline differences, it was estimated that over the 30-year period the risk for developing borderline-high LDL was greater than 80% and the risk for developing high LDL was 50% [9]. There was a 25% percent risk for women and 65% risk for men of developing low HDL and a 20-50% risk of developing low HDL and high LDL levels [9].

1.2.1 Dyslipidemia Classification

Dyslipidemia is categorized as primary or secondary [10]. Primary dyslipidemia is caused by an overproduction of lipoproteins or a decreased clearance [10]. Secondary dyslipidemia is the result of a medical condition such as diabetes mellitus, obesity, or liver disease among several others [10].

Dyslipidemia is also classified into five categories based on presentation [11]. Type-I hyperlipidemia is an uncommon form of dyslipidemia, caused by inactivation of lipoprotein lipase, which normally clears TGs and chylomicrons [11]. This dysfunction results in decreased rate of clearing of TGs resulting in elevated levels of TGs [11].

Type-II hyperlipidemia is the most common form of dyslipidemia and is divided into Type-II-a and Type-II-b. Type II-a is caused by a defective LDL receptor and is known as familial hypercholesterolemia. [11]. Type II-a also includes a polygenic form that is the most frequent variety of dyslipidemia. The cause of this is thought to be multi-factorial [11]. Type II-b involves increased levels of cholesterol and TGs and is known as familial combined hyperlipidemia [11]. This is a result of overproduction of apolipoprotein (apo) B-100 [11].

Type III hyperlipidemia, known as, dysbetalipoproteinemia, involves elevated levels of chylomicrons and beta very low density lipoproteins (VLDL) [11]. This is the result of an impaired apo- E, which is normally recognized by the LDL receptor, and removes apo-E containing lipoproteins. In the altered state apo-E is not recognized and hence lipoproteins are not removed [11]. While in circulation the particles interact with lipoprotein lipase, which removes TGs and leaves the particles rich in cholesterol [11]. These particles are taken up by macrophages and deposited in peripheral tissue, which results in coronary artery atherosclerosis [11].

Type IV, familial hypertriglyceridemia, consists of elevated levels of VLDLs, which results in elevated levels of TGs [11]. Type V is similar in nature to type IV but it also has elevated levels of chylomicrons. The elevation of these two particles results in increased levels of TGs [11].

1.2.2 Genetics and Dyslipidemia

In 1990, the National Health and Nutrition Examination Survey (NHANES) in the United States reported that 33% of men and 17% of women had low HDL (<40mg/dl) [12]. It is hypothesized that these values may be related to genetics, particularly mutations in *ABCA1*, *APOA1*, and *LCAT,* which are the three principle genes involved in the metabolism of HDL [12].

The province of Newfoundland and Labrador is a fairly genetically homogenous population [13]. A study involving third generation Newfoundland population looked at Retinol-binding protein 4 (RBP4), which is an adipokine thought to be implicated in insulin resistance of dyslipidemia, found that specific minor alleles of two noncoding single nucleotide polymorphisms (SNP) had a significant association with serum HDL [13]. This study provides evidence and support for the theory that genetics may play a significant role in being partially responsible for differences in serum HDL within the Newfoundland population [13].

Another example of the role of genetics in the lipid profile of Newfoundlander's comes from a study done by Anjilvel in 1973 that examined the lipid profiles of 102 members of two families of the Baie Verte Peninsula [14]. Out of the total study population, 39 were found to have familial hyperlipoproteinemia. Consanguinity was found to be present in both families [14].

The study examined 11 cases of ischemic heart disease that were present in the 102 members of the two families. All 11 cases were found to have hyperlipoproteinemia [15]. The diet in these 11 individuals frequently included fish and brewis with scrunchions and jigs dinner – both of these are high in saturated fats, carbohydrates and salt [15]. With the genetic information gathered from this study, the researchers felt that they could predict those with genetic predispositions to CVD and partially curb their disease through lifestyle and diet modification [15].

1.3 Factors Influencing Dyslipidemia

1.3.1 Age and Sex Differences in Lipid Profiles

Blood lipid profiles are comparable between sexes until puberty [16]. At this time testosterone begins to rise in boys and there is a resultant drop in HDL, while levels remain stable in girls [16]. Studies have shown a significant negative correlation between sex-hormone binding globulin (SHBG) and testosterone with TGs [16]. These hormones were found to have a positive correlation with HDL. Estradiol was found to have a significant positive correlation with TGs. No significant relationship has been found between sex hormones and LDL [16]. It is suggested that SHBG may play a central role in hormonal regulation of the lipid profile [16].

Post-menopausal women experience a significant increase in Total Cholesterol, LDL, TG and apolipoprotein-B [17]. These changes have been shown to increase with body mass index (BMI) [17]. Several studies have shown significant differences in HDL between men and women. [18]. It has been hypothesized that higher HDL levels partially explain why women suffer fewer myocardial infarctions (MI) than men. These differences are present worldwide, with the smallest difference documented in China at 0.06mmol/L and the largest difference in Canada at 0.40mmol/L. The differences remain significant after adjustment for BMI, smoking, alcohol use and heart rate [18].

Limited research has been conducted in North America on lipid profile variation with age. A study conducted in Nepal, found that women tended to have higher lipid levels in all age ranges [19]. Researchers concluded that the normal range of lipids for women is higher than that of men [19].

A study conducted in Poland [20] showed no statistically significant difference in lipid profiles for men and women age 25-32. Older men, around age 50 had lower TGs and higher HDL levels than the other age groups (men and women age 25-32,

men and women age 58-66, and women age 60-65). In the 58-66 age group lipid profiles for sedentary men and women were similar [20].

NHANES III examined the prevalence of isolated low HDL in different age groups with respect to BMI [21]. The age groups used were: 20-39, 40-59, 60-79, and 80+. In men with a BMI <25, and a BMI 27-30 the prevalence of low HDL increased with each age group. For men with a BMI ≥30, the prevalence increased from the 20-39 age group to the 40-59 age group and then decreased to the lowest value in the 60+ age group. For women with a BMI<25 the prevalence decreased from the 20-39 to the 40-59 group and then increased to the maximum value of 18.9% in the 60+ group. Women with a BMI ≥30 had levels decrease from 50.1% to 34.6% in the 60+ age group. The study reports that the odds for developing low HDL is highest for the younger age group [21].

1.3.2 Obesity and Dyslipidemia

The relationship between BMI and CVD is well documented. Many studies have divided BMI into different distributions of body fat and evidence shows that waist circumference and waist-to-hip ratio are the best predictors of CVD [22].

The classification of BMI can be seen in the following table taken from Statistics Canada [22]:

Table 2.1 Classification of Obesity by Body Mass Index (BMI)

Classification	BMI Category (kg/m^2)	Risk of Developing Health Problems
Underweight	<18.5	Increased
Normal Weight	18.5 - 24.9	Least
Overweight	25 - 29.9	Increased
Obese Class I	30 - 34.9	High
Obese Class II	35.0 - 39.9	Very high
Obese Class III	≥40.0	Extremely high

Weight issues have become a health epidemic. From 2008 to 2012 the number of adults over the age of 18 who self-identified as either overweight or obese increased

from 12,389,673 to 13,485,120 [23]. Nearly 19% of the individuals in 2012 were classified as obese with males making up 7,722,703 of this total. The highest rate of overweight/obesity was found in the 45-64 age group and the prevalence decreased with age greater than 65[23].

Atlantic Canada has the highest rates of obesity in Canada. Newfoundland has the second highest rate of obesity of all provinces at 26.3% [24]. In addition to this, Newfoundland ranks 9th among the provinces and territories for percent smoke-free, 10th for physical activity and 11th for adequate consumption of fruits and vegetables. Combing all health behaviors, Newfoundland and Labrador ranked 12th out of 13 [25].

The most common comorbidity of obesity is dyslipidemia [26]. As fat accumulates it becomes an active endocrine and inflammatory tissue that can result in metabolic disorders [26]. When large amounts of fat accumulate, the result is organelle dysfunction, particularly the mitochondria and the endoplasmic reticulum [26]. These dysfunctions cause hormone dysregulation, impaired storage of fatty acids, increased circulating free fatty acids, and the production of reactive oxygen species [26]. The increased inflammatory reaction comes from increase activation of adipose-tissue associated macrophages, which contributes to the development of atherosclerosis [26].

With an increased level of adipose tissue there is an increase in circulating free fatty acids [26] which results in an increased output of hepatic VLDLs [26].This results in an elevated fasting level of TG [26]. In circulation, VLDLs bind to other components of the lipid profile making them TG rich [26]. For instance, when VLDL binds to HDL, it is acted on by lipases, which reduces the size of the HDL molecule. When the HDL particle becomes smaller it is more likely to be metabolized and can be excreted in the urine [26]. This causes a decreased level of circulating HDL particles. When VLDL interacts with LDL, the particle again becomes smaller and more dense, contributing to the development and or progression of atherosclerosis [26]. Weight

loss is recommended to combat these atherogenic changes. A loss of 4.5kg can reduce LDL levels by up to 8% [26] and physical activity has been shown to be helpful in increasing the size of HDL particles and to total HDL level [26].

1.3.3 Tobacco Smoking and Dyslipidemia

Smoking increases the risk of developing atherosclerosis, coronary artery disease (CAD) and peripheral vascular disease [27]. In adults and adolescents, smoking was associated with an increase in the levels of Total Cholesterol, LDL, VLDL, TG and decreases the level of HDL [28] [29]. Passive smoking in adults has also been shown to have the same effect [30].

There are several proposed mechanisms through which smoking causes these changes. Nicotine, a component in tobacco smoke, acts on the sympathetic nervous system causing an increased release of catecholamines [28]. This results in lipolysis and a subsequent increased secretion of free fatty acids from the liver into the bloodstream [28]. Effects of smoking are also illustrated by a decrease in HDL, which is hypothesized to be caused by a decrease in estrogen [28].

There is evidence of a dose dependent relationship between smoking and some components of the lipid profile [28]. Those who smoke 11-20 cigarettes per day have significantly increased levels of LDL and TGs compared to those who smoke 1-10 cigarettes per day [28]. Levels of HDL are significantly lower than non-smokers regardless of the number of cigarettes smoked per day [28].

In children with hyperlipidemia, there was an association between exposure to second hand smoke in the house and the lowers levels of HDL [30]. Hyperlipidemic children not exposed to second hand smoke on average had 11.2% higher levels of HDL [30]. This information is extremely useful in preventing disease in those who are at risk of early onset CVD.

1.3.4 Diabetic Dyslipidemia

A common comorbidity of dyslipidemia is diabetes, and patients who have both diseases are said to have diabetic dyslipidemia [31]. Those with diabetes have a two to fourfold increased risk for developing CAD, cerebrovascular events and peripheral arterial disease [31]. Close to 80% of people with type-2 diabetes die of a macrovascular complication [32] and dyslipidemia accounts for a large proportion of this elevated risk [32].

In healthy individuals, insulin facilitates glucose uptake by cells [26]. It is thought that insulin resistance is dependent on the accumulation of intracellular TG [26]. Studies have shown that intracellular accumulation of lipids results in the activation of protein kinase C (PKC), which causes an impaired signaling cascade and is hypothesized to be the cause of impaired glucose transport [26].

In the liver, insulin works by inhibiting gluconeogenesis and promoting glycogen synthesis [26]. In obese people, there is an increased amount of diacylglycerol (DAG) in the liver [26] that is associated with increased activation of PKC and causes hepatic insulin resistance [26].

People with diabetes tend to develop an atherogenic lipid triad [33] consisting of high serum TG, low HDL, and a high level of small, dense LDL [33]. This triad contributes to microvascular complications including retinopathy and nephropathy [34]. Subsequently, dyslipidemia causes a more rapid decline in the glomerular filtration rate, which results in earlier development of nephropathy [34]. The early detection of kidney disease from dyslipidemia is monitored by the presence of microalbuminuria [35].

The use of lipid-lowering agents in patients with diabetes results in up to a 25% reduction in the risk of macrovascular disease [32]. Studies support the use of moderate doses of statins in patients with diabetic dyslipidemia [32].

1.3.5 Hypertension and Dyslipidemia

Hypertension is defined as a systolic pressure of 140mmHg or greater, and a diastolic of 90mmHg or greater [36]. Several studies, including the Framingham study have shown a direct link between hypertension and cardiovascular events [36]. The prevalence of hypertension has increased from 1998/9 to 2006/7 and the numbers are expected to continue rising [37]. The prevalence of patients with both hypertension and diabetes is also high and these patients experience higher mortality rates over those who suffer from only one of these conditions alone [37].

Approximately 20% Canadian adults (age 20+) were diagnosed with hypertension in 2006/7 [38]. Geographic trends have been observed with Atlantic Provinces having a greater prevalence than the national average. As previously mentioned, Newfoundland has the second highest age standardized incidence rates [37].

Hypertension has been referred to as the "silent killer" and is one of the major modifiable risk factors for CVD [37]. Hypertension is frequently detected through routine BP measurements, as it typically does not present with symptoms [37]. Like most risk factors for CVD, hypertension affects all age groups but the risk of developing it increases with age [37]. For patients who suffer from hypertension it is very important that they closely monitor their lipid profile as dyslipidemia can increase the damage of hypertension [37]. Evidence suggests there is an interaction between hypertension and dyslipidemia that increases the development of atherosclerosis and subsequently CVD [39].

1.4 Geography

1.4.1 Geographic Classifications in Canada

There are several parameters that can be used to classify a region as rural or urban[40]. In Canada there are at least six definitions of rural. Depending on which definition is chosen, the size of the overall rural population can vary significantly

[40]. This is illustrated by the fact that the rural population of Canada can range from 22% to 38% based on the definition used [40].

A rural region consists of several building blocks. The dissemination area, which is a group of houses, is the smallest of these blocks [40]. Adding enumeration areas together generates census sub-divisions, which are towns and communities [40]. Census sub-divisions are grouped to create census-consolidated subdivisions. Finally, a census division is the largest block, which represents an intermediate between municipality and province [40].

There are various definitions of what a rural regions is. Examples of Canadian definitions of rural are as follows:

1. *Rural postal code*- 0 as the second character in their postal code [41]
2. *Rural and small town (RST)*- census sub-divisions that are not a part of a Census Metropolitan Area (CMA) or Census Agglomerations (CA) (Rural and Small Town Canada Analysis Bulletin) [42].
    a. *Strong Metropolitan Influenced Zone (MIZ)*- 30% or more of residents commute to a CMA or CA for employment
    b. *Moderate MIZ*- 5-29% of residents commute to a CMA or CA for employment
    c. *Weak MIZ*- more than 0% but less than 5% commute to a CMA or CA for employment
    d. *No MIZ*- no residents commute to a CMA or CA for employment

1.4.2 Rural-urban Health Risk Factor Variations in Newfoundland

In the province of Newfoundland and Labrador there is a shortage of research into rural and urban health disparities. Kettle [43] conducted a cross-sectional study in Newfoundland comparing the prevalence of various risk factors for CVD between young adults living in urban and rural areas. Rural was defined as an area with a population of less than 10,000. A total of 540 participants including both males and

females between the ages of 18 and 34 were included. Variables of interest included: cigarette smoking, measurements of body size (BMI, waist circumference), education level and family income level.

No difference was found between the two regions in regular smoking and BMI. More rural women than urban women had a waist-circumference above the accepted cut-off. The main finding of the paper was that young adults in both regions suffer from a high prevalence of modifiable risk factors.

The province of Newfoundland has a shortage of physicians. Mathews and Edwards [44] studied adults, over the age of 20, living in urban, semi-urban and rural regions that did not have a family physician. Rural was defined as a population of less than 10,000, semi-urban as 10,000-99,999 and urban as a population greater than 100,000. They used data that was collected from a 1995 random dialing survey and information was collected from 11,789 households. The researchers found that 15% of respondents did not have a family physician. A large amount of those without a family physician were young, unmarried males living in rural areas that worked either part-time or had seasonal employment. Overall, the researchers found that rural residents were less likely to have a family physician.

Fodor [45] compared lipid profiles of school aged children in Newfoundland to children in the United States. The study included 1,033 students between the ages of 8-10 and 14-16 on both the east and west coast of Newfoundland. Compared to the age, sex and race matched children in the United States, children in Newfoundland had higher total cholesterol.

1.5 Literature Review- Geographic Variation in Lipid Profiles and Dyslipidemia

To identify peer-reviewed articles comparing lipid profiles between rural and urban inhabitants a systematic search in the electronic databases including PubMed, EMbase, CINHAL was performed in June 2013, and again in May 2015. Key words included: rural, urban, lipid, dyslipidemia, Canada, and North America. There has been little research in North America comparing lipid profiles between rural and urban inhabitants. Therefore the studies presented here were conducted in other regions of the world.

1.5.1 Lipid Profile and Rural-urban Migrations in Tanzania

Unwin et al [46] conducted a cohort study examining lipid profiles in adult men and women age 15 to 59 who migrated from rural Morogoro, to urban Dar es Salaam.

Participants were recruited by informants that were in place within the village from a previous surveillance system project. Adults that were migrating to Dar es Salaam and intended to stay for at least six months were recruited. Data was collected on participants at least one week before and no more than one month prior to migration. These values were then repeated 12 months following the participants move.

The study involved 103 men and 106 women. Both sexes had an increase in HDL and a decrease in BP from baseline to the 12-month follow up. For women, the Total Cholesterol/HDL ratio dropped. Men exhibited a significant increase in Total Cholesterol and a significant decrease in serum TGs at the end of the 12-month follow-up period. Women had an initial decrease in TGs but the levels increased later in the study.

The increase in HDL in both men and women was not predicted, nor was the decrease in BP. It is important to remember that this study was conducted in Tanzania, which is considered to be a low to middle income country.

1.5.2 Rural-urban Risk Factors for Dyslipidemia, Shanghai

Jia-Yu Wu et al [47]., conducted a study comparing the prevalence of dyslipidemia and risk factors for dyslipidemia in 2 rural and 4 urban regions in Shanghai, China. A total of 1,400 participants over the age of 16 were randomly selected. Researchers conducted physical and laboratory assessments on the participants after a 12-hour fast.

Data regarding demographics, medical history and health-related habits were collected through the use of questionnaire. Weight, height, waist and hip circumference, BMI and waist-to-hip ratio were recorded. Blood samples were drawn for Total Cholesterol, TG, and HDL.

Overweight was classified as a BMI ≥ 25 kg/m^2 and obesity was defined as a BMI ≥ 30 kg/m^2. Dyslipidemia was diagnosed by the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP) criteria.

The results of the study showed that the prevalence of dyslipidemia among adults in Shanghai was 36.5%. The researchers suggest that the high prevalence of dyslipidemia represents in the impact of increasing urbanization. Dyslipidemia was more prevalent in males (40.2%) than females (33.8%). The prevalence increased by age, with a peak at age 35-44 for males and 65+ for females. Statistical analyses showed that male gender and advanced age were strongly associated with dyslipidemia.

Geography was an independent risk factor for dyslipidemia. Dyslipidemia was more prevalent in rural (44.2%) than in urban (32.4%) regions. Isolated high TGs and

isolated low HDL were found to be significantly more prevalent in rural regions. In contrast, urban regions had more high Total Cholesterol and mixed hyperlipidemia. Rural residents had a high mean level of TGs and a relatively low mean Total Cholesterol and HDL level. The authors cite diet as the reason for these findings as urban Shanghai is becoming increasingly westernized with respect to a high fat diet but rural regions still consume more complex and simple carbohydrates. Both smoking and alcohol consumption were shown to be risk factors for dyslipidemia. The fact that urban Shanghai is becoming more and more westernized may allow this study to be applied to the western world for comparison.

1.5.3 Rural-urban Variations in High Total Cholesterol, Saudi Arabia

AL-Nuaim [48] conducted a similar study in Saudi Arabia using a cross-sectional study design. Data was collected on randomly selected adults age 25-64 living in both urban and rural regions. The study focused on the distribution and prevalence of high Total Cholesterol.

A BMI ≥30kg/m^2 was used to define obese participants. Mild high Total Cholesterol was defined as 5.3-6.2mmol/l. Moderate to severely high Total Cholesterol was defined as a cholesterol concentration of >6.2mmol/l.

The results of the study showed that Total Cholesterol levels were higher in rural than urban regions for men and women. HDL was found to be higher in rural regions and rural residents had a higher Total Cholesterol/HDL ratio. LDL concentrations were found to be higher in urban regions.

Total Cholesterol levels increased with age for both sexes. Men age 56-65 had the highest level in urban regions. The highest levels for rural men were those age 46-55. The mean serum Total Cholesterol was lower for urban males compared to rural counterparts for all age groups. The only statistically significant difference was in the 25-35 age category.

Women age 56-65 had the highest level of serum Total Cholesterol in both rural and urban regions. The serum Total Cholesterol level was lower for urban women in the younger age categories but was higher for the older age categories. There was no significant difference at any age group.

No statistical significance was found between rural (13%) and urban (12%) for the prevalence of high Total Cholesterol (5.2-6.2mmol/l). The prevalence of high Total Cholesterol (>5.2mmol/l) was 18% and 23% for urban and rural males ($p<0.0001$). The prevalence of moderate to severely high Total Cholesterol (>6.2mmol/l) for urban males was 6% and 11% for rural males ($p<0.001$).

For urban and rural females, the prevalence of high Total Cholesterol (5.2-6.2mmol/l) was 12% and 13%. The prevalence of moderate to severely high Total Cholesterol (>6.2mmol/l) was 9% for urban and 10% for rural women. The prevalence of high Total Cholesterol (>5.2mmol/l) was 21% among urban females and 23% for rural females. None of these differences were statistically significant.

The discrepancy of high Total Cholesterol between rural and urban regions is not consistent with previous studies in similar communities. Suggested reasons for this are that Saudi communities have gone through a period of urbanization, which might be responsible for the narrow gap between the rural and urban regions.

1.5.4 Rural-urban Variations in Lipids and Other CVD Risk Factors, Sweden

Thelin et al [49]., conducted a cross-sectional study in 2001 in Sweden examining lipid levels and other CVD risk factors such as tobacco smoking, diet, BP and BMI of males living in rural regions. Their study population included 1,013 farmers and 769 non-farmers who were born between 1930 and 1949.

Famers had a healthier lipid profile than non-farmers, however, there was little difference between Total Cholesterol levels. The study found a significant positive relationship of total cholesterol with BMI, tobacco consumption, and diastolic BP for both groups. The TG level of farmers was 1.80 mmol/L, which was significantly lower than non-farmers (2.00 mmol/L). The HDL level for farmers (1.22 mmol/L) was significantly higher than that of non-farmers (1.15 mmol/L). HDL concentration was found to have a positive relationship with physical workload, alcohol consumption and a negative relationship with BMI, waist-hip ratio and smoking. Farmers were also found to have lower BP. The overall findings showed that diet was a minor determinant for lipid profiles and that physical activity, body weight, waist-hip ratio, smoking, alcohol consumption were the independent factors affecting lipid profiles.

1.5.5 Dyslipidemia in Canada

Lipid profiles are a popular focus of research in North America. Petrella in 2008 [50] conducted a study in Southwestern Ontario that focused on the prevalence and treatment of both hypertension and dyslipidemia in primary care. Through the use of a retrospective cohort design they collected data on all clinical visit diagnoses, symptoms supporting the diagnosis, BP, smoking status, height, weight, serum lipid levels, glucose concentration, medications, and more.

The study included 46,322 subjects age 18 and older. The most common risk factors were: male, age ≥55, smoking, diabetes, family history of coronary heart disease and other CVDs. Hypertension (17.6%) was more prevalent than dyslipidemia (12.3%) and the prevalence of the two as comorbities was 8%. Almost 65% of subjects with dyslipidemia also had hypertension, whereas only 54.8% of those with hypertension had dyslipidemia. Subjects who were over the age of 55 were much more likely than those under the age of 55 to be hypertensive, dyslipidemic or both. Prevalence increased until age 75.

The treatment of dyslipidemia, with statin therapy, was three times more likely in subjects who were also diagnosed with hypertension compared to those with only dyslipidemia (60.9% vs 20.2%). Those diagnosed with hypertension and dyslipidemia were twice as likely to receive treatment than patients with only hypertension (65.1% vs 34.2%). No significant differences were found in treatment between men and women.

In patients with uncomplicated dyslipidemia, those who had a family history of CHD were the group that received the highest treatment rate at 58%. This value was more than double the treatment rate of participants with other comorbidities and approximately 3 times that of the total study population.

Of those patients with uncomplicated dyslipidemia only 7% achieved their treatment goal. Those patients who had a family history of CHD had the highest lipid level control at 53%, smokers 25%, and history of stroke at 21%. The achievement of treatment goals did not vary with sex. Patients over the age of 55 were more likely to receive treatment with lipid-lowering agents.

This study was not only supported by previous studies showing a high prevalence of hypertension and dyslipidemia but also brought attention to the high rate of under treatment. The prevalence of dyslipidemia, 11.2%, in this study was much lower than the 26% determined by the Canadian Heart Health Surveys (CHHS) conducted in 1992. The reason suggested for this discrepancy was better pharmacologic control. This would account for the decrease in the number of residents with a serum Total Cholesterol of ≥5.2mmol/L.

Petrella found that there was a large gap between the recommended treatment guidelines and what was actually being provided in clinical care. They identified that there is a large underutilization of treatment for patients. The interaction of a number of risk factors appears to play a role as to whether or not the physician provides treatment for dyslipidemia or hypertension.

The findings of this study have been replicated elsewhere, including the DYSlipidemia International Study (DYSIS), which found that close to 50% of Canadians who were at high risk for CVD did not achieve the treatment targets outlined in the Canadian guidelines [51]. The reason for this gap is attributed to difficulty in taking evidence-based research and applying it to clinical practice [51]. It was also observed that patients tended to be on mono-therapy of low to medium doses of HMG-CoA reductase inhibitors [51].

Older age and male sex were independent predictors of successful treatment [51]. This finding was consistent with results from America and other countries [51]. Women were less likely to achieve target lipid levels, which continues to highlight the difference of managing the disease between the sexes [51]. Overall high Total Cholesterol/HDL ratio was present in 23% of patients [51]. The researchers suggest that there needs to be more emphasis on multi-targeted therapy to better achieve lipid goals [51].

Asghari et al in 2015 conducted a study that examined the prevalence of single and multiple dyslipidemia in primary care across Canada [52]. Using the Canadian Primary Care Sentinels Surveillance Network (CPCSSN) database they included patients age 20 or older that had a complete lipid test done between 2010 and 2012. They used the 2009 Canadian Cardiovascular guidelines to define dyslipidemia. Of the 134,074 individuals in the study 16,319 (14.6%) had isolated high LDL, 8,382 (7.9%) had isolated high TG, and 14,776 (13.2%) had low HDL. With respect to multiple dyslipidemia 3,114 (2.8%) had elevated LDL and low HDL, 5,328 (4.8%) had high LDL and high TG, 10,883 (9.7%) had elevated TG and low HDL. Finally, 2,601 (3.2%) had high LDL, high TG and low HDL.

This study also examined the relationship between rural geography, which was defined using the second digit of the FSA, and dyslipidemia. Rural residence was associated with significant increased odds of having low HDL (OR 1.12). Rural

residents had a significant relationship with high TG with an OR of 1.24. There was also a significant relationship between rural residence and multiple dyslipidemia. For low HDL and high TG the OR was 1.34. The odds ratio for having low HDL, high LDL and high TG in rural regions was significant at 1.33.

There has been research examining possible differences in dyslipidemia between Newfoundland and Labrador and the rest of Canada. Asghari et al 2015, conducted a study that sought to detect differences in the prevalence of dyslipidemia between Newfoundland and Labrador and the rest of Canada [53]. They conducted a cross-sectional study using the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) including adults age 20 and older, and excluded pregnant women. To define dyslipidemia they used the 2009 Canadian Cardiovascular Society guidelines.

The study found several significant results. Newfoundland and Labrador had a significantly higher prevalence of high LDL (29 vs 25%, $p < 0.0001$), low HDL (38 vs 27%, $p < 0.0001$), and high TG (29 vs 26%, $p < 0.0001$) compared to the rest of Canada. The researchers also conducted a multivariate logistic regression model for dyslipidemia. This showed that Newfoundland and Labrador residents were more likely to have dyslipidemia of total Cholesterol (OR: 1.16, $p < 0.0001$), HDL (OR 1.52, $p < 0.0001$), LDL (OR: 1.38, $p < 0.0001$), and total cholesterol/HDL ratio (OR 1.53, $p < 0.0001$).

Overall there is a high prevalence of both single and multiple dyslipidemia in Canada. There is evidence to support that geography may be an independent variable in predicting the odds of developing dyslipidemia. The province of Newfoundland and Labrador appear to have a more dyslipidemic lipid profile than the rest of Canada. It remains to be examined whether the prevalence of dyslipidemia varies between rural and urban regions within Newfoundland and Labrador.

1.5.6 Summary

Dyslipidemia is one of the major modifiable risk factors for the development of CAD and therefore has significant morbidity and mortality associated with it. From review of the literature it is evident that there is a large burden of disease in various populations across the world including within Canada. Evidence also shows that health status and disease prevalence is independently associated with rural-urban environments.

Chapter 2 Research Objectives/Research Question/Hypothesis

2.1 Purpose

The purpose of this thesis is to assess geographic variation in lipid profiles between rural and urban locations in the province of Newfoundland and Labrador.

2.2 Research Questions

2.2.1 Is there a statistically significant difference in the lipid profile of people who live in rural areas compared to those who live in urban areas in Newfoundland and Labrador in 2009-2010? Specifically, are there rural-urban differences in:

- Serum HDL level
- Serum LDL level
- Total serum cholesterol level
- Serum TG level
- Ratio of total serum cholesterol/HDL?

2.2.2 Is there a statistically significant difference in the prevalence of dyslipidemia, as defined by the 2009 Canadian Cardiovascular Society Guidelines, in 2009-2010 between rural and urban areas in Newfoundland and Labrador? Specifically, are there rural-urban differences in:

- Prevalence of HDL dyslipidemia
- Prevalence of LDL dyslipidemia
- Prevalence of TG dyslipidemia
- Prevalence of Total Cholesterol dyslipidemia
- Prevalence of Total Cholesterol/HDL ratio dyslipidemia
- Prevalence of single dyslipidemia?

2.2.3 Is there a statistically significant difference in the prevalence of multiple dyslipidemia between rural and urban areas in Newfoundland and Labrador in 2009-2010?

2.3 Null Hypothesis

2.3.1There is no statistically significant difference in the levels of lipid profiles between rural and urban areas of Newfoundland and Labrador in 2009-2010.

2.3.2 There is no statistically significant difference in the prevalence of dyslipidemia between rural and urban areas of Newfoundland and Labrador in 2009-2010.

2.3.3 There is no statistically significant difference in the prevalence of multiple dyslipidemia between rural and urban areas of Newfoundland and Labrador in 2009-2010.

2.4 Study Objectives

2.4.1 To examine rural-urban differences in lipid profiles (HDL, LDL, TG, Total Cholesterol, Total Cholesterol/HDL ratio) in Newfoundland and Labrador in 2009-2010.

2.4.2 To examine rural-urban differences in the prevalence of dyslipidemia (low HDL, high LDL, high TG, high Total Cholesterol, high Total Cholesterol/HDL ratio) in Newfoundland and Labrador in 2009-2010.

2.4.3 To examine rural-urban differences in the prevalence of multiple dyslipidemia in Newfoundland and Labrador in 2009-2010.

2.5 Significance

Throughout Canada, measures of health have shown significant differences between rural and urban inhabitants, with rural regions tending to have a poorer health status [43][44]. Internationally, studies have shown rural and urban differences in the prevalence of dyslipidemia, which is an important modifiable risk factor for CVD[46][47][48][49] and the focus of this thesis. Within Canada it has been found that the prevalence of dyslipidemia is high and that there is a large proportion of people with dyslipidemia who are not being optimally treated [50][51].

It is known that dyslipidemia is one of the major modifiable risk factors for CVD[2]. Preventing risk factors, such as dyslipidemia, could potentially reduce the massive burden of CVD on the Canadian population [2]. This is highlighted by the fact that 20% of Canadians die from coronary disease and 7% die of cerebrovascular disease [2].

The information provided from this study will allow health professionals to target specific groups at risk with remedial intervention programs that promote normal lipid profiles and hence decrease CVD morbidity and mortality among Newfoundlanders. If geographic location is shown to be a risk factor for dyslipidemia, this study could be expanded to look at other potential differences such as genetic factors, nutrition, availability of exercise facilities and other health factors as potential causes. The methodology used in this study is transferable to other risk factors for CVD such as obesity, diabetes, smoking and hypertension. If this method was used to explore geographic trends in these risk factors, it may allow for a more holistic approach to preventative medicine in areas with high prevalence of these modifiable risk factors.

Newfoundland and Labrador ranks near the bottom of all provinces and territories in various health determining factors. As previously mentioned, Newfoundland and Labrador ranked 12th out of 13 in combined health behaviors [25]. The province was found to be 9th in smoke-free, 10th in physical activity and 11th in health

consumption of fruits in vegetables. Finally, Newfoundland and Labrador was ranked 13th in the healthy weight category with only 33.3% of the population having a healthy weight [25]. These facts are evidence that the province has a poor health status and lend support for the importance of investigating geographic differences in other major modifiable risk factors for CVD such as dyslipidemia.

2.6 Rationale

A large proportion of Newfoundland and Labrador resides in rural regions. As mentioned above, research has shown that rural regions tend to have poorer health status than urban regions. This was part of our rationale for the development of this study.

Furthermore, using secondary data from the Eastern Health Laboratory Information System provided us with a low cost approach to test our hypothesis and develop a methodology to use the available data that could be replicated in future studies. This, to our awareness, was the first study in Newfoundland and Labrador that used existing laboratory data to identify geographic variations in lipid profiles and dyslipidemia.

As it is known that dyslipidemia is a strong risk factor for CVD, it is important to investigate both the prevalence of the disease as well as trends. In doing this we will be able to identify regions with a higher prevalence of disease, which could later be targeted for health education and intervention to determine the cause of the higher rate of disease. This could reduce CVD risk level for the people of Newfoundland. If this occurred there would be a reduction in the burden of disease on the patient, health care system and a decreased economic burden.

Chapter 3 Methods

3.1 Ethics

The Health Research Ethics Board of Newfoundland and Labrador approved the study.

3.2 Study Design

We used a retrospective cross-sectional study design using laboratory data from Eastern Health.

3.3 Data Source

Newfoundland and Labrador residents are provided with a lifetime Medical Care Plan number. For each laboratory service, the patient's identification, date of service, and laboratory test result are entered into the Eastern Health Laboratory Information System (EHL). All blood lipid tests from the Eastern Health Lab between January 1st, 2009 and December 31st, 2010 were extracted for the purpose of this study. The de-identified data was transferred to a secure computer at Primary Healthcare Research Unit for this research. Table 3.1 shows the variables extracted from the EHL and their applications to this thesis.

Table 3.1 Variables Used and Their Purpose in this Thesis

Category	Variable Name	Case Detection Criteria for EHL Data	Purpose
Demographic (Independent Variable)	ID	De-identified ID	To define individual level data
	Age	Birth Year	To describe and compare groups by demographics
	Sex	Sex	
Geographic (Independent Variable)	Postal Code	Postal Code	For data linkage, Geo-referencing
	Urban/Rural	Postal Code (Second digit of FSA)	To describe/compare groups by rural/urban areas
Lipid Profile (Dependent Variable)	Total Cholesterol	Most recent lab result, (lab result, lab date)	To describe and compare Lipid profiles /dyslipidemia
	LDL	Most recent lab result, (lab result, lab date)	
	HDL	Most recent lab result, (lab result, lab date)	
	Triglycerides	Most recent lab result, (lab result, lab date)	
	Total Cholesterol/HDL ratio	Most recent lab result, (lab result, lab date)	

3.4 Study population

3.4.1 Inclusion/Exclusion Criteria

Adults over the age of 20 in the Eastern Health Lab database who had a complete (HDL, LDL, TG, Total Cholesterol) lipid profile done between January 1st, 2009 and December 31st, 2010.

All pregnancy events were used to exclude the pregnant women from the study. If data regarding postal-code was missing, incomplete or invalid, patients were also excluded. Postal-codes that corresponded to regions outside of the province were excluded.

3.5 Data Cleaning and Definition and Derivation of Variables

3.5.1 Data Cleaning and Quality of Data

Prior to beginning our analyses, the data that we received was cleaned. This first involved transforming the text data format to a data format readable by STATA (data analysis and statistical software). To ensure the quality of the data, a preliminary descriptive analysis was performed. The missing data, variables deemed to be out of the expected range, and duplicate cases were removed. The database was then evaluated for the study inclusion and exclusion criteria. Once it was cleaned the data was recoded into different variables such as rural or urban.

Variables created included: rural/urban, age groups, low HDL, high LDL, high TG, high Total Cholesterol, high Total Cholesterol/HDL ratio, single dyslipidemia and multiple dyslipidemia. Rural/urban was coded based on the forward sortation area (FSA) for each patient. The three age groups were generated, which were <40, 40-64, ≥65.

3.5.2 Definition and Derivation of Variables

Place of Residence

Canada is divided into geographic regions defined by a six-digit postal code [40]. The postal codes are unique and represent locations in the real world. The first digit represents a province and the second is used to designate a specific region as rural or urban [40]. In our study we used the first digit to identify postal codes within Newfoundland. We used the second digit to classify each data point as rural or urban.

For the purpose of individual level analysis, the definition we used for determining rural or urban residence was taken from Statistics Canada [40]. Rural Postal Codes were areas serviced by rural route delivery from a post office or postal station. “0” in second position of a postal code denotes a “rural” postal code (also referred to as “rural” FSA – the first three digits of a postal code) [40].

For the purpose of visualization, in the maps, urban centres demonstrates Statistics Canada definition using FSA (Figure 3.1) , *an area with a population of at least 1,000 and a density of 400 or more people per square kilometer* [54][55]. In the statistical analysis, place of residence was a categorical variable classified as rural and urban.

Figure 3.1 FSA codes in Newfoundland and Labrador.

Demographic Variables

Demographic variables include age and sex. The age was classified into one of three groups: less than 39 years old, between 40 and 64 years old and equal or older than 65 years old. These age-groups have been used in dyslipidemia studies previously [55].

Lipid Variables

The Canadian Cardiovascular Society generates national screening guidelines for dyslipidemia and target levels. It is recommended that men over age 40 and women over age 50 have routine screens [4]. In addition it is also suggested that, all postmenopausal women, and anyone living with diabetes, hypertension, obesity, smoking or with a first degree relative under the age of 60 with CVD also undergo screening [4]. The screening test includes the full lipid panel (Total Cholesterol, HDL, LDL, and TG). Our study used the most recent lipid profile for each individual. We also generated the Total Cholesterol to HDL ratio by dividing the two.

Dyslipidemia

We used the 2009 Canadian Cardiovascular Society Guidelines for the definition of dyslipidemia (Table 3.2) [4]. If one lipid profile value was not within the limits, they were classified as having dyslipidemia. The forms of dyslipidemia that were examined included: high cholesterol, high levels of LDL, low levels of HDL, high TG, and an elevated Total Cholesterol/HDL ratio.

Table 3.2 Classification of Dyslipidemia as per the 2009 Canadian Cardiovascular Society Guidelines

High-Density Lipid Dyslipidemia	
Male	<1.0 mmol/L
Female	<1.3 mmol/L
High Low-Density lipid	≥3.4 mmol/L
High Triglyceride	≥1.7 mmol/L
High Total-Cholesterol	≥5.2 mmol/L
Total Cholesterol/HDL ratio	< 5.0

3.5.3 Outcome Measures

Overall Dyslipidemia: We defined overall dyslipidemia as having at least one of the lipid components outside of the recommended range.

Single Dyslipidemia: We defined mutually exclusive dyslipidemia (single dyslipidemia) as the presence of only one lipid component (HDL, LDL, TG, Total Cholesterol) outside of the recommended range.

Multiple Dyslipidemia: We defined multiple dyslipidemia as more than one lipid component (i.e. HDL, LDL, TG,) outside of the recommended range. Total cholesterol and ratio were not considered here as they both contain elements of the other three components.

3.6 Statistical Analysis

Descriptive analyses are presented as means ± standard deviations and frequencies. Continuous variables were compared using the Student *t*-test and categorical variables were compared using the chi-square test. Comparisons were made between rural and urban for each of the dyslipidemia measures.

Prevalence of dyslipidemia for each lipid component was calculated as total number of individuals with dyslipidemia in a geographic location divided by total number of individuals who had a lipid test in the same geographic location during the same time.

Linear regression models were used to assess for a possible variation in lipid levels between rural and urban regions controlling for sex, age group, and the other components of the lipid profile. Total Cholesterol was removed from the linear regression models to assess the rural and urban differences in HDL or LDL and vice versa to avoid co-linearity.

Logistic regressions controlling for the same covariates as above, were conducted to assess a possible rural/urban variation in overall dyslipidemia as well as the dyslipidemia in every component of the lipid profile. Dyslipidemia of Total Cholesterol was removed from the Logistic regressions models to assess the rural

and urban differences in HDL or LDL dyslipidemia and vice versa. A multinomial logistic regression was used to assess for multiple dyslipidemias. This included: low HDL and high TG, high TG and high LDL, high LDL and low HDL, and the presence of all three high LDL, low HDL and high TG. A two-sided *p* value of less than 0.05 for all tests was considered significant. The outcome base for the multinomial logistic regression was no lipid disorder

We conducted a second multinomial logistic regression where we compared single dyslipidemia, dyslipidemia of two lipid variables, and dyslipidemia in three lipid variables. The base outcome was no lipid disorder.

3.7 Geographic Representation

3.7.1 Georeferencing

All individuals in this study were geo-referenced using 3 digit postal-code product and were subsequently assigned to communities. This means that from the FSA we were able to map them to the corresponding region of Newfoundland. ArcGIS 10 was used in our mapping process. We obtained our postal-code conversion file from Statistics Canada. The shape file, NLFSA, based on FSA was from the Census of Population, 2006 (56).

The postal code conversion file (PCCF) is a geospatial reference file that can be available by Statistics Canada upon request and is not readily available to the public. The file provides hierarchical geographic attribute data, which allows for the aggregation and disaggregation of spatially referenced data. The PCCF provided the required information to associate other levels of geography and the non-spatial data attributed to them to the FSA level of geography used in this study. A shapefile is a container file that houses both the geospatial information necessary to map the points, lines or polygons (e.g. geographic coordinates and projection) as well as the attribute data that is tied to each of the mapped polygons. For the purposes of this study we used polygons. Therefore using both PCCF and shapefiles, we were able to

map administrative health data to each of the 35 FSAs and their associated polygons.

3.7.2 Visualization and Spatial Analysis

A choropleth map was used to show proportions of a diagnosed dyslipidemia across the area of the map. This is a thematic map that is divided into specific regions and shaded different densities to represent the proportion of a specific variable, for example dyslipidemia.

To determine if the pattern of diagnosed dyslipidemia and the community characteristics are (similarly or dissimilarly) clustered, dispersed, or random, spatial autocorrelation (both global and local Moran's I) were performed. When Moran's I statistic is greater than zero, one can expect to see high or low values for a given variable clustering with other high or low values (e.g. high/high cluster or low/low cluster). A negative value indicates dispersion since the pattern exhibited is a result of high values repelling low values. A value close to zero means that low and high values do not have any effect on one another and with themselves and therefore result in a random pattern.

Chapter 4 Results

4.1 Study Population

Initially 96,060 people were included, but after excluding 1448 patients with missing information (1.5%) (e.g., wrong or missing postal code, unknown sex, no recorded age) and duplicates, 94,612 (98.5%) of the original individuals were included in the study. Among these individuals nearly 92, 339 (98%) who had a complete lipid profile (HDL, LDL, TG, Total Cholesterol) were eligible for multivariate analyses.

4.2 Characteristics of Study Population

Table 4.1 shows the demographic characteristics for the patients with lipid profile tests done in this study. Of the 94,612 patients, nearly 54% were female. The ages of patients ranged from 20-100 with an overall mean of 53.83 (± 14.95) years. The mean age of men was 53.83 (±14.49) and the mean age of women was 53.84 (±15.35).

Table 4.1 Demographics and Baseline Characteristics of the Study Population

	Total (n=94,612)	**Female (n=50,846)**	**Male (n=43,766)**
Age; mean (SD)	53.83(14.96)	53.84 (15.35)	53.83 (14.49)
Urban; n (%)	80,055 (84.61)	43,433(85.42)	36,662 (83.68)
Rural; n (%)	14,557 (15.39)	7,413(14.58)	7,144 (16.32)

4.3 Lipid Profile

4.3.1 Lipid Profile by Lipid Components

Table 4.2 shows the mean lipid levels for all four components of the lipid profile test; HDL, LDL, TG and Total Cholesterol reported in *mmol/L*. The mean lipid levels of the study population for all four components, for the total population were within normal limits according to the 2009 Canadian Cardiovascular Society guidelines [4].

Table 4.2 Mean and Confidence Interval of Lipid Components in Adults who Had a Lipid Test in Eastern Health Laboratories in 2009-2010

Lipid Component	N	Mean (CI)
High Density Lipid	93,685	1.26 (1.25 - 1.26)
Low Density Lipid	92,420	2.98 (2.97 - 2.98)
Triglyceride	93,871	1.50 (1.49 - 1.50)
Total Cholesterol	94,445	4.90 (4.89 - 4.90)
Total Cholesterol/HDL ratio	93,704	4.15 (4.14 - 4.16)

4.3.2 Rural-urban Differences in Lipid Profile

Table 4.3 shows the results of *t-test* with respect to mean lipid profile. The mean level of HDL was significantly lower in rural inhabitants compared to urban residents (1.21 vs 1.27; *p* for t-test ≤ 0.001). The mean level of TGs was significantly higher in rural regions compared to urban regions (1.59 vs 1.48; *p* for t-test ≤ 0.001). Rural residents had a significantly higher level of Total Cholesterol/HDL ratio than urban residents (4.27 vs 4.13; *p* for t-test ≤ 0.001). The mean level of LDL and Total Cholesterol were significantly higher among urban inhabitants (2.98 vs 2.93; *p* for t-test ≤ 0.001) and (4.91 vs 4.84; *p* for t-test ≤ 0.001), respectively.

Table 4.3 Mean and Confidence Interval of Lipid Components in Rural and Urban Adults who Had a Lipid Test in Eastern Health Laboratories in 2009-2010 by the Place of Residence

Lipid Component	Rural Mean (CI)	Urban Mean (CI)	*p* value
High Density Lipoprotein	1.21 (1.20 –1.22)	1.27 (1.26 – 1.28)	≤0.001
Low Density Lipoprotein	2.93 (2.91 – 2.94)	2.98 (2.97 – 2.99)	≤0.001
Triglyceride	1.59 (1.57 – 1.61)	1.48 (1.47 – 1.49)	≤0.001
Total Cholesterol	4.84 (4.82 – 4.86)	4.91 (4.90 – 4.91)	≤0.001
Total Cholesterol/HDL ratio	4.27 (4.24 – 4.30)	4.13 (4.14 – 4.16)	≤0.001

p value for *t-test*

4.3.3 Rural-urban Differences in Lipid Profile Controlling for Covariates

Table 4.4 shows the results of adjusted analysis using linear regression. As shown in the table below, after adjusting for age, sex, and other lipid components, persons living in urban areas are more likely to have higher levels of HDL by approximately 0.04 units, ($p \leq 0.001$) and lower levels of TG by 0.05 units ($p \leq 0.001$), higher level of Total Cholesterol by 0.083 units ($p \leq 0.001$) and higher levels of LDL by approximately 0.04 units, ($p \leq 0.001$).

The linear regression also shows that persons living in urban regions are more likely to have a lower mean Total Cholesterol/HDL ratio by 0.078 units holding sex, age and other lipid components constant.

Table 4.4 Linear Regression Models Assessing Rural-urban Differences in Lipid Profile (HDL, LDL, TG, Total Cholesterol, Total Cholesterol/HDL ratio) in Newfoundland and Labrador in 2009-2010.

		Cholesterol	HDL	LDL	Triglycerides	Total Cholesterol/HDL ratio
		β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Place of Residence		0.083 (0.064 - 0.102) **	0.036 (0.030 - 0.042) **	0.039 (0.022 - 0.0557) **	-0.0466 (-0.0595 - -0.0338) **	-0.0783 (-0.0984 - -0.058)**
Sex		0.352 (0.338 - 0.366) **	0.232 (0.227 - 0.237)**	0.0399 (0.027 -0.0526) **	0.034 (0.247 - 0.044) **	-0.492 (-0.507 - -0.478) **
Age	**40-64**	0.161 (0.142 - 0.179)**	0.092 (0.085 - 0.098)**	0.021 (0.004 - 0.37) *	0.187 (0.175 - 0.199) **	-0.183 (-0.203 - -0.163) **
	65≥	-0.31 (-0.331 - -0.289)**	0.093 (0.086 - 0.100)**	-0.425 (-0.444 - -0.406)**	0.226 (0.211 - 0.241)**	-0.527 (-0.549 - -0.5040)**
Triglycerides		0.269 (0.263 - 0.274) **	-0.172 (-0.175 - -0.169) **	0.135 (0.127 - 0.143) **	-----	0.573 (0.567 - 0.579)**
LDL		-----	0.051 (0.048 - 0.0533) **	-----	0.079 (0.075 - 0.085) **	-----
HDL		-----	-----	0.35 (0.342 - 0.376) **	-0.72 (-0.733 - -0.708) **	-----

*:P≤ 0.01,** P: ≤0.001, ns : Non-significant
Reference group for sex (male), Reference group for age (age < 40), Reference group for place of residence (rural)

4.4 Dyslipidemia

4.4.1 Dyslipidemia by Lipid Components

As shown in Table 4.5, 74.26% of the study population had dyslipidemia in at least one lipid component. Approximately 44% of the study population was found to have low HDL. Thirty-two percent of the population had high LDL. Twenty-nine percent had high TG. Thirty-eight percent had high Total Cholesterol, and 23% had high Total Cholesterol/HDL ratio.

Table 4.5 Prevalence of Dyslipidemia in Adults who Had a Lipid Test in Eastern Health Laboratories in 2009-2010

Type of Dyslipidemia	%
High Density Lipid	44.36
Low Density Lipid	32.39
Triglyceride	29.62
Total Cholesterol	37.81
Total Cholesterol/HDL ratio	23.05
Overall Dyslipidemia	74.26

4.4.2 Rural-urban Differences in Dyslipidemia

Approximately, 74.26% of the study population had dyslipidemia in at least one lipid component including 76.56% in rural areas, and 73.84% in urban regions. The results of bivariate analysis using chi square test shows, significant differences between rural and urban regions for low HDL (48.13% vs 43.68%; *p for* chi square test ≤ 0.001), high TG (33.53% vs 28.91%; *p for* chi square test ≤ 0.001), high Total Cholesterol (36.85% vs 37.98%; *p for* chi square test ≤ 0.01) and high Total Cholesterol/HDL ratio (25.54.2% vs 22.61%; *p for* chi square test ≤ 0.001). No significant difference was found for high LDL, between the rural and urban regions. These results are depicted in Figure 4.1.

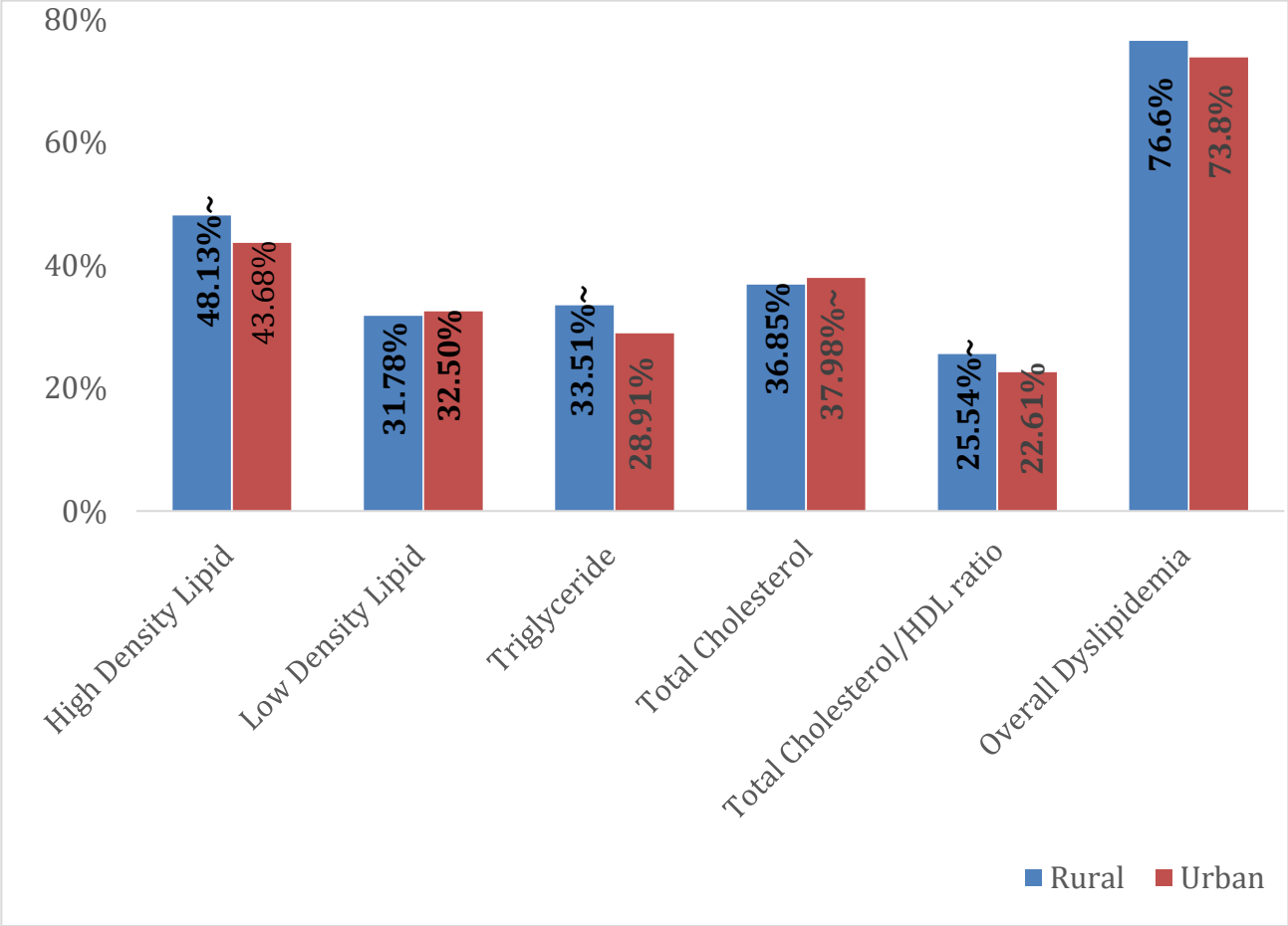

Figure 4.1 Prevalence of Dyslipidemia in Adults Who Had a Lipid Test in Eastern Health Laboratory in 2009-2010 by the Place of Residence.
Significance Represented by ~ (based on p value for chi square test).

4.4.3 Single and Multiple Dyslipidemia

Among patients who had a complete lipid profile, approximately 40.64 % had single dyslipidemia. As seen in Table 4.6, 16% of the study population had only high LDL, 20% had only low HDL and 14% had only high TG. Table 4.6 also shows patients with multiple dyslipidemia nearly 23.63% had dyslipidemia of two lipid components and 5.88% dyslipidemia of three lipid components. Seven percent of the study population had low HDL and high LDL, 5% had low HDL and high TG, 12% had high LDL and high TG, and 6% had low HDL, high LDL and high TG.

Table 4.6 Prevalence of Single and Multiple Dyslipidemia in Adults who Had a Complete Lipid Test in Eastern Health Laboratory in 2009-2010 by the Place of Residence (N= 92,437)

Type of Dyslipidemia		%
Single Dyslipidemia	LDL	15.91%
	HDL	20.47%
	TG	6.12%
Multiple Dyslipidemia	HDL, LDL	7.38%
	HDL, TG	4.70%
	LDL, TG	12.63%
	HDL LDL TG	5.88%
No lipid disorder		26.92%

4.4.4 Rural Urban Differences in Single and Multiple Dyslipidemia

As shown in Figure 4.2, approximately 23% of rural residents did not have any lipid disorder. Thirteen percent had only high LDL, 6.1% had only high TG and 20% had only low HDL. Approximately 7% of rural residents had high LDL and low HDL, 14% had high TG and low HDL, and 6% had high TG and high LDL. Seven percent of rural residents had high LDL, low HDL and high TG.

As shown in Figure 4.3, approximately 26% of urban residents did not have any lipid disorder. Fifteen percent had only high LDL, 19% had only low HDL, and 6% had only high TG. Nearly 7% of urban residents had high LDL and low HDL, 12% had low HDL and high TG, and 5% had high TG and high LDL. Six percent of urban residents had high LDL, low HDL and high TG.

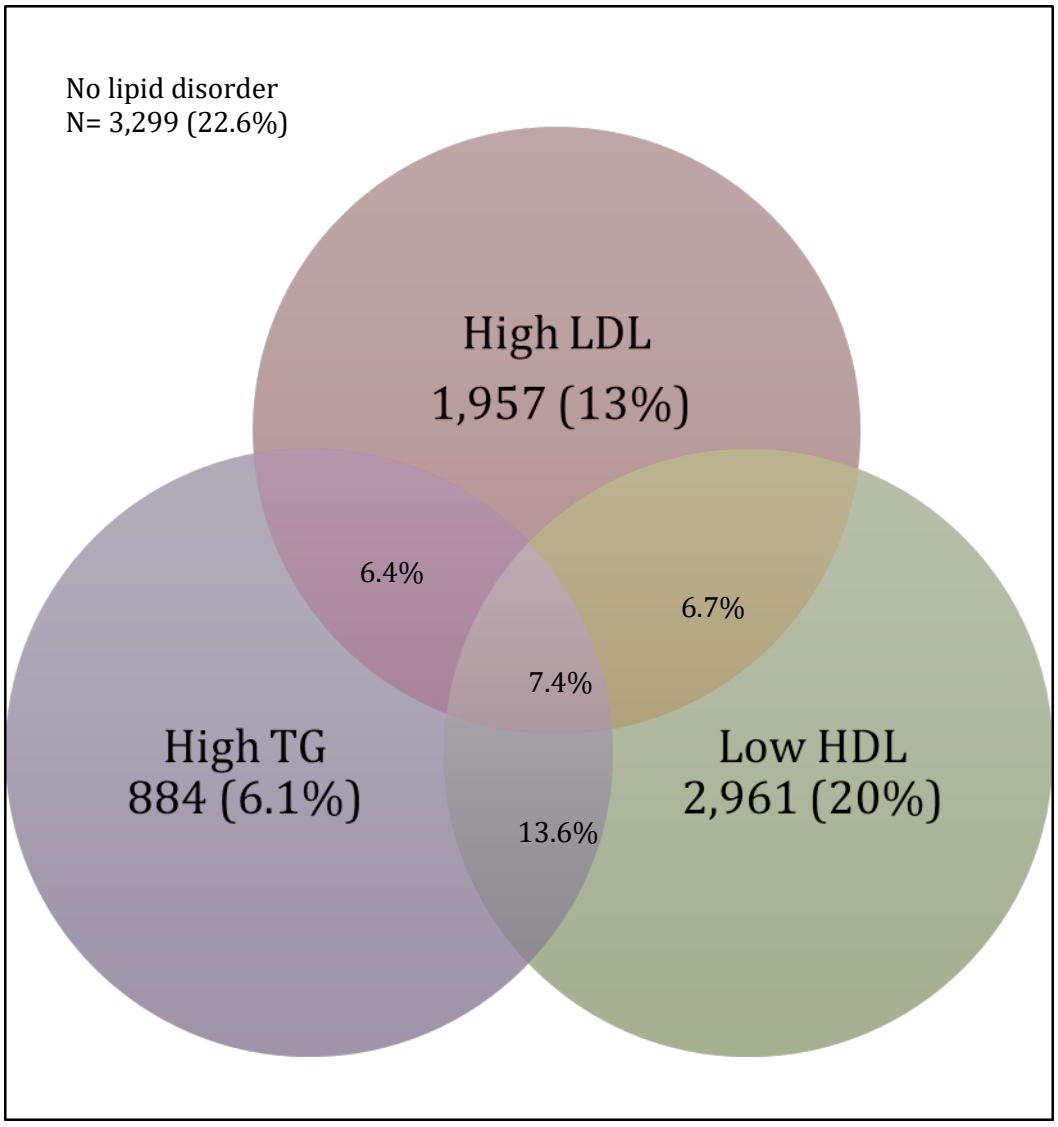

Figure 4.2 Single and Multiple Dyslipidemia in Adults in Rural Regions Who Had a Lipid Test in Eastern Health Laboratory in 2009-2010

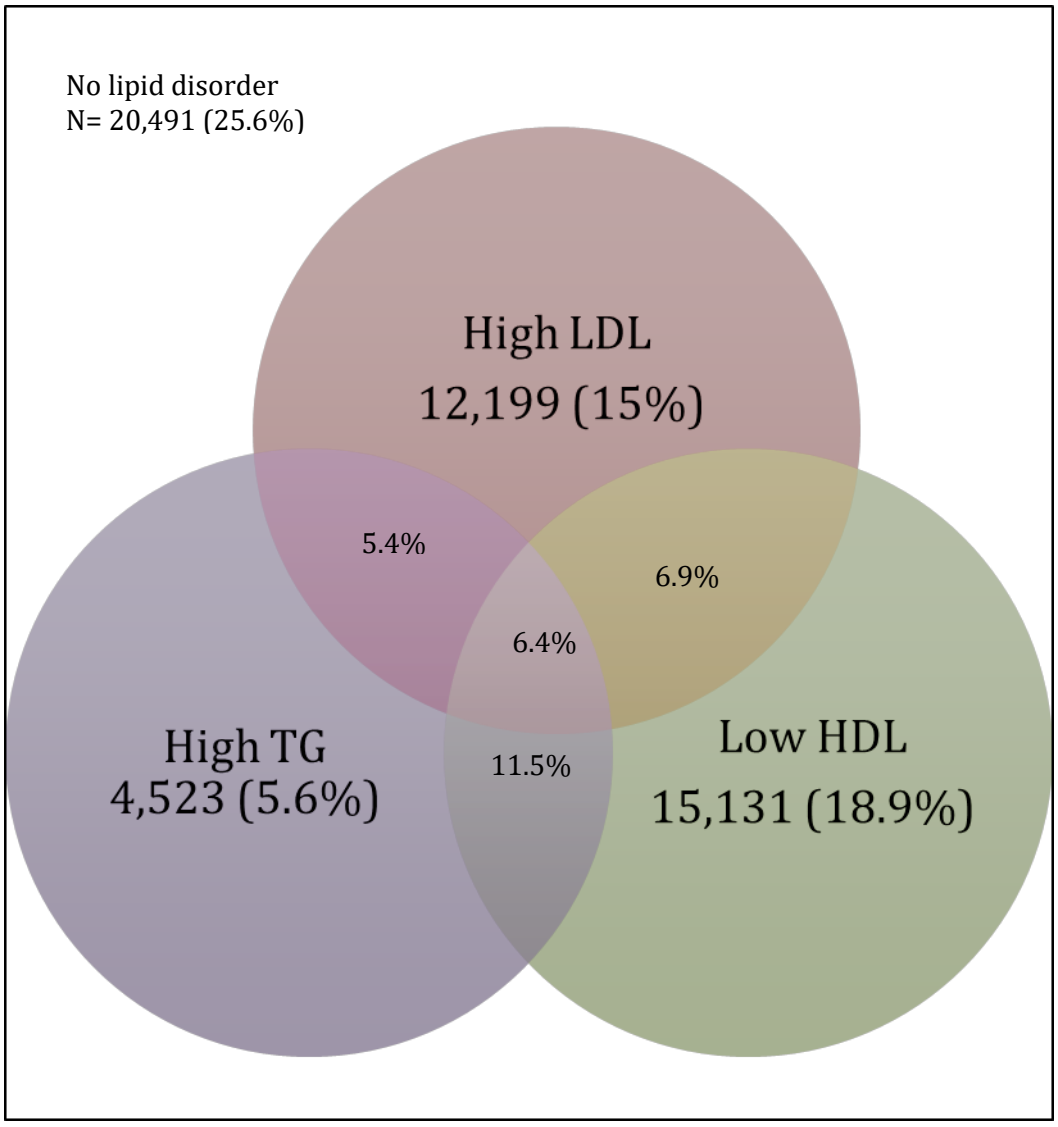

Figure 4.3 Single and Multiple Dyslipidemia in Adults in Urban Regions Who Had a Lipid Test in Eastern Health Laboratory in 2009-2010

4.4.5 Rural-urban Differences in Dyslipidemia Controlling for Covariates

As shown in Table 4.7, after controlling for covariates, urban residents were 15% less likely to have overall dyslipidemia than rural residents (OR: 0.85, CI: 0.81-0.88; $p \leq 0.001$). The results of the logistic regression also shows that persons living in urban regions were 15% less likely to have low HDL (OR: 0.85, CI: 0.82 - 0.88; $p \leq 0.001$), 14% less likely to have high TG (OR: 0.86, CI: 0.83 - 0.89; $p \leq 0.001$), and 17% less likely to have a high Total Cholesterol/HDL ratio (OR: 0.83, CI: 0.79 - 0.86; $p \leq$

0.001), respectively. Persons living in urban regions were 7% more likely to have high Total Cholesterol (OR: 1.07, CI: 1.03 - 1.11; $p \leq 0.001$).

The logistic regression also suggests women were 28% more likely than men to have overall dyslipidemia (OR: 1.28, CI: 1.25-1.32; $p \leq 0.001$), 57% more likely to have dyslipidemia of Total Cholesterol (OR: 1.57, CI: 1.52-1.61; $p \leq 0.001$), 50% more likely to have low HDL (OR: 1.50, CI: 1.45-1.54; $p \leq 0.001$) and 17% more likely to have high LDL (OR: 1.17, CI: 1.14-1.20; $p \leq 0.001$), respectively.

Table 4.7 Logistic Regression Models Assessing Rural-urban Differences in Dyslipidemia in Newfoundland and Labrador in 2009-2010.

		Overall Dyslipidemia	Cholesterol	HDL	LDL	Triglycerides	Total Cholesterol/ HDL ratio
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Place of residence		0.85 (0.81 - 0.88) **	1.07 (1.03 - 1.11) **	0.85 (0.82 - 0.88) **	0.99 (0.96 - 1.04) ns	0.86 (0.83 - 0.89) **	0.83 (0.79 - 0.86) **
Sex		1.28 (1.25 - 1.32) **	1. 57 (1.53 - 1.61) **	1.50 (1.45 - 1.54) **	1.17 (1.14 - 1.20) **	0.62 (0.60 - 0.64) **	0.42 (0.41 - 0.44) **
Age	**40-64**	1.29 (1.24 - 1.34) **	1.57 (1.51 - 1.63) **	0.74 (0.71 - 0.77) **	1.26 (1.22 - 1.31) **	1.40 (1.34 - 1.46) **	0.80 (0.76 - 0.83) **
	65≥	0.96 (0.92 - 1.00) ns	0.80 (0.76 - 0.83) **	0.79 (0.76 - 0.82) **	0.64 (0.61 - 0.67) **	1.46 (1.40 - 1.54) **	0.46 (0.44 - 0.49) **
Triglycerides		----------	2.12 (2.06 - 2.18) **	3.09 (3.00 - 3.18) **	1.74 (1.69 - 1.79) **	----------	----------
LDL		----------	----------	0.66 (0.64 - 0.67) **	----------	1.76 (1.70 - 1.81) **	----------
HDL		----------	----------	----------	0.66 (0.64 - 0.67) **	3.11 (3.01 - 3.20) **	----------

*= P≤ 0.01, **=P ≤0.001, ns = Non-significant
Reference group for sex (male), Reference group for age (age < 40), Reference group for place of residence (rural)
Overall dyslipidemia: having at least one of the lipid components outside of the recommended range

4.4.6 Rural-urban Differences in Single and Multiple Dyslipidemia Controlling for Covariates

Table 4.8 shows the result from multinomial logit for multiple dyslipidemia including type of dyslipidemia. After controlling for sex and age, urban residents were 14% less likely to have combined low HDL and high LDL (OR: 0.86, CI: 0.80 – 0.93, $p \leq 0.001$). Urban residents were 26% less likely to have combined low HDL and high TG (OR: 0.74, CI: 0.7 – 0.79, $p \leq 0.001$), 17% less likely to have combined high LDL and high TG (OR: 0.83, CI: 0.76 – 0.91, $p \leq 0.001$), and 26% less likely to have combined low HDL, high LDL and high TG (OR: 0.74, CI: 0.69 – 0.81, $p \leq 0.001$).

Table 4.9 shows the result from the multinomial logit for single and multiple dyslipidemia. After controlling for sex and age, place of residence was significantly associated with having single and multiple dyslipidemia. Urban residents were 13% less likely to have single dyslipidemia (OR: 0.87, CI: 0.83-0.91; $p \leq 0.001$), 22% less likely to have dyslipidemia in two lipid components (OR: 0.78, CI: 0.75-0.83; $p \leq 0.001$), and 26% less likely to have dyslipidemia in three lipid components (OR: 0.74, CI: 0.69-0.81; $p \leq 0.001$), respectively.

Table 4.8 Multinomial Logistic Regression Model Assessing Rural-urban Differences in Single and Multiple Dyslipidemia in Newfoundland and Labrador in 2009-2010.

		Single Dyslipidemia			Multiple Dyslipidemia			
		HDL	**LDL**	**TG**	**HDL& LDL**	**HDL& TG**	**LDL& TG**	**HDL&LDL& TG**
		OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Place of residence		0.78 (0.75-0.83) **	1.01 (0.94-1.07) ns	0.84 (0.78-0.91) **	0.86 (0.80-0.93) **	0.74 (0.70-0.79)**	0.83 (0.76-0.91) **	0.74 (0.69-0.81) **
Sex		1.23 (1.18-1.28) **	1.03 (0.99-1.07) ns	0.49 (0.46-0.53) **	1.77 (1.67-2.01) **	0.93 (0.89-0.97) **	0.56 (0.53-0.61) **	1.31 (1.24-1.39) **
Age	**40-64**	0.77 (0.73-0.81) **	1.79 (1.69-1.90) **	1.84 (1.68-2.02) **	0.95 (0.89-1.02) ns	1.37 (1.28-1.46) **	1.63 (1.48-1.78) **	1.21 (1.11-1.31) **
	65≥	0.87 (0.81-0.92) **	0.95 (0.89-1.02) ns	1.70 (1.54-1.88) **	0.43 (0.39-0.46) **	1.52 (1.42-1.63) **	0.86 (0.76-0.96) *	0.64 (0.58-0,71) **

*= P≤ 0.01, **=P ≤0.001, ns = Non-significant

Reference group for sex (male), Reference group for age (age < 40), Reference group for place of residence (rural), base outcome no lipid disorder

Overall dyslipidemia: having at least one of the lipid components outside of the recommended range

Table 4.9 Multinomial Logistic Regression Model Assessing Rural-urban Differences in Single and Multiple Dyslipidemia in Newfoundland and Labrador in 2009-2010.

		Single Dyslipidemia	Dyslipidemia in two components of lipid	Dyslipidemia in 3 components of lipid
		OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**
Place of residence		0.87 (0.83-0.91) **	0.78 (0.75-0.83) **	0.74 (0.69-0.81) **
Sex		1.01 (0.97-1.04) ns	1.02 (0.98-1.05) ns	1.31 (1.23-1.39) **
Age	**40-64**	1.16 (1.11-1.21) **	1.24 (1.18-1.30) **	1.21 (1.12-1.39) **
	65≥	0.97 (0.93-1.02) ns	0.96 (0.91-1.02) ns	0.64 (0.58-0.71) **

*= P≤ 0.01,**=P ≤0.001, ns = Non-significant
Reference group for sex (male), Reference group for age (age < 40), Reference group for place of residence (rural)
Base outcome: No lipid disorder

4.5 Geographical Representation of Lipid Tests and Dyslipidemia

4.5.1 Geographic Representation of Number of Lipid Tests

Figure 4.4, shows the spatial distribution of lipid tests performed during the study period in the Eastern Health laboratory region. The number of the tests per FSA varied between 20 and 13000. The majority of lipid tests were done in FSAs that mapped to regions on the Avalon Peninsula. Western Newfoundland and Labrador had fewer lipid tests completed than the Eastern Health District. The distribution of lipid tests was found to be spatial autocorrelated (I=0.48, Z-score=6.05, p=0.000001). Since the z-score is both positive and significant, we therefore reject Moran's I null hypothesis which assumes the random distribution of lipid tests among the FSA regions. This means that the pattern exhibited by number of lipid tests are unlikely due to random chance and instead display a clustered pattern as demonstrated by the Avalon Peninsula in figure 4.4.

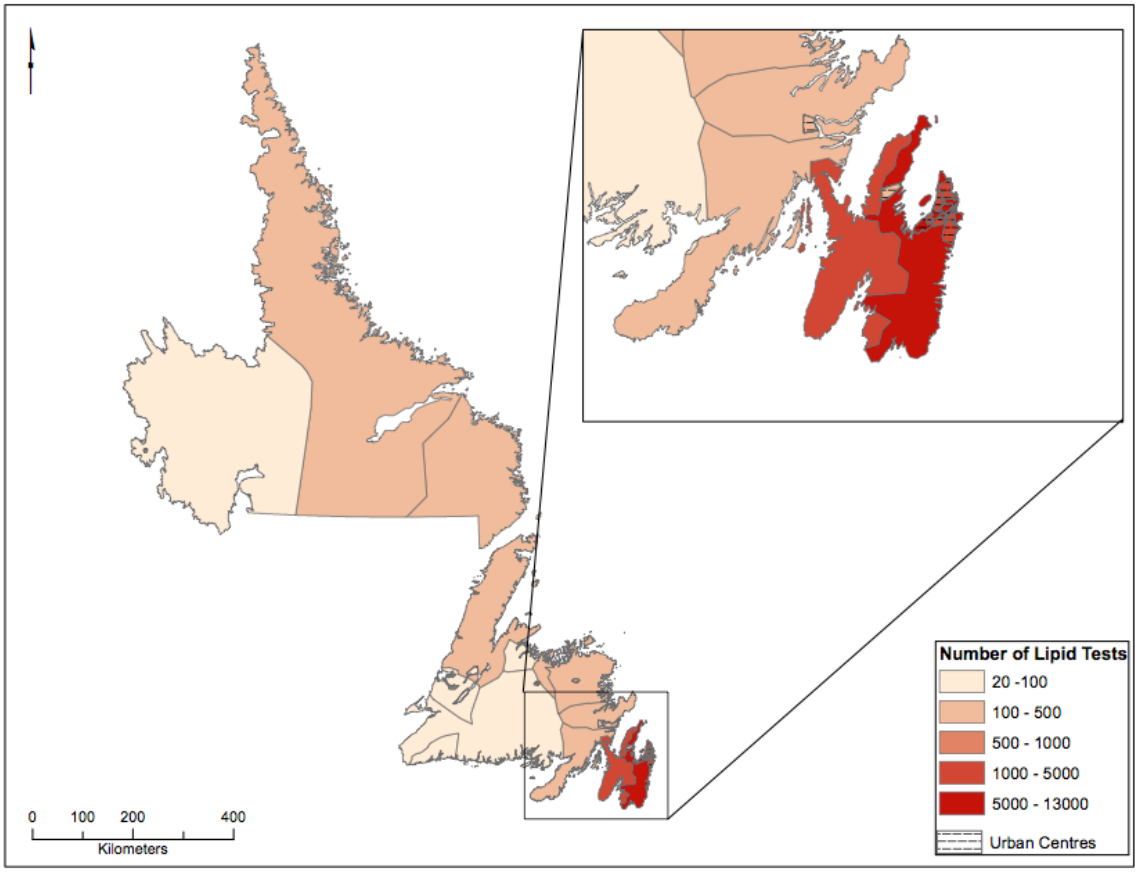

Figure 4.4 Number of Lipid Tests Performed between 2009 and 2010 in Eastern Health Laboratory in NL by the Place of Residence

4.5.2 Geographic Representation of Dyslipidemia

Spatial representations of dyslipidemia using the lab tests for the Eastern Health Region in the form of maps were generated to enable visual examination of potential trends based on Forward Sortation Areas (FSA) (Figures 4.5, 4.6, 4.7, 4.8. 4.9, 4.10). The dashed areas in each of the maps represents urban centers based on FSA (St. John's(A1A-A1H), Torbay (A1K), Paradise(A1L), Mount Pearl,(A1N) Portugal Cove – St Phillips (A1M), Goulds (A1S), Gander(A1V), Manuels (A1W), Carbonear (A1Y), Conception Bay South(A1X), Clarenville(A5A), , Grand Falls (A2A)-Grand Falls-Windsor (A2B), Deer Lake (A8A), Corner Brook (A2H), Stephenville (A2N), Labrador City (A2V)) [57]. Although FSA is not primarily used to designate a place/town/city, the urban centers listed above can be associated with a particular FSA since each

one only appear within the boundaries of that particular place/town/city. The results below will refer to the associated place/town/city rather than the FSA code. The prevalence of dyslipidemia in the entire population was 74.86% (Figure 4.5). The areas that had the highest prevalence of dyslipidemia include Grand Falls-Windsor (A2B) (100%), Springdale (A0J) (88%) and Mary's Harbour (A0K) (86%). The areas that had the lowest prevalence of dyslipidemia include St. John's (Southwest) (69%), St. John's (North) (73%) and Paradise (A1L) (74%).

The areas that had the highest prevalence of low HDL include Springdale (Northern Newfoundland) (A0J) (68%), Grand Falls-Windsor (A2B) (68%) and Labrador City (A2V) (62%) (Figure 4.6). Some of the areas with the lowest prevalence of HDL dyslipidemia include St. John's (North) (40%), Paradise (A1L) (40%), Torbay (A1K) (40%) (Figure 4.6).

The areas that had the highest prevalence of high LDL include Grand Falls-Windsor (A2A) (48%), Stephenville (A2N) (46%), and Paradise (A1L) (46%). Some of the areas with the lowest prevalence of high LDL include Port-Aux-Basque (A0M) (22%), Deer Lake (A8K) (23%) and Port-au Port Peninsula region (A0N) (28%) (Figure 4.7).

The areas that had the highest prevalence of high Total Cholesterol include Grand Falls-Windsor (A2A) (48%), Paradise (A1L) (47%), and Torbay (A1K) (41%) (Figure 4.8). Some of the areas with the lowest prevalence of high Total Cholesterol include Churchill Falls (A0R)(29%), Carbonear (A1Y) (30%), Deer Lake (A8A) (31%) (Figure 4.8).

The areas that had the highest prevalence of High Total Cholesterol/HDL ratio include Paradise (A1L) (53%), Stephenville (A2N) (46%), Labrador City (A2V) (44%) and (Figure 4.9). Some of the areas with the lowest prevalence of high Total Cholesterol/HDL ratio include Churchill Falls (A0R) (16%), St. John's (North) (21%), and St. John's (22%) (Figure 4.9).

The areas that had the highest prevalence of high TG include Grand Falls-Windsor (A2A) (51%), Paradise (A1L) (46%) and Grand Falls-Windsor (A2B) (45%) (Figure 4.10). These regions are darker in color on the maps. Some of the areas with the

lowest prevalence of high TG include St. John's (Southwest) (24%), Goulds (A1S) (27%), and Carbonear (A1Y) (28%) (Figure 4.10).

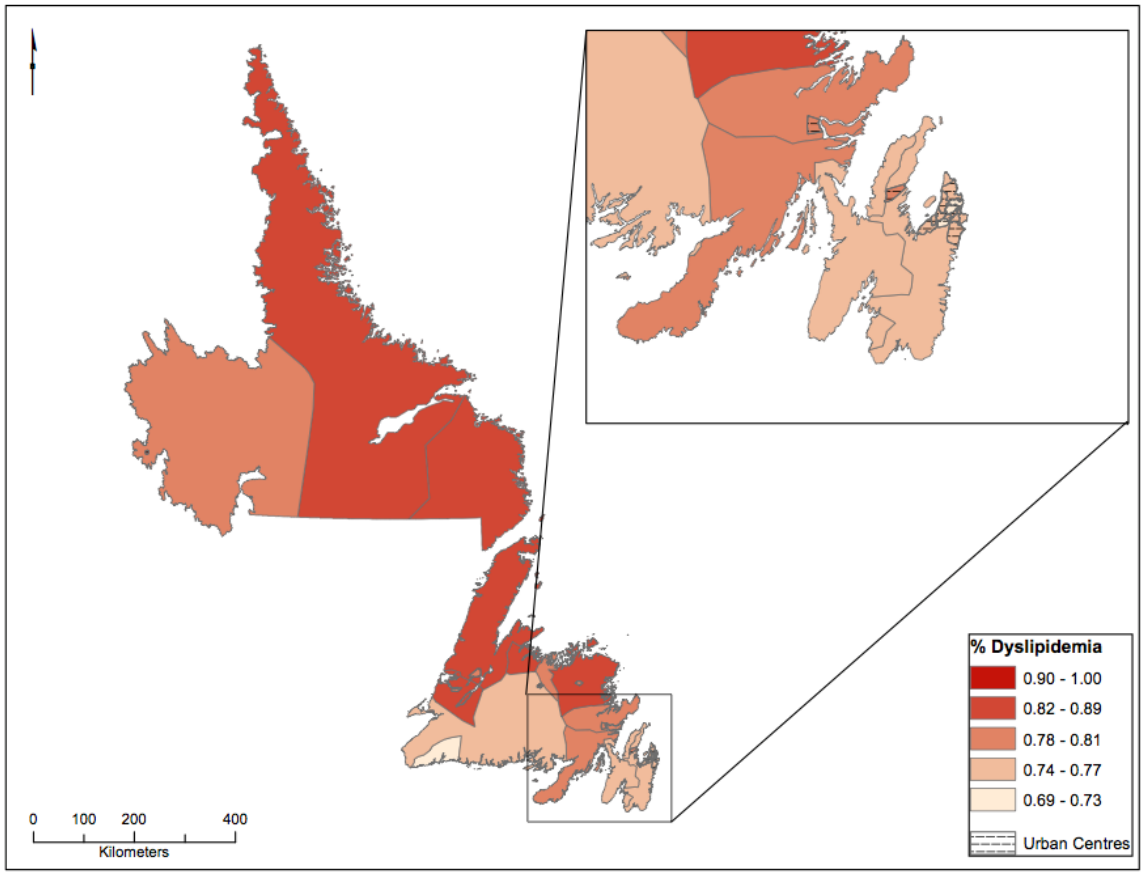

Figure 4.5 Prevalence of Overall Dyslipidemia among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

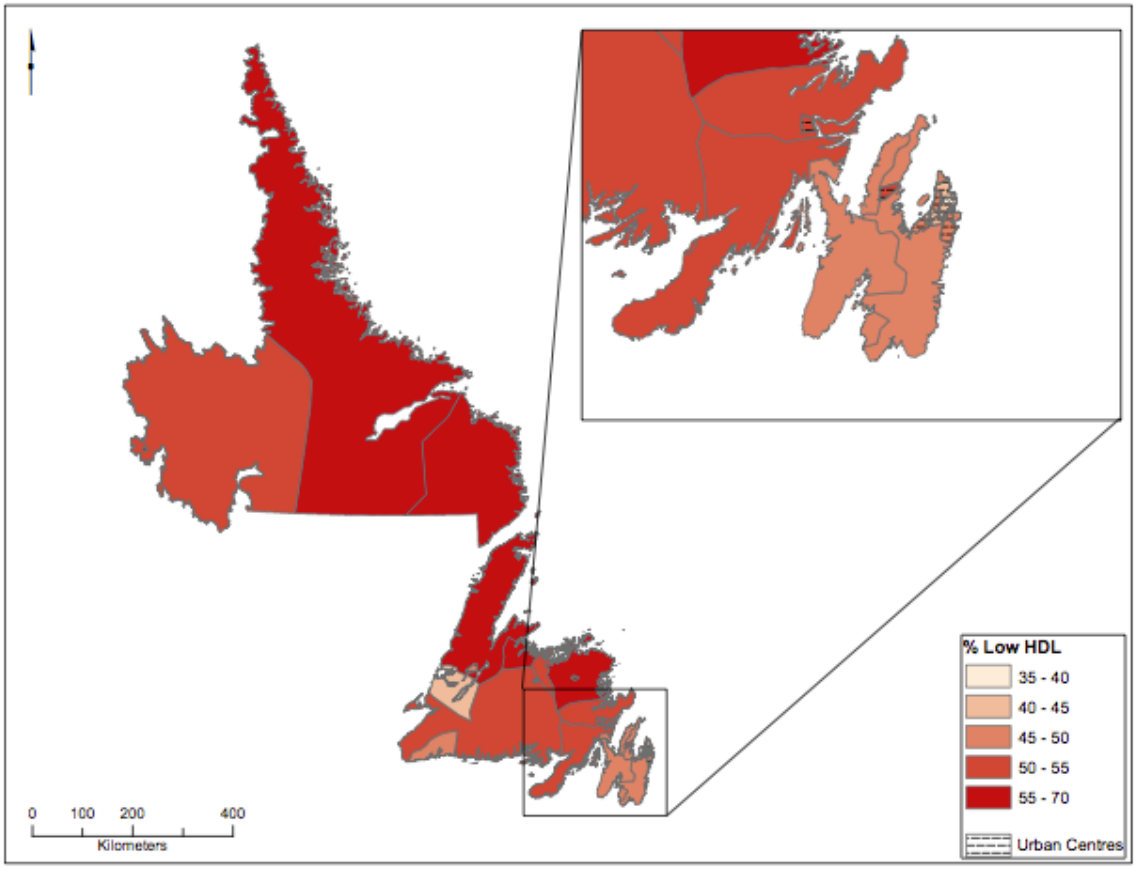

Figure 4.6 Prevalence of Low HDL among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

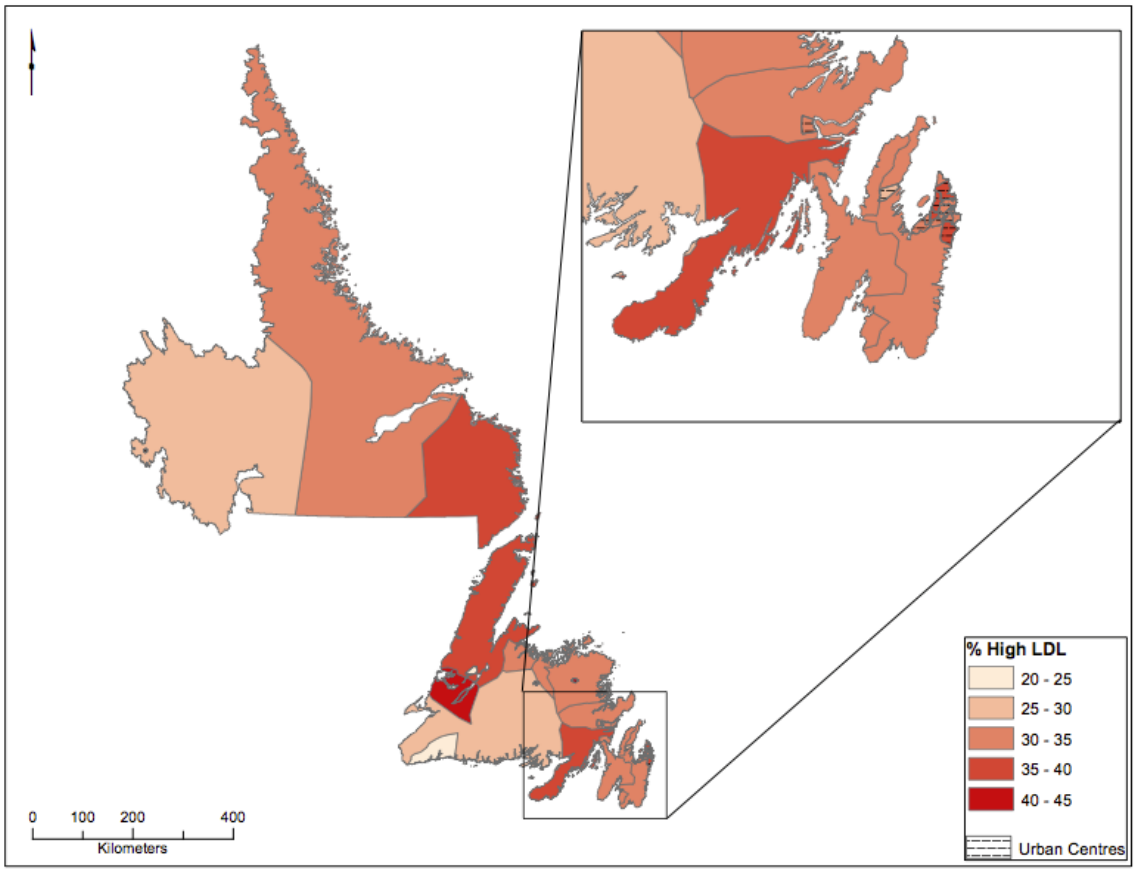

Figure 4.7 Prevalence of High LDL among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

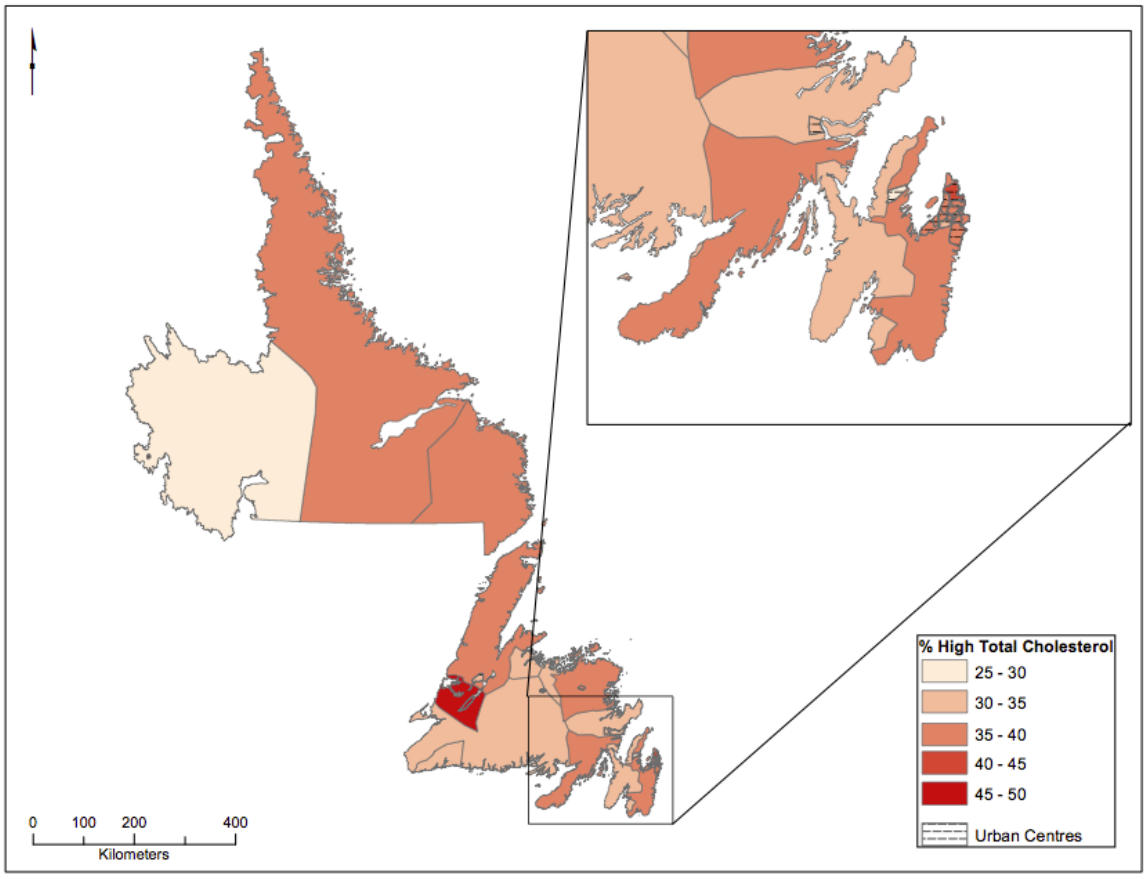

Figure 4.8 Prevalence of High Total Cholesterol among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

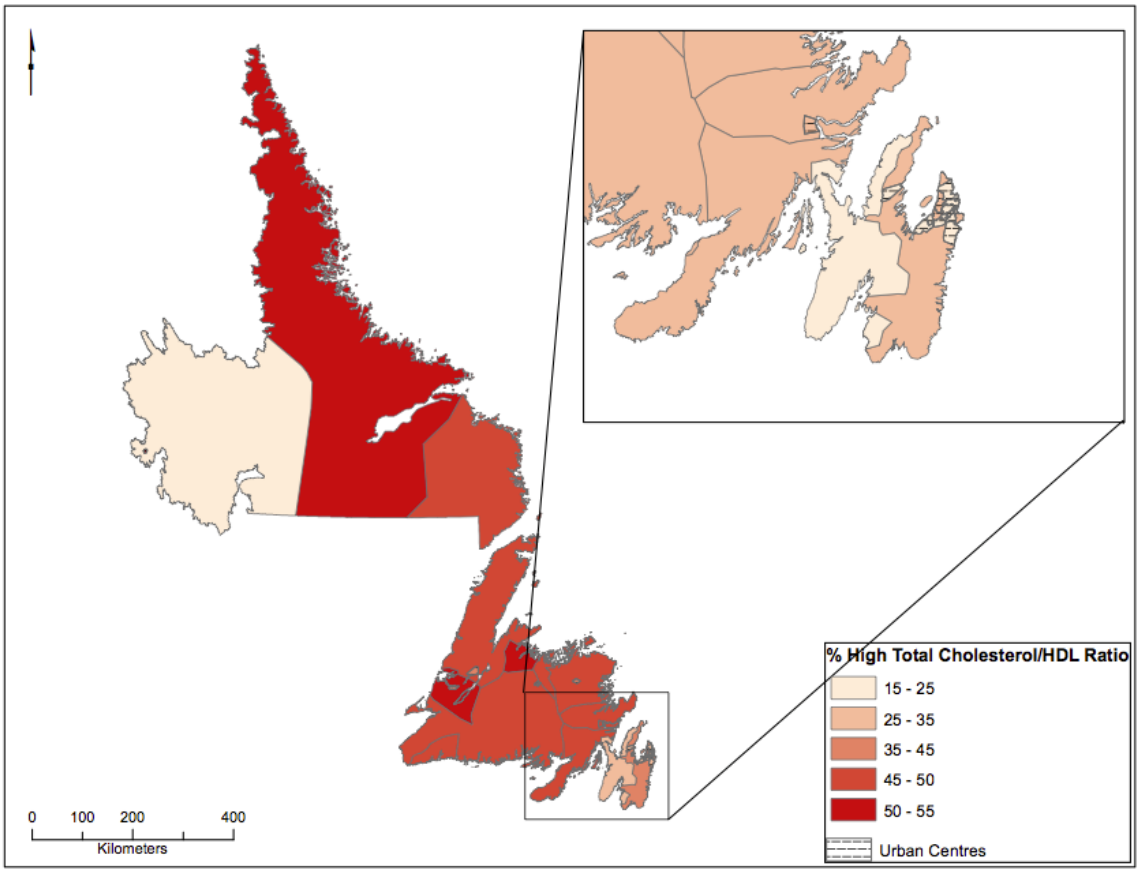

Figure 4.9 Prevalence of High Total Cholesterol/HDL Ratio among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

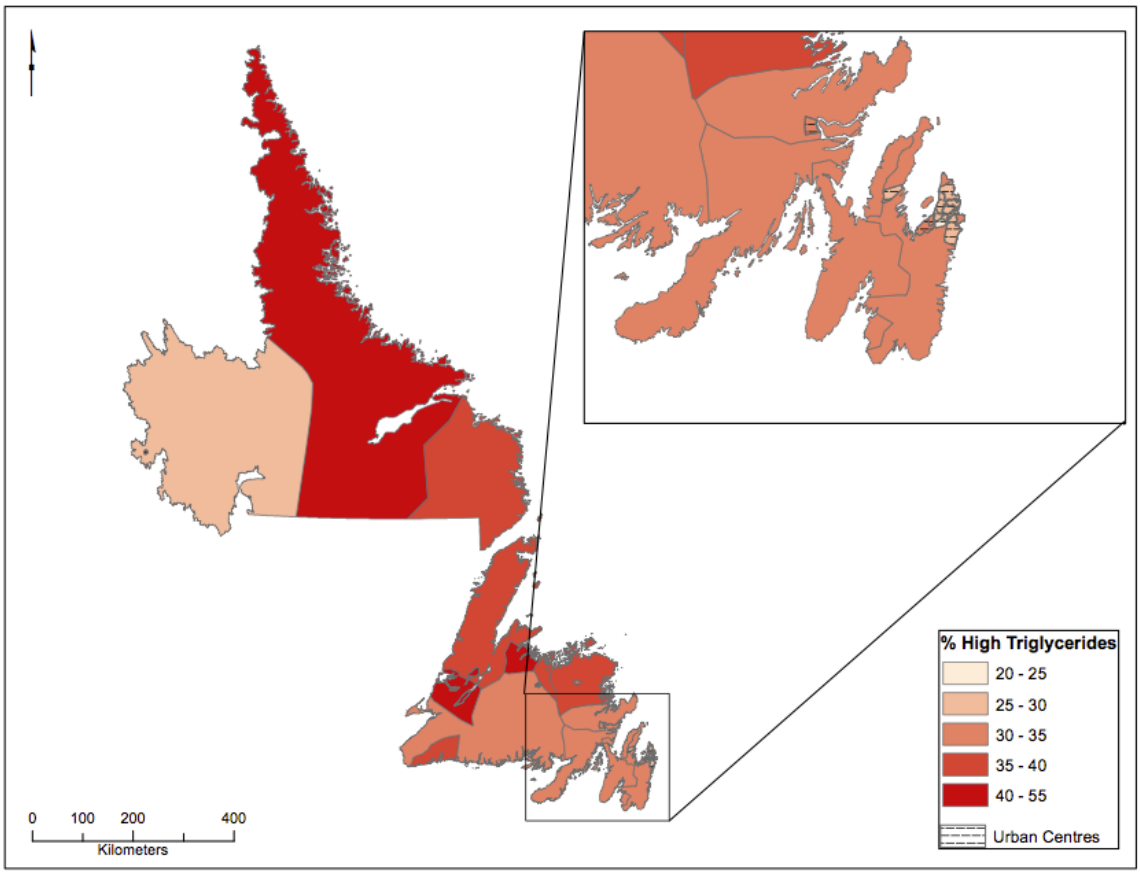

Figure 4.10 Prevalence of High TG among Adults who Had a Lipid Test in Eastern Health Laboratory in NL by the Place of Residence

4.6 Spatial Correlation

4.6.1 Spatial Autocorrelation

Moran's *I* was used *t*o assess for global spatial autocorrelation. As shown in table 4.11, Moran's *I* was found to be significant for overall dyslipidemia, HDL, TG and Total Cholesterol/HDL ratio suggesting spatial correlation in these lipid abnormalities. The index for overall dyslipidemia was found to be 0.47, 0.45 for HDL, 0.59 for TG, and the index for Total Cholesterol/HDL ratio was found to be 0.245. The Z-scores were 6.05, 5.5, 7 and 3.07 respectively, which means that there is a less than one percent likelihood the observed clustered patterns is a result of random chance.

Table 4.10 Spatial Autocorrelation- Moran's I Statistic

Dyslipidemia	Moran's Index	Z-score	p-value
Overall Dyslipidemia	0.47493	6.0525	≤0.001
LDL	-0.16367	-1.538	Non-significant
HDL	0.455829	5.501	≤0.001
Cholesterol	-0.11296	-0.9552	Non-significant
TG	0.5938	7.073	≤0.001
Total Cholesterol/HDL Ratio	0.244816	3.07223	≤0.01

Chapter 5 Discussion

5.1 Summary

This study, using a secondary analysis of the data from Eastern Health Laboratory Database, suggests a high prevalence of dyslipidemia among adults who had a lipid test done in Newfoundland and Labrador in 2009-2010. The study also suggests that patterns of dyslipidemia differ between rural and urban regions, with rural having a greater prevalence of dyslipidemia**.**

The study also showed significant differences in the mean levels of all four lipid components between rural and urban regions. Rural regions had lower levels of HDL, higher levels of TGs and a higher mean Total Cholesterol/HDL ratio, while urban regions had higher levels of LDL and Total Cholesterol. The mean values for these lipid components were not found to be outside the recommended range for general population.

5.2 Lipid Profile

For the overall population no mean values of any lipid component were found to be outside the range recommended by the Canadian Cardiovascular Society [4]. While this finding is somewhat reassuring, it must be noted that despite these mean values, this study found a high percentage of dyslipidemia in the study population.

Urban regions had significantly higher levels of LDL and Total Cholesterol. None of the mean levels for rural or urban were found to be at an unhealthy level. Unfortunately, we found no studies within Canada that have been conducted comparing lipid levels between rural and urban regions. Studies in Tanzania [46] have shown that upon migration from rural to urban regions there is a significant increase in cholesterol, HDL and TGs. There was a non-significant increase in LDL. Our findings are consistent with this study for HDL, and Total Cholesterol; however,

our results differ for TGs and LDL. It is difficult to say whether or not we can generalize the results from Tanzania to our study in Newfoundland given the likely differences in culture and or genetics.

Rural regions had significantly lower levels of HDL and significantly higher levels of TGs than urban regions. This finding was expected based on previous research [47].

Holding age, sex, and other lipid components constant, people living in urban regions were more likely to have lower levels of HDL, high levels of TGs, high levels of Total Cholesterol and higher levels of LDL. The differences between rural and urban values were small, with the largest difference being 0.083 for Total Cholesterol. This may indicate that in addition to geography other factors, such as biological factors may be at play. The cause is likely multi-factorial including diet, income, education and physical exercise [58].

5.3 Dyslipidemia

Our results showed 75 % of the study population had dyslipidemia in at least one component of the lipid profile including 44% of the population low HDL, 34% high LDL, 30% high TG, 38% high Total Cholesterol and 24% a high Total Cholesterol/HDL ratio. Our results differ from those of the Canadian Health Measures Survey (CHMS) [6], which found that 36% of Canadians had high LDL, 30% had low HDL, 25% had high TG 41% had high Total Cholesterol and up to 23% had a high Total Cholesterol/HDL ratio. This finding supports the anecdotal claim that the lipid pattern in Newfoundland could be different from the rest of Canada. The finding that rural residents have a higher prevalence of dyslipidemia is consistent with previous Canadian literature showing that rural regions have worse health status than urban regions [44], [58], [59], [60], [61], [62]. One study in NL done by Chockalingham and Fodor [61] found the prevalence of high Total Cholesterol to be 60% in the rural population of Old Perlican (A0A). Unfortunately we do not have data for Old Perlican alone. Our data for the FSA A0A yielded a

prevalence of high Total Cholesterol of 30%. It is important to keep in mind that their study was done in one location within an FSA, whereas ours took numerous rural regions under the same FSA into account. Despite this it does seem that they found a much larger percentage of elevated cholesterol than our study did in that region.

Unfortunately, we found no studies within Canada have been conducted comparing lipid levels between rural and urban regions. Studies in Tanzania [46] have shown that upon migration from rural to urban regions there is a significant increase in Total Cholesterol, HDL and TGs. There was a non-significant increase in LDL. Our findings are consistent with this study for HDL, Total Cholesterol and LDL; however, our results differ for TGs. Our findings are also supported by those in various parts of the world that have shown rural to urban migrations result in a significant increase in HDL [48]. The finding that low HDL and high TGs are significantly more prevalent in rural regions was also found in Shanghai [47].

These results may imply that environment has a stronger influence on HDL and TGs than LDL and Total Cholesterol. The cause is likely multi-factorial including diet, income, education and levels of physical exercise [58], [62].

5.4 Multiple Dyslipidemia

Our results showed that place of residence was associated with having multiple forms of dyslipidemia. Rural residents throughout the country have poorer health than urban residents [62]. Living in an urban environment was associated with significantly decreased odds of having 1, 2 and 3, forms of dyslipidemia. The finding that living in a rural environment is significantly associated with increased odds of having multiple forms of dyslipidemia was expected. Our finding that rural inhabitants have an increased odds of multiple dyslipidemia is consistent with other studies in Newfoundland that have shown rural regions to have poor health, and

several modifiable risk factors for CVD [40]. Dyslipidemia is a known modifiable risk factor for CVD. Our finding of a higher prevalence of dyslipidemia in rural regions parallels the finding in Quebec that showed rural residents had more MI than urban residents [58].

The Canadian Institute for Health Information (CIHI) has examined the health of rural Canadians. Compared with urban regions, rural regions tend to have lower income, less than secondary education and a higher proportion of people who smoke and do not exercise regularly [60], [61]. They also tend to have less healthy diets [56]. These factors could contribute to the dyslipidemia in this study population.

The finding that dyslipidemia is more likely in rural regions is consistent with previous research showing that health of rural residents is worse than urban [64]. The finding of this study could suggest that there needs to be increased surveillance of dyslipidemia in Newfoundland, particularly in rural areas.

5.5 Limitations

This cross-sectional study using laboratory data was aimed to provide a snapshot of rural-urban differences in dyslipidemia in Newfoundland and Labrador. The data for this study came from the Eastern Health Laboratory Database so the data may have failed to capture the lipid tests performed in other health regions in Newfoundland and Labrador; however, a breakdown of the tests performed in different health regions in NL from laboratory information system between 2009 and 2014, shows more than 73% of the lipid tests in NL are performed in Eastern Health laboratories (data not shown).

After adjusting the number of tests performed by the population of the adults 20 years and older in the area, on average more than 50% of population in urban centers in the Avalon area had a lipid test during the study period. Approximately 25% of the population living in rural area in Avalon Peninsula had a lipid test. Less

than 5% of population had a lipid test in other Eastern Region and lest than 1% of NL population who live in other regions had a lipid test in Eastern Health Labs during the study period.

Eastern Health area is home to more than 60% of the population of the province. Approximately one out of three people in this region had a lipid test during the study period. Furthermore, there was no significant change in rural urban patterns and distribution of dyslipidemia and lipid profile in the sensitivity analysis we performed by limiting the study population to people who live in Avalon peninsula, or to people who live only in Eastern Health region compared to all NL population.

The study population includes the individuals who had a lipid test during the study period; therefore, the sample may not be representative of people who did not have a lipid test during the study period.

The choropleth map and spatial autocorrelation suggests that there is a relationship between prevalence of diagnosed dyslipidemia and living in rural areas, but many other factors including SES and demographic factors, health condition and access to healthcare services likely play a role in dyslipidemia.

Similar to other studies using secondary data there is also potential for incomplete and inaccurate data. The place of residence was identified using the first three digits of a patient's postal code, which did not provide representative information for advanced geospatial analysis. Geospatial analysis was limited to visualization and global spatial autocorrelation. The use of FSA areas for mapping and spatial autocorrelation and the use of "0" postal codes to identify rural areas also introduce issues of both ecological fallacy and the modifiable areal unit problem (MAUP). Ecological fallacy refers to the incorrect interpretation of individual behavior inferred from group level results. The modifiable areal unit problem is the introduction of statistical bias as a result of aggregating to a higher level of geography without adjusting variables accordingly. Since variables have the

capacity to vary over time and space, assuming that a variable will exhibit the same patterns at different levels of aggregation is improper. Both ecological fallacy and MAUP were introduced through the summarizing of patient data by FSA region, which creates aggregates that are no longer representative of the individuals and regions that were used to create them. With respect to ecological fallacy, we are applying population-wide proportions to the sortation area as a whole, but individual communities within these areas may have different rates of dyslipidemia. Regarding the modifiable areal unit problem, zero postal code is somewhat arbitrary in their composition and may not be the ideal unit of study for this type of data. However, the data in this study was collected at the individual level and then aggregated to higher order geographic levels. There was no significant change in rural/urban differences in distribution of dyslipidemia and lipid profile when we performed the analysis within different geographic units e.g., Avalon area, Eastern Health region, Central Health Region and the province of Newfoundland.

One may question the possibility of selection bias in this study. We have a relatively small number of lipid tests per FSA in a large area of the province. This could be due to the fact that our data is only from the Eastern Health Laboratory Information System. Therefore one must be careful in generalizing the results of this study to the entire province. Furthermore, The Eastern Health region is a tertiary center that provides healthcare to the entire province. Therefore our data for patients who resided outside of the Eastern Health region were likely those with multiple comorbidities and chronic illnesses. Therefore the prevalence that was obtained for regions outside of Eastern Health should be interpreted with caution. With respect to the calculation of prevalence of dyslipidemia, in order to be true prevalence this would need to be a population based calculation, however ours was conducted with the sample of data that we had available. Therefore while this does reflect the true prevalence of dyslipidemia for our study population, people who were screened for dyslipidemia according to records of lipid tests in Eastern Health Laboratory System during the study period. Generally speaking, these are the people who likely have

risk factors and a high clinical suspicious of disease for this reason, they may not be a completely accurate representation of the whole population of the province.

5.6 Implications

To our knowledge, this study is the first study using a large database to assess lipid profiles and dyslipidemia in Newfoundland and Labrador. The results of this study can help guide future research about dyslipidemia as well as other risk factors for CVD and chronic disease in Newfoundland and Labrador and Canada.

The finding that rural inhabitants were more likely to have one and multiple forms of dyslipidemia, provides evidence that perhaps these regions could be targeted for education, and a preventative medicine approach to curb the disease. The combined fact that dyslipidemia is a major modifiable risk factor for CVD and Newfoundland and Labrador has the highest mortality rates for CVD and IHD in Canada [1], highlight the need for targeted therapy and prevention in the province of Newfoundland and Labrador.

5.7 Conclusions

This study found that rural residents had a higher prevalence of high TG, low HDL and high Total Cholesterol/HDL ratio than urban residents. It also found that rural residents had increased odds of having dyslipidemia, and multiple dyslipidemias. There are possible explanations for this; however, this study did not have the other variables required to examine possible reasons for the difference.

Future research should focus on risk factors for dyslipidemia, as well as other risk factors for CVD between rural and urban regions. The fact that 41% of the inhabitants of Newfoundland and Labrador live in rural regions [65], and the fact that health indicators get worse with increasing rurality as highlighted, further highlights the need for investigation for health differences between rural and urban regions.

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