SPATIAL ANALYSIS OF PREGNANCY COMPLICATIONS ASSOCIATED WITH MATERNAL CARDIOVASCULAR DISEASE RISK IN ONTARIO

by

Jessica Nichole Stortz

A thesis submitted to the Department of Community Health and Epidemiology

In conformity with the requirements for

the degree of Master of Science

Queen's University

Kingston, Ontario, Canada

July, 2012

Abstract

Aim: The aim of this study was to: 1) investigate the geographic distribution of six pregnancy complications associated with future maternal cardiovascular disease risk in the province of Ontario and 2) to identify regions where women are likely to benefit from post-partum cardiovascular disease screening, based on the development of complications during pregnancy.

Rationale: Cardiovascular disease is the leading cause of death in Canadian women. Pregnancy has been likened to a cardiovascular stress test and provides an early opportunity to assess a female's lifetime risk of cardiovascular disease.

Methods: This study was a retrospective analysis of data collected for the Niday Perinatal Database, provided by the Better Outcomes Registry & Network. Crude and age-standardized cumulative incidences of six pregnancy complications, and one or more pregnancy complications, were calculated for each Public Health Unit area in Ontario. The cumulative incidence of one or more pregnancy complications for women with no previous history of cardiovascular disease or traditional cardiovascular risk factors was calculated at the Public Health Unit and census subdivision area levels. Spatial statistics were applied to locate statistically significant clusters of high cumulative incidence.

Results: Crude and age-standardized cumulative incidences of each pregnancy complication and one or more pregnancy complications varied across Public Health Unit areas in Ontario. The crude cumulative incidence of one or more complications ranged from 74 to 224 cases per 1000 pregnancies. The spatial analysis identified one statistically significant cluster of high cumulative incidence at the Public Health Unit area level, spanning the Lambton, Chatham-Kent, and Windsor-Essex Health Unit areas. Seven statistically significant clusters of high cumulative

incidence census subdivisions were located within the following Public Health Unit areas: Chatham-Kent, Lambton, Middlesex-London, Ottawa, Leeds, Grenville and Lanark, Renfrew County, Simcoe Muskoka, Grey Bruce, and Eastern Ontario.

Conclusion: Regional variation in the cumulative incidence of six pregnancy complications associated with cardiovascular disease risk was observed in Ontario. Statistically significant clusters of high cumulative incidence of one or more of these pregnancy complications were identified. These regions in particular may benefit from post-partum screening clinics and increased awareness regarding the association between pregnancy complications and cardiovascular disease.

Co-Authorship

This thesis contains the work of Jessica Stortz in collaboration with her thesis supervisors, Dr. Duncan Hunter, Dr. Graeme Smith, and Dr. Dongmei Chen. The study was designed by Jessica Stortz, Dr. Hunter, Dr. Smith, and Dr. Chen. The mapping, statistical analyses and interpretation of results were completed by Jessica Stortz, with input and guidance from Dr. Hunter, Dr. Smith and Dr. Chen. This thesis was written by Jessica Stortz, with editorial feedback from Dr. Hunter, Dr. Smith, and Dr. Chen.

Acknowledgements

This study is based on data provided by the Better Outcomes Registry and Network (BORN), administered by the Children's Hospital of Eastern Ontario. The interpretation and conclusions contained herein do not necessarily represent those of BORN Ontario.

I would like to acknowledge the following groups and individuals for their contributions, guidance and assistance in this project:

Dr. Ann Sprague, Mr. Daniel Bedard, and Ms. Joan Mongeon (BORN Ontario) for assistance throughout this project, including answering the many questions I had about the data, handling the data request, arranging the research agreement, and providing feedback on the methodology,

The Maps, Data and Government Information Center (Queen's University) for providing the geographic boundary files,

Ms. Nam Bains and Mr. Mike Pacey (Ontario Ministry of Health and Long-Term Care) for providing input on mapping of health data,

Ms. Laurie Vaughan-Evans (Office of Research Services, Queen's University) for coordinating the data sharing agreement in an incredibly timely manner,

Members of the Laboratory of Geographic Information and Spatial Analysis (LaGISA, Queen's University) for assistance with GIS and spatial analysis,

Ms. Heather Ramshaw, Ms. Jessica Pudwell, and Ms. Michelle Roddy (Queen's Perinatal Research Unit) for allowing me to observe pregnancy-related research and gain background knowledge relevant to this project.

Thank you to my thesis supervisors:

Dr. Duncan Hunter has been greatly supportive and encouraging, always made himself available to meet, and kept me on track and organized,

Dr. Graeme Smith has been an incredible source of knowledge and expertise throughout this entire project,

Dr. Dongmei Chen agreed to co-supervise this project knowing I had never heard of ArcGIS before beginning it and provided invaluable knowledge.

I would also like to thank:

Kim Crowe, Michelle Dimitris and Ally Mahar for being wonderful and supportive roommates and making my time in Kingston so enjoyable,
My sister, Danielle Stortz, for the love, laughs, and encouragement,
Family and friends back home for your support and encouragement throughout the completion of this degree.

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List of Acronyms

Acronym	Definition
CVD	Cardiovascular disease
SGA	Small for gestational age
GIS	Geographic information systems/sciences
BORN	Better Outcomes Registry & Network
CHEO	Children's Hospital of Eastern Ontario
PARAT	Privacy Analytics Re-Identification Risk Assessment Tool
eHIL	electronic Health Information Laboratory
PHU	Public Health Unit
CSD	Census subdivision
PCCF	Postal Code Conversion File
BMI	Body mass index
CIHI	Canadian Institute for Health Information
ICES	Institute for Clinical Evaluative Sciences

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Chapter 1

Introduction

1.1 General Introduction

Cardiovascular disease (CVD) is a group of disorders that involve injuries to the blood vessels, heart, and brain. These disorders may cause changes in blood flow to the heart and brain, potentially resulting in heart attacks and or strokes. Disorders classified as CVD include coronary/ischemic heart disease, cerebrovascular disease, peripheral vascular disease, heart failure, rheumatic heart disease, and congenital heart disease [1]. According to the World Health Organization, CVD was responsible for approximately 17 million deaths worldwide in 2004[1,2]. It is projected that by 2030, the number of yearly deaths due to CVD will increase to 23.6 million[1,2]. Many risk factors for CVD are modifiable and in many cases CVD is preventable. Early identification of risk factors is therefore important. Collection of data on prevalence of CVD risk factors is essential for enhancement of prevention and care[3]. In Canada, regional differences in the prevalence and types of CVD exist between and within provinces[4]. Regional variation in prevalence of traditional risk factors for CVD has also been shown between provinces[5]. With the aid of GIS technology, this study will determine whether there is regional variation in the distribution of six pregnancy complications associated with CVD risk in Ontario. The aim of this thesis is to identify areas in Ontario where women are likely to benefit from post-partum CVD screening, based on the development of complications during pregnancy.

Regional distribution of risk factors for CVD is relevant to program planning, design, and implementation within Public Health Units. Information on geographic distribution of risk factors and prevalence of CVD is useful for identification of populations that may benefit from prevention and treatment programs[5]. The results of this study will be useful in decision making

related to CVD screening programs for women post-partum in certain regions in Ontario. This study will also provide information on regions where increased education and awareness of the association between pregnancy complications and CVD may be particularly important. Combining screening programs which identify personal risk factors and methods to reduce personal risk, and education about risk factors is an effective strategy in CVD prevention[3].

This thesis is structured as follows. Chapter 2 presents a literature review on the topics of CVD and risk factors (including pregnancy complications), and also the use of GIS for health research purposes. Chapter 3 describes the methods of study, including study design, data source, and the analytical approach. In Chapter 4, results of the analyses are presented. These results are discussed in Chapter 5 and implications for future research and practice are suggested.

Chapter 2

Literature Review

2.1 Cardiovascular disease risk factors

Behavioural risk factors, including unhealthy diets, physical inactivity, and tobacco use, account for 80% of coronary and cerebrovascular diseases[2]. These behavioural risk factors manifest as intermediate physical risk factors such as high blood pressure, glucose, and lipid levels, overweight, obesity, and diabetes[2,1]. On a broader scale, poverty and stress have been labeled determinants of CVD as they may influence the development of risk factors[2]. Education and income have been shown to be associated with the prevalence of self-reported modifiable CVD risk factors. A higher prevalence of CVD risk factors was observed in individuals with lower income and education compared to those with higher income and education[6]. Similarly neighborhood deprivation, a composite measure of material deprivation and social deprivation[7], has been found to be associated with the prevalence of CVD risk factors. Individuals living in high deprivation neighborhoods were significantly more likely to be physically inactive, obese, and cigarette smokers compared to individuals living in neighborhoods of moderate deprivation[8].

Genetics also plays a role in susceptibility to CVD. Some DNA mutations related to CVD are population specific, predisposing certain ethnic groups to developing CVD[6]. This may account for some of the variation in CVD prevalence seen across ethnic groups[6]. Additionally, prevalence of modifiable CVD risk factors were different according to race/ethnicity when Caucasian, Chinese, South Asian, Black, and Southeast Asian groups were compared in Canada[6].

Societal and environmental variables are also relevant to cardiovascular health as area level variables are associated with CVD risk. A recent Canadian study found high area level

unemployment was associated with elevated body mass index (BMI) and higher total cardiometabolic risk scores when compared to lower area level unemployment quartiles, after adjusting for other individual level variables[9]. CVD mortality was found to be associated with higher levels of area level deprivation categories, a composite measure of unemployment, overcrowding, car ownership, and social class[10] . This association was attenuated when CVD risk factors were adjusted for, possibly explained by unequal distribution of other risk factors according to socioeconomic characteristics of residential areas[10]. Studies have found that residents of disadvantaged neighborhoods were at higher risk of coronary heart disease compared to residents of advantaged neighborhoods, after controlling for individual level variables[11,12]. Neighbourhood income and education levels were both found to be associated with coronary heart disease incidence, after adjusting for individual level variables[13]. Numerous mechanisms have been suggested to explain increases in CVD prevalence, incidence, and mortality in disadvantaged neighborhoods. These mechanisms include differences in prevalence of traditional CVD risk factors, exposures such as air pollution, the built environment, local food environment, and social environment including social norms, neighbourhood disorder, and crime[14,15].

2.2 Cardiovascular disease in Canada

Despite declining rates of heart disease and stroke in Canada over the past 40 years, in 2008, 29% of all deaths were related to CVD[16]. Of these deaths, 54%, 23%, and 20% were due to ischemic heart disease, heart attack, and stroke, respectively[16]. In 2007, nine in ten Canadians reported having one or more of the following CVD risk factors: daily tobacco smoking, physical inactivity in leisure time, inadequate consumption of vegetables or fruits, being overweight or obese, high stress, high blood pressure, and diabetes[6].

2.2.1 Regional variation of cardiovascular disease risk factors and cardiovascular disease

Regional variation of CVD risk factors has been shown in Canada as rural areas had a higher proportion of daily smokers, overweight and obese individuals, and individuals experiencing high

stress levels compared to urban areas[6]. Variation in prevalence of a number of risk factors (smoking, hypertension, obesity, diabetes, sedentary lifestyle, and low income) in Canadian provinces and health regions has also been observed[5]. A study that investigated prevalence of overweight and obesity across Canada observed spatial heterogeneity and clustering at the health region level[17]. Clustering in the prevalence of type 2 diabetes was observed in Winnipeg at the neighbourhood level, and variations in prevalence were associated with variations in population characteristics including aboriginal status and smoking, environmental characteristics including crime and the presence of vacant houses, and socioeconomic variables[18]. Similarly, regional variation in the crude prevalence of CVD has been reported in Canada. Regional variation in self-reported prevalence of heart disease, myocardial infarction, angina, and congestive heart failure occurred across the country, and variation existed at both the provincial and health regional levels[4]. Proposed explanations for the observed regional variations in CVD prevalence include differences in cardiac risk factors, ethnic distribution, and socioeconomic characteristics of regions[4].

2.3 Cardiovascular disease in women

In 2008, CVD was the leading cause of death in Canadian women, resulting in more deaths than cancer[16]. In 1999, the first guidelines for prevention and treatment of CVD specific to women were published by the American Heart Association[19]. In addition to traditional risk factors which affect both genders, there are CVD risk factors unique to women, including hormone therapy and pregnancy[20]. The guidelines were most recently updated in 2011 and for the first time specific pregnancy complications were identified as risk factors for the development of CVD. During pregnancy, the body is placed under elevated metabolic and cardiovascular stress. Physiological changes in normal pregnancy, relative to pre-pregnancy, include hypervolemia, insulin resistance, thrombophilia, and immunosuppression. Underlying or early dysfunctions or disease may become apparent as a result of these changes brought on by pregnancy[21]. In certain individuals, pregnancy

complications may result. There are three hypotheses concerning the biological mechanisms behind the association between pregnancy complications and CVD outcomes. The association may be due to: 1) common causes and shared risk factors for pregnancy complications and CVD or 2) vascular damage caused by pregnancy complications or 3) a combination of both of these[22,23].

A history of preeclampsia, gestational hypertension, or gestational diabetes increases the risk of developing CVD later in life[20]. In addition to these three complications, other pregnancy conditions associated with an increased maternal risk of CVD are placental abruption, giving birth to a small for gestational age infant, and preterm delivery[24-26]. The American Heart Association guidelines recommend that a detailed patient history of pregnancy complications, specifically gestational diabetes, preeclampsia, preterm delivery, or delivery of a small for gestational age infant, be obtained by health care practitioners to assess CVD risk[20].

2.3.1 Preeclampsia/eclampsia

Preeclampsia is characterized by the onset of hypertension and proteinuria later than 20 weeks gestation and affects 3% to 8% of pregnancies[27,24,22,28,29]. Eclampsia is a more severe form of preeclampsia and affects only 0.1% of pregnancies[23]. Preeclampsia and eclampsia are conditions unique to pregnancy and typically resolve with delivery[22,30]. Women with a history of preeclampsia are at increased risk of CVD later in life. A systematic review and meta-analysis conducted in 2007 calculated the relative risks for hypertension (3.7; 95% C.I. 2.7-5.1), ischemic heart disease (2.2; 95% C.I. 1.9-2.5) , stroke (1.8; 95% C.I. 1.5-2.3) , and venous thromboembolism (1.8; 95% C.I. 1.4-2.3), between 5 and 15 years after experiencing a preeclamptic pregnancy, compared to women who did not develop preeclampsia[22]. A more recent cohort study found that women who experienced preeclampsia or eclampsia 10 years prior were at increased risk of stroke, myocardial infarction, heart failure, any major adverse cardiovascular

event, any non-stroke major adverse cardiovascular event, and any major adverse cardiovascular event-related death, compared to women who did not develop preeclampsia or eclampsia. Hazard ratios in this study ranged from 2.3 to 14.5 after adjusting for clinical and demographic variables[31]. In a study conducted in Ontario, women with preeclampsia were matched to pregnant women who did not develop preeclampsia according to age, race, and parity. The group which developed preeclampsia had significantly higher BMIs, blood pressure readings, insulin levels and total cholesterol levels compared to the control group when examined one year post-partum[32]. The same study used mathematical modeling to calculate 10 year cardiovascular event risk scores and women who had developed preeclampsia were at twice the risk of experiencing a cardiovascular event compared to women who did not develop preeclampsia during pregnancy[32]. Women from the same cohort were followed up to three years post-partum and the only significant difference between the two groups was blood pressure levels. The preeclampsia group had significantly higher mean systolic and diastolic blood pressure readings than the control group[33]. The preeclampsia group had a higher relative risk of developing metabolic syndrome at one year (2.7; 95% C.I. 1.2-5.9) and three years (3.4; 95% C.I. 1.1-11.1) post-partum compared to the control group[33]. Another study conducted in Ontario found an association between preeclampsia and heart failure or cardiac arrhythmias after adjusting for demographic and clinical variables; the hazard ratio for women who developed preeclampsia compared to those who did not was1.6 (95% CI 1.2-2.0) and the hazard ratio for women who developed severe preeclampsia compared to those who did not was 2.0 (95% CI 1.2-3.3), after a median duration of 7.8 years[34].

2.3.2 Gestational hypertension

Gestational hypertension is hypertension without proteinuria first occurring after 20 weeks of gestation[23]. The incidence of gestational hypertension in pregnancy has been estimated at approximately 4-6% [35,36] . Multiple studies have found gestational hypertension increased the risk of CVD later in life. Women with gestational hypertension were at increased risk of ischemic

heart disease (relative risk of 1.5; 95% CI 1.1-2.0, incidence rate ratio of 1.6; 95% CI 1.3-2.0) and acute cardiovascular disease events (hazard ratio of 2.8; 95% CI 1.6-4.8)[23]. Two studies of Ontario women have also shown an increased risk of CVD in women with gestational hypertension after adjusting for demographic and clinical variables, with a hazard ratio of 1.8 (95% CI 1.4-2.2) for CVD[24] and 1.8 (95% CI 1.4-2.4) for heart failure or cardiac arrhythmias[34]. The median durations of follow-up in these studies were 8.7 years[24] and 7.8 years[34].

2.3.3 Gestational diabetes

Gestational diabetes is defined as carbohydrate intolerance which is first diagnosed during pregnancy[37,38]. Between 2% and 6% of pregnancies in the developed world are affected by gestational diabetes[21,37]. Normal glucose tolerance is usually restored after delivery in individuals who develop this complication[38]. Gestational diabetes is associated with an increased risk of developing type 2 diabetes, which is also a risk factor for CVD. Within five years of pregnancy, 20% to 60% of women with a history of gestational diabetes developed type 2 diabetes[39]. A history of gestational diabetes has also been found to increase the risk of obesity, hypertension, and dyslipidemia[38]. In a cohort study involving pregnant women in Ontario with a median follow-up period of 11.5 years, the unadjusted hazard ratio for CVD was 1.7 (95% C.I. 1.1-2.7) when women with gestational diabetes were compared to women without gestational diabetes[40]. After adjusting for the development of type 2 diabetes, the hazard ratio was no longer statistically significant. The investigators attributed the increased risk of CVD to the development of type 2 diabetes in women with a history of gestational diabetes. Another study found that among women with a family history of type 2 diabetes, women with a history of gestational diabetes had increased odds of developing hypertension (odds ratio of 1.9; 95% CI 1.3-2.6), dyslipidemia (odds ratio of 1.8; 95% CI 1.3-2.4), type 2 diabetes (odds ratio of 10.1; 95% CI 6.0-16.8), and CVD (odds ratio of 1.9; 95% CI 1.2-2.8) compared to women that did not develop gestational diabetes[41]. The Canadian Diabetes Association recommends all women who develop gestational

diabetes be screened for impaired glucose tolerance and type 2 diabetes six weeks to six months following delivery and regularly thereafter[42].

2.3.4 Placental abruption

Placental abruption is a complication in which the placenta separates from the uterine lining prior to delivery, affecting 0.6-1% of pregnancies[43]. In a study examining women in Ontario, the hazard ratio (median follow-up of 8.7 years) for CVD was 1.7 (95% CI 1.3-2.2) for women with placental abruption and infarction compared to women without these placental complications[24].

2.3.5 Delivery of a small for gestational age infant

Small for gestational age (SGA) is broadly defined as an infant that is small in birth weight, after standardization for gestational age and gender[44]. Between 5 and 9% of pregnancies result in the birth of SGA infants[25,45,46]. The cut-off values for SGA were not standard in the literature; two studies used a weight less than 2 standard deviations below the mean birth weight for gestational age[44,47], one used the lowest birth weight quintile (after adjustment for age and gender)[48], and another used a definition of delivery of an infant weighing less than 2500g, at or after 37 weeks gestation[49]. Women who gave birth to SGA offspring were more likely to die of cardiovascular events than those who gave birth to offspring of normal birth weight after a mean follow-up duration of 14.8 years (hazard ratio of 2.6; 95% CI 2.2-3.0)[44]. Similarly, women who gave birth to infants in the smallest birth weight quintile had a hazard ratio of 2.4 (95% CI 1.3-4.4) for death due to ischemic heart disease compared to the amalgamated top 4 birth weight quintiles[48]. In another study, women who delivered SGA infants were 1.9 times more likely to develop ischemic heart disease in comparison to women who gave birth to non-SGA infants, even after adjustment for other risk factors for ischemic heart disease (95% CI 1.2-3.0)[49]. There is evidence to suggest a dose response relationship exists between SGA and maternal risk of CVD. For women with one, two, and three or more SGA offspring, the hazard ratios for CVD compared to women with no SGA offspring were 1.4 (95% CI 1.4-1.5), 1.7 (95% CI 1.6-1.9), and 1.9 (95% CI

1.4-2.6), respectively, after a mean follow up period of 20 years and adjustment for demographic variables[47] .

2.3.6 Preterm delivery

Preterm delivery is defined as delivery before 37 weeks gestation. Preterm deliveries occur in 8-11% of pregnancies[46,50,51]. The hazard ratio for cardiovascular mortality for women who delivered preterm compared to those who delivered at term was determined to be 2.0 (95% CI 1.6-2.4) in one study with a mean follow up duration of 14.8 years[44]. In another study, women who delivered prior to 37 weeks gestation were 1.9 times more likely to experience major stroke compared to women who delivered at term (95% CI 1.4-2.7) after adjusting for demographic variables[52]. When this condition was combined with low infant birth weight, the relative risk of major stroke increased to 2.7 (95% CI 1.4-5.1)[52].

2.3.7 Multiple pregnancy complications

The combined effects of pregnancy complications on CVD risk have been investigated and evidence suggests an increased risk of CVD with a greater number of pregnancy complications developed. The hazard ratio for death from cardiovascular causes in women who delivered preterm, SGA infants was higher than the ratio for either condition alone in comparison to women with neither condition[44]. Similarly, the hazard ratio for cardiovascular death in women with preeclampsia, and preterm delivery of SGA infants was higher than the ratio for any one complication independently[44]. Women who had preeclampsia and gave birth to a preterm, SGA infant were 7 times more likely to experience ischemic heart disease compared to women with none of these conditions[48]. The same study found women with preeclampsia alone to be only 2 times more likely to develop heart disease compared to women without preeclampsia[48]. In a large study conducted in Ontario, women who experienced a maternal placental syndrome, defined as preeclampsia, gestational hypertension, and placental abruption and/or placental infarction, had a hazard ratio of 1.80 (95% CI 1.42-2.29) for future hospitalization for heart failure compared to

women who did not develop maternal placental syndromes, after adjusting for demographic and other health related variables[34]. Similar to the findings of other studies, women with a greater number of pregnancy complications were at the highest risk of CVD. Hazard ratios for heart disease or cardiac arrhythmias in women with maternal placental syndromes in combination with preterm delivery and poor fetal growth were higher than the hazard ratio for this outcome in women with maternal placental syndromes only, compared to women with no pregnancy complications[34]. The hazard ratio for future hospitalization for heart disease or cardiac arrhythmias was higher for women with preeclampsia and preterm delivery, compared to those who only developed preeclampsia[34].

2.4 Cardiovascular disease screening and risk assessment

In 2009, the Canadian Cardiovascular Society published recommendations for prevention of CVD in adults[53]. Plasma lipid profile screening was recommended to begin in all postmenopausal women or women above the age of 50, unless specific CVD risk factors were already present. If these risk factors are present, screening should begin at an earlier time[53]. CVD risk factors identified in the recommendations were diabetes, hypertension, current cigarette smoking, obesity, family history of premature coronary artery disease, inflammatory diseases, chronic renal diseases, atherosclerosis, certain HIV treatments, and hyperlipidemia[53]. Pregnancy history is also an important component in assessing a female's cardiovascular risk later in life[20]. It has been suggested that women who experience pregnancy complications associated with increased risk of CVD begin screening prior to or at the onset of menopause[26]. The American Heart Association's 2011 Guidelines for Prevention of Cardiovascular Disease in Women recommend post-partum referral to a cardiologist or primary care physician for cardiovascular risk monitoring in women who have experienced pregnancy complications which are known to be associated with CVD[20].

Traditional methods of CVD risk assessment have calculated individual risk scores to determine whether intervention is necessary. Algorithms for risk scores incorporate well-established CVD risk factors including age, smoking, blood pressure, and blood lipid levels in calculations[54]. Individuals with calculated risk scores which exceed a predefined threshold value are recommended to undergo intense lifestyle modifications and or pharmacotherapy[54]. Methods for calculating 10 year, 30 year, and lifetime CVD risk have been developed and there has been debate surrounding which method is most appropriate[54,55]. CVD risk scores were calculated and compared between Ontario women with and without preeclampsia at one year post-partum. Women who developed preeclampsia had significantly higher 10 year, 30 year, and lifetime CVD risk scores than women who did not develop preeclampsia[55]. Lifetime CVD risk scores calculated one year post-partum identified a larger proportion of women with preeclampsia at increased risk in comparison to the 10 year and 30 year risk estimates. It has been proposed that of the commonly used methods for assessing CVD risk, lifetime CVD risk scores are most appropriate to assess risk in post-partum women[55].

The results of a 2007 survey of prenatal care providers in Ontario revealed that increased CVD risk in women with certain pregnancy complications is not always communicated. Approximately 60% of care providers reported informing patients who developed preeclampsia or gestational hypertension of increased CVD risk, while 40% reported informing primary care physicians of the need for follow up in patients with gestational hypertension[56]. The results of this survey suggest that many prenatal care providers may not be aware of the association between certain pregnancy complications and increased CVD risk. Only 64% and 54% of care providers surveyed correctly identified that women with gestational hypertension and preeclampsia, respectively, were at increased long-term risk of hypertension compared to nulliparous women[56].

2.5 Standard antenatal care

Virtually all pregnant women in Ontario are utilizing health care services during pregnancy, and therefore pregnancy is an optimal time to identify cardiovascular risk factors[32]. In Canada, information on cardiovascular risk factors is collected by prenatal care providers throughout pregnancy. Fasting plasma glucose levels, oral glucose tolerance tests, and multiple weight and blood pressure measurements are recorded during pregnancy using standardized antenatal forms to detect complications including preeclampsia/eclampsia, gestational diabetes, and gestational hypertension. Delivery outcomes and complications including placental abruption, SGA, and preterm birth, are also recorded. A post-partum follow up at 6 weeks is also standard care in Canada, during which maternal and child health is assessed. This visit presents an opportunity for counseling regarding cardiovascular risk factors developed during pregnancy and suggestions regarding lifestyle modifications to decrease the risk of complications in subsequent pregnancies and risk of CVD later in life[32,21,26]. These lifestyle modifications include increased physical activity and consuming a healthier diet[26,57]. Screening in women who develop one or more pregnancy complications associated with CVD could begin after the post-partum visit, and include routine measurements of blood pressure, weight and waist circumference, fasting lipids, and glucose concentrations[26].

2.6 Cardiovascular disease awareness

A survey carried out in the United States in 2005 showed that CVD awareness has increased over time among American women. Of the women surveyed, 55% identified heart disease/heart attack as the leading cause of female death, compared to 30% of women who correctly answered the same question in 1997[57]. Despite the increase in CVD mortality awareness, 30% of women surveyed underestimated levels of personal CVD risk[57].

Results from this study suggest that increased knowledge and awareness of CVD and risk factors are associated with healthy lifestyle modifications related to CVD. Knowledge of heart disease, awareness of healthy cholesterol levels, a high perceived level of CVD risk, and personal history of CVD and risk factors were all associated with lifestyle modifications[57]. These modifications included increased physical activity, healthier diet, weight loss, and smoking cessation.

2.7 Geographic Information Systems

Geographic information systems (GIS), commonly referred to as geographic information sciences, is a computerized tool used to create, store, manipulate, analyze, and visualize spatial data [58,59]. Originally developed for the purpose of geographic land inventory in the 1960's, its use has broadened into many other disciplines in addition to physical geography. Current applications include utilities and resources management, urban and regional planning, vehicle routing, telecommunications, and parcel delivery[58]. Many health organizations and researchers have also taken advantage of GIS to analyze and visualize health-related data.

2.7.1 Health applications of GIS

GIS has been used in the fields of public health and epidemiology to monitor population health status. Through the combination of cartography and spatial analysis techniques, GIS allows researchers to simultaneously examine spatial relationships between disease and place, while presenting results visually via maps[60]. It is useful for generating and/or confirming hypotheses including identification of risk factors for diseases, environmental exposure assessment and assessment of health-care accessibility and planning. GIS also has surveillance applications including examining geographic burden of disease and detecting spatial clustering, identifying specific geographic areas in which public health intervention may be necessary, and monitoring outcomes of health interventions and programs[60-65].

One of the earliest and most well-known examples of disease mapping was the investigation of the London cholera outbreaks in the mid-1800s by John Snow. Similar, more technologically advanced methods have continued to be used in the study of communicable diseases, including sexually transmitted infections[66,67]. GIS has also been used to analyze the spatial distribution of pneumonia and influenza hospitalizations within Ontario, at the census division level[68,69]. It has aided in environmental epidemiology studies which investigate associations between environmental variables and disease outcomes, such as temperature and vector-borne diseases[70,71] air pollution and various disease outcomes[72] and soil arsenic level and risk of birth defects[70]. GIS has also proven to be useful in assessment of healthcare systems including service provision, healthcare delivery, and disease reporting. Researchers utilized GIS to better understand population-level variables influencing mammography rates and physician visits across Toronto, Ontario[73]. GIS has been used to evaluate completeness of hospital reporting of birth defects and to investigate clustering of birth malformations[74]. In chronic, non-communicable disease research, studies have employed GIS to investigate geographic variation in cancer incidence rates. The spatial distribution of cancer has been examined at the neighbourhood (dissemination area) and Public Health Unit area levels in Ontario[75,76], at the county level in California[77], and across the entire U.S.A.[78].

2.7.2 GIS and cardiovascular disease research

GIS has also been used to investigate CVD in terms of service provision, disease mortality, and risk factors. Geographic access to cardiac care has been examined utilizing GIS in Canada[79] and the United States[80]. GIS has been used to map the prevalence of obesity, fast food-outlets, and green space at the neighbourhood level, and these maps were used to inform obesity interventions tailored to neighborhoods in Austin, Texas[81]. In Canada, spatial analysis of the prevalence of overweight and obesity has been undertaken at the health region level across the country[17]. Additionally, physical activity and the characteristics of the built environment were investigated

in Australia[82]. Another study examined clustering of congenital heart malformations and risk factors in Baltimore/Washington[83]. Geographic distribution of CVD mortality and associated risk factors were investigated at the American state and neighbourhood level[84,85] and the state level in India[86]. The association between traffic-related air pollution and risk of CVD mortality has been investigated by multiple studies in North America and Europe[87]. Geographic variation and clustering of diabetes risk/prevalence has been investigated in the United Kingdom[88], Canada[18], and the U.S.A.[89]. To date, no research related to pregnancy complications in the context of CVD risk involving GIS has been published.

Chapter 3

Methods

3.1 Objectives

The objectives of this thesis are:

1) To describe the characteristics of the study population and calculate crude and age-standardized cumulative incidences of pregnancy complications for each Public Health Unit area in Ontario

2) To analyze the spatial pattern and geographic distribution of one or more pregnancy complications at the Public Health Unit area level for detection of clusters of high cumulative incidence

3) To analyze the spatial pattern and geographic distribution of one or more pregnancy complications at the census subdivision level for detection of clusters of high cumulative incidence

3.2 Study Design

The study was a retrospective analysis of data from the Niday Perinatal database, a provincial maternal-child registry, provided by the Better Outcomes Registry & Network (BORN) Ontario (n = 658,744, 2005-2009 fiscal years), administered by the Children's Hospital of Eastern Ontario (CHEO).

3.3 Study population

The study population consisted of pregnant women residing in Ontario and delivering in an Ontario hospital at ≥20 weeks gestation (live and stillbirths), between April 1, 2005 and March

31, 2009 (n= 652,118). Women with a permanent residence outside of Ontario during pregnancy, but delivered in an Ontario hospital, were excluded.

3.4 Data sources

3.4.1 Better Outcomes Registry and Network (BORN) Ontario

Pregnancy data for this thesis was obtained from BORN Ontario, formerly known as the Ontario Perinatal Surveillance System. Record-level data was requested following the process outlined on the BORN Ontario website[90]. BORN is a prescribed registry under Ontario's Personal Health Information Protection Act, and obtained this designation in 2009. It integrates data from five founding members; the Fetal Alert Network (congenital anomalies), Prenatal Screening Ontario, Niday Perinatal Database (labour, birth and newborn data) , Ontario Midwifery Program (home birth data) , and Newborn Screening Ontario. The data used in this thesis was originally collected and held within the Niday Perinatal Database (Niday), established in 1997, which by the fiscal year 2006-2007 captured 95% of all births in Ontario[91]. Standardized, web-based entry forms were used to enter data into the database, but records used in data abstraction were not consistent across data entry sites. Records from which data may have been abstracted include admission, labour, delivery, antenatal, medication, and post-partum records, discharge summaries, laboratory results, nurse's notes, and doctor's orders.

3.4.2 Data request

A record-level data request was submitted to BORN Ontario. The following variables were requested: maternal age at time of birth, year of birth (delivery), Public Health Unit (area) of residence, census subdivision of residence, and potential indicators of cardiovascular risk - smoking status, preeclampsia, gestational hypertension, gestational diabetes, placental abruption, small for gestational age/intrauterine growth restriction, preterm labour, chronic hypertension, diabetes (insulin-dependent), diabetes (non-insulin dependent), and heart disease. The original

record-level data request submitted for this thesis and definitions of each variable can be found in Appendix A. Variables provided in the final dataset received from BORN Ontario are presented in Table 1.

Table 1. Variables obtained from BORN Ontario

Variable	Classification	Missing Data
Age	<15, one year age intervals, 50+	0.15%
Smoking	No smoking, ≤ 20 weeks, > 20 weeks gestation, ≤ 20 weeks and > 20 weeks	9.79%
Pregnancy complications		11.41%
Preeclampsia	Yes/No	
Gestational hypertension	Yes/No	
Gestational diabetes	Yes/No	
Placental abruption	Yes/No	
Preterm labour	Yes/No	
Delivery of a small for gestational age infant	Yes/No	
Maternal health complications		11.72%
Heart disease	Yes/No	
Chronic hypertension	Yes/No	
Diabetes (insulin dependent)	Yes/No	
Diabetes (non-insulin dependent)	Yes/No	
Residence		
Public Health Unit area	Public Health Unit code	0.33%
Census subdivision	Census subdivision code	2.39%

For all record-level data requests that include either personal identifiers or quasi-identifiers, BORN Ontario completes an analysis that measures risk of re-identification using the Privacy Analytics Re-Identification Risk Assessment Tool (PARAT). This tool, developed by the electronic Health Information Laboratory (eHIL) at CHEO, provides an objective measure of re-identification risk of persons in the dataset and BORN requires this risk to be below a determined identifiability threshold set a-priori before data is provided. Strategies to reduce risk by de-

identification are provided, and BORN and the researcher work together to find the lowest risk level and de-identification strategies that will still allow the researcher to answer the question. Of the variables requested, three were found to be quasi-identifiers, with a potential risk of re-identification in the cohort. To meet to re-identification threshold of 0.2 determined for this request, mother's age of less than 15 years and ages 50 years and above were treated as categorical, rather than continuous variables. The final De-identification Report for this thesis provided by eHIL is provided in Appendix B.

Access to the Statistics Canada Boundary Files for Public Health Unit areas and census subdivisions was requested and obtained through the Maps, Data, & Government Information Centre at Queen's University.

3.5 Ethical considerations

Ethics approval for this study was obtained from the Queen's University Research Ethics Board and the CHEO Research Ethics Board. Letters of ethics approval are provided in Appendix C and Appendix D. Data was received from BORN on an encrypted CD-ROM and no personal identifiable information was included in the dataset. The dataset was stored in a password-protected folder on a secure server at the Laboratory for Geographic Information and Spatial Analysis (LaGISA) at Queen's University.

3.6 Analytical strategy

3.6.1 Variable re-classification

Variables obtained in the data received from BORN Ontario were modified to create new variables required to conduct this study. Smoking status was dichotomized (Yes/No) and type 1 and type 2 diabetes were grouped into one variable, diabetes. Six pregnancy complications (preeclampsia, gestational hypertension, gestational diabetes, placental abruption, delivery of a

SGA infant, and preterm labour) were grouped together to create a new variable, one or more pregnancy complications. CVD diagnoses and traditional CVD risk factors (smoking, diabetes, chronic hypertension, heart disease, and age>50) were grouped together to create another variable, one or more cardiovascular complications or traditional risk factors. This definition was based on data availability from BORN Ontario and Canadian Cardiovascular Society Guidelines[53].

3.6.2 Descriptive analysis

The total study population was described according to variables obtained for the study. Public Health Unit (PHU) areas were described by number of pregnancies during the study period and cumulative incidence of pregnancy complications associated with CVD risk. A map of PHU areas in Ontario is provided in Appendix E. Crude and age-standardized cumulative incidence rates for each PHU area were calculated. The denominator for the incidence calculations was the total study population (number of pregnancies) in each PHU area. The numerator was the total number of cases of a particular pregnancy complication in each PHU area. Women with missing pregnancy complication data were excluded from incidence calculations. To calculate age-standardized rates, the 1991 Canadian Census population was used. The choice of reference population for the age-standardization was arbitrary, but this reference population has been used in recent Canadian literature[92]. Age-standardized cumulative incidence rates were visually displayed using maps generated by Esri's ArcGIS 10[93].

3.6.3 Spatial Analysis

Spatial analysis was carried out at two different levels of aggregation: PHU and census subdivision (CSD). For more information on CSDs, see Appendix F. To generate the study population for the spatial analysis, women with one or more cardiovascular complications or traditional risk factors were excluded. This was necessary to obtain of a group of women who were not likely undergoing cardiovascular screening prior to pregnancy, to allow for

identification of geographic areas in which women may benefit from screening, based only on the development of pregnancy complications know to be associated with increased CVD risk. The resulting study population for the spatial analysis was 568, 009 pregnancies. The spatial distribution of cumulative incidences of one or more pregnancy complications was examined at the global level, using a test for spatial autocorrelation, and the local level, using a hot spot analysis. Each test was performed twice in total, once for each of the two levels of aggregation (PHU area and CSD). The chosen method for conceptualization of spatial relationships was first-order polygon contiguity. In this method, only polygons (PHU areas/CSDs) which share one or more edges with the polygon of interest influence spatial calculations. This type of conceptualization was chosen based on methods in similar studies conducted in Ontario[73,75]. All spatial analysis functions were carried out using Esri's ArcGIS 10[93]. For a schematic diagram of the spatial analysis, see Appendix G.

3.6.3.1 Public Health Unit area level analysis

The crude cumulative incidence of one or more pregnancy complications was calculated from the spatial analysis population at the PHU area level. The numerator for the incidence calculation was number of cases of one or more pregnancy complications in each PHU area. The denominator was the number of pregnancies in each corresponding PHU area. Women with missing pregnancy complication data were excluded from incidence calculations. Spatial analysis functions were performed for all 36 PHU areas in Ontario.

3.6.3.1.1 Global spatial pattern analysis

The global spatial pattern analysis was carried out by conducting a test for spatial autocorrelation. Spatial autocorrelation is based on Tobler's First Law of geography which states "everything is related to everything else, but near things are more related than distant things" [94]. It is a measure of the degree to which characteristics at one location are similar (or dissimilar) to nearby locations and can be used to analyze the overall spatial pattern in a data set. The test for spatial

autocorrelation in this study was based on the global Moran's I statistic. The mathematical formula for Moran's I, as calculated in ArcGIS, is presented in Appendix H. A z-score and corresponding p-value were calculated from this statistic. For this analysis, the null hypothesis was that the cumulative incidences of one or more pregnancy complications associated with CVD risk were randomly distributed spatially. The value of Moran's I can range between -1.0 and +1.0. A value close to +1.0 (positive autocorrelation) indicates a clustered pattern while a value close to -1.0 (negative autocorrelation) indicates a dispersed pattern. A clustered pattern occurs when nearby locations are similar in characteristics. A dispersed pattern is when characteristics at one location are dissimilar to characteristics at nearby locations. A Moran's I value near 0 with an insignificant p-value indicates that the data is randomly spatially distributed[95]. A p-value of 0.05 was considered to be significant in this study.

3.6.3.1.2 Detection and visualization of local clusters

Local spatial analysis methods were employed to locate and display clusters of areas with high and low cumulative incidences. A hot spot analysis was performed to determine whether statistically significant clusters existed in the data set. Hot spot analysis was based on the Getis-Ord (Gi*) statistic (a z-score) which identifies clusters of points with values higher or lower in magnitude than would be expected by chance if the spatial distribution is random[95]. The mathematical formula for calculation of the Gi* statistic in ArcGIS is presented in Appendix I. A z-score and corresponding p-value were output for each PHU area, the probability that a particular area is within a cluster. For this analysis, the null hypothesis was that the spatial distribution of cumulative incidences across PHUs was random. In other words, the unit of analysis (PHU area) was not located within a cluster of high or low cumulative incidence of one or more pregnancy complications. A p-value of 0.05 was considered significant in the hot spot analysis for this study. A positive z-score and significant p-value indicated a statistically

significant cluster of high cumulative incidence while a negative z-score and significant p-value indicated a statistically significant cluster of low cumulative incidence.

3.6.3.2 Census subdivision level analysis

Population sizes of many CSDs in this study were extremely small because population counts consisted only of pregnant women. BORN Ontario routinely suppresses cell sizes of less than 5, and as a result, data was available for approximately 60% of the 585 census subdivisions in Ontario, or 97% of the total study population. The geographic distribution of CSD data availability was examined, and it was found that approximately 80% of CSDs with suppressed data were located in PHU areas in the Northern region (North East and North West) of Ontario, based on Ministry of Health and Long-Term Care PHU classification[96]. PHU areas from this region contributed only 5% of the pregnancies in the total study population. For these reasons, CSDs located in the Northern region of Ontario were excluded from the spatial analysis at the CSD level. The global spatial pattern analysis and test for local level clustering was performed for CSDs within PHU areas in Eastern, Central, and Southwestern Ontario, and are collectively referred to as Southern Ontario in this thesis.

The crude cumulative incidence of one or more pregnancy complications was calculated from the spatial analysis study population at the CSD level. The numerator for the incidence calculation was the total number of cases of one or more pregnancy complications in each CSD. The denominator was the number of pregnancies in each corresponding CSD. Women with missing pregnancy complication data were excluded from the cumulative incidence calculations. For CSDs with suppressed data in Southern Ontario (n=43), cumulative incidences were assigned using the cumulative incidence of the PHU area in which the CSD was located.

Four CSDs within Southern Ontario were excluded from the analysis; Akwesasne (Part) 59 (n =179), Frontenac Islands (n= 49), Pelee (n=11), and Christian Island 30 (n=5). This was necessary due to incompatibility with the polygon contiguity conceptualization of spatial relationships method, as none of the islands shared boundaries with any CSDs. Overall, spatial analysis functions at the CSD level were performed using 295 units in Southern Ontario.

3.6.3.2.1 Global spatial pattern analysis

The test for spatial autocorrelation using Moran's I statistic, as described in section 3.6.3.1.1, was performed for CSDs in Southern Ontario.

3.6.3.2.2 Detection and visualization of local clusters

The hot spot analysis using the Gi* statistic, as described in section 3.6.3.1.2, was performed for CSDs in Southern Ontario.

Chapter 4

Results

4.1 Descriptive Analysis

The study population was first described in terms of age, pregnancy complications, and cardiovascular complications or traditional risk factors. The age distribution of the study population is presented in Table 2. The age span of study subjects was wide, ranging from less than 15 to over 50 years. The majority of women were between the ages of 25 and 34 years. Approximately 0.02% of the population was under 15 years of age and individuals 50 years of age and above constituted 0.01% of the study population.

Table 2. Age distribution of pregnant women in Ontario (2005-2009)[*]

Age (years)[†]	Percent (%)
<15	0.02
15-19	3.4
20-24	13.5
25-29	28.1
30-34	33.7
35-39	17.5
40-44	3.5
45-49	0.2
50+	0.01

The crude cumulative incidence of pregnancy complications for the study population is presented in Table 3. The crude cumulative incidence of one or more pregnancy complications was 136.8 per 1000 pregnancies. Gestational diabetes, gestational hypertension, and preterm labour were the most common complications, with cumulative incidences of 45.1, 34.5, and 31.2 cases per 1000

[*] Study population, n = 652, 118
[†] Age at time of delivery

pregnancies, respectively. Delivery of an SGA infant and preeclampsia were less common, and crude cumulative incidences were calculated at 18.7 and 17.2 cases per 1000 pregnancies, respectively. Placental abruption was the rarest of the pregnancy complications examined in this study, with a crude cumulative incidence of 5.7 cases per 1000 pregnancies.

Table 3. Crude cumulative incidence of pregnancy complications in Ontario (2005-2009)[‡]

Pregnancy Complications	Incidence (per 1000 pregnancies)
Preeclampsia	17.2
Gestational hypertension	34.5
Gestational diabetes	45.1
Placental abruption	5.7
Delivery of an SGA infant	18.7
Preterm labour	31.2
One or more	136.8

For women who did develop pregnancy complications, the vast majority, approximately 90%, developed a single complication. Approximately 10% of women with pregnancy complications developed two complications, and less than 1% developed 3 or more complications.

The prevalence of cardiovascular complications and traditional cardiovascular risk factors is shown in Table 4. The prevalence of one or more cardiovascular complications and traditional risk factors was 129 per 1000 pregnant women, lower than the cumulative incidence of one or more pregnancy complications. Diabetes was the most prevalent at 16 cases per 1000 pregnancies. The prevalence of heart disease was 7.4 cases per 1000 pregnancies, and chronic hypertension was less common, with a prevalence of 5.1 cases per 1000 pregnancies. For every 1000 pregnant women in Ontario, approximately 119 reported smoking during pregnancy.

[‡] Study population, n = 658, 118

Table 4. Prevalence of cardiovascular complications and traditional cardiovascular risk factors in pregnant women in Ontario (2005-2009)[§]

Cardiovascular complications or traditional risk factors	Prevalence (per 1000 pregnancies)
Chronic hypertension	5.1
Diabetes	16.0
Smoking	118.9
Heart disease	7.4
Age >50	0.1
One or more	129.0

The number of pregnancies and pregnancy rates by PHU area can be found in Table 5. Across PHU areas, the number of pregnancies ranged from 207 to greater than 150,000 during the study period. The greatest number of pregnancies occurred in the Toronto, Peel, York Region, and Ottawa PHU areas. Timiskaming, Huron County, and Northwestern PHU areas contributed the fewest pregnancies. Pregnancy rates over the entire study period, calculated by dividing the number of pregnancies by the total population in each PHU area, ranged from 6.0 to 70.4 per 1000 people. PHU areas in the Greater Toronto Area had the highest pregnancy rates, specifically Peel (70.4 per 1000 people), Toronto (61.7 per 1000 people), York (59.0 per 1000 people), and Halton (58.8 per 1000 people) regions. Ottawa PHU area had the 6th highest pregnancy rate of all health regions in Ontario, at 56.7 pregnancies per 1000 people. Timiskaming Health Unit area had the lowest pregnancy rate (6.0 per 1000 people), followed by the Niagara Region Health Unit area (24.0 per 1000 people) and Wellington-Dufferin-Guelph Health Unit area (29.4 per 1000 people)

[§] Study population, n = 652,118

Table 5. Pregnancies in Public Health Unit areas in Ontario (2005-2009)[**]

Public Health Unit	Total Population (2006)[††]	Number of pregnancies (2005-2009)	Pregnancy rate (per 1000 people)
Algoma Public Health Unit	116,252	4,512	38.8
Brant County Health Unit	125,136	6,195	49.5
Chatham-Kent Health Unit	108,589	4,969	45.8
City of Hamilton - Public Health & Social Services	504,559	20,266	40.2
Durham Region Health Department	561,258	31,609	56.3
Eastern Ontario Health Unit	190,583	9,538	50.0
Elgin-St. Thomas Health Unit	85,351	4,565	53.5
Grey Bruce Health Unit	157,760	5,811	36.8
Haldimand-Norfolk Health Unit	107,775	3,583	33.2
Haliburton, Kawartha, Pine Ridge District Health Unit	171,671	6,442	37.5
Halton Region Health Department	439,256	25,849	58.8
Hastings and Prince Edward Counties Health Unit	155,970	7,657	49.1
Huron County Health Unit	59,325	2,866	48.3
Kingston, Frontenac and Lennox & Addington Health Unit	184,407	9,260	50.2
Lambton Health Unit	128,204	5,705	44.5
Leeds, Grenville and Lanark District Health Unit	162,991	7,311	44.9
Middlesex-London Health Unit	422,333	23,834	56.4
Niagara Region Public Health Department	427,421	10,246	24.0
North Bay Parry Sound District Health Unit	122,848	4,615	37.6
Northwestern Health Unit	80,532	2,868	35.6
Ottawa Public Health	812,129	46,033	56.7
Oxford County Public Health & Emergency Services	102,756	5,664	55.1
Peel Public Health	1,159,405	81,568	70.4
Perth District Health Unit	74,344	4,005	53.9
Peterborough County-City Health Unit	133,080	5,901	44.3
Porcupine Health Unit	84,159	3,583	42.6
Region of Waterloo, Public Health	478,121	27,886	58.3
Renfrew County and District Health Unit	99,369	4,941	49.7
Simcoe Muskoka District Health Unit	479,767	19,091	39.8
Sudbury and District Health Unit	192,391	9,254	48.1
Thunder Bay District Health Unit	154,067	7,565	49.1
Timiskaming Health Unit	34,217	207	6.0
Toronto Public Health	2,503,281	154,447	61.7

[**] Study population, n = 652,118
[††] Canadian Census (2006), Statistics Canada

Wellington-Dufferin-Guelph Health Unit	254,861	7,484	29.4
Windsor-Essex County Health Unit	393,402	21,911	55.7
York Region Public Health Services	892,712	52,698	59.0
Ontario	12,160,282	652,118	53.6

Crude and age-standardized cumulative incidences of preeclampsia, gestational hypertension and gestational diabetes are displayed in Table 6 and age-standardized cumulative incidences are also presented in Figures 1, 2, and 3. Crude and age-standardized cumulative incidences of placental abruption, delivery of a SGA infant, and preterm labour are displayed in Table 7 and age-standardized cumulative incidences are also presented in Figures 4, 5, and 6. Crude and age-standardized cumulative incidences of one or more pregnancy complication are displayed in Table 8. Age-standardized cumulative incidences are also presented in maps in Figure 7. The crude cumulative incidence for preeclampsia ranged from 4.3 to 35.9 cases per 1000 pregnancies. Algoma, Windsor-Essex, and Niagara Region Health Unit areas had the lowest age-standardized cumulative incidences, while Thunder Bay, Toronto, and Middlesex-London had the highest. The crude cumulative incidence of gestational hypertension across health regions was between 20.0 and 78.1 cases per 1000 pregnancies. North Bay Parry Sound, Peterborough, and Hamilton health regions had the lowest age-standardized cumulative incidences of gestational hypertension, and York, Durham, and Porcupine had the highest age-standardized cumulative incidences. The crude cumulative incidence rates for gestational diabetes ranged from 17.3 to 71.9 cases per 1000 pregnancies. Peterborough, Haliburton, Kawartha Pine Ridge, and Perth health regions had the lowest age-standardized cumulative incidences and Hamilton, Peel, and Middlesex-London had the highest age-standardized cumulative incidences. For placental abruption, the crude cumulative incidence was between 2.6 and 15.6 cases per 1000 pregnancies. North Bay Parry Sound, Algoma, and Sudbury had to lowest age-standardized cumulative incidences, while Toronto, Eastern Ontario, and Timiskaming had the highest age-standardized cumulative incidences. The range of crude cumulative incidence of delivery of a SGA infant was 8.9 to 41.7 cases per 1000 pregnancies. North Bay Parry Sound, Sudbury, and Algoma had the lowest and Wellington-Dufferin-Guelph, Niagara, and Eastern Ontario Health Unit areas had the highest age-standardized cumulative incidences. Crude preterm labour cumulative incidences ranged from

15.6 to 67.7 cases per 1000 pregnancies. Algoma, Kingston, Frontenac Lennox & Addington, and Northwestern had the lowest age-standardized cumulative incidences of preterm labour and Peel, Middlesex-London, and Toronto had the highest. Crude cumulative incidences of one or more pregnancy complications ranged from 74.0 to 224.0 cases per 1000 pregnancies. Algoma, North Bay Parry Sound, and Kingston, Frontenac Lennox & Addington had the lowest age-standardized cumulative incidences and Peel, Middlesex-London, and Toronto had the highest age-standardized cumulative incidences. Overall, of all PHU areas, Algoma and North Bay Parry Sound regions appeared in the lowest age-standardized cumulative incidence categories of pregnancy complications most frequently. Middlesex-London, Toronto, and Peel Health Unit areas appeared in the highest age-standardized cumulative incidence categories most frequently.

Table 6. Crude and age-standardized cumulative incidence (per 1000 pregnancies) of preeclampsia, gestational hypertension, and gestational diabetes in Ontario (2005-2009)[‡‡]

Public health unit	Preeclampsia			Gestational Hypertension			Gestational Diabetes		
	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence
Algoma Public Health Unit	23	5.2	2.1	98	22.0	12.3	99	22.2	19.2
Brant County Health Unit	107	19.0	10.2	210	37.3	18.0	166	29.5	16.1
Chatham-Kent Health Unit	90	18.3	10.3	235	47.8	26.1	353	71.9	46.0
City of Hamilton - Public Health & Social Services	245	12.9	13.8	492	25.9	12.3	697	36.7	130.3
Durham Region Health Department	458	16.1	8.7	1499	52.5	69.5	1283	45.0	30.6
Eastern Ontario Health Unit	212	29.9	15.9	377	53.1	24.3	251	35.4	20.9
Elgin-St. Thomas Health Unit	75	18.6	9.7	125	31.0	17.2	108	26.8	14.6
Grey Bruce Health Unit	84	15.2	6.2	209	37.8	29.4	113	20.5	11.9
Haldimand-Norfolk Health Unit	56	16.7	7.7	119	35.4	16.3	99	29.5	24.3
Haliburton, Kawartha, Pine Ridge District Health Unit	97	19.1	9.1	175	34.5	18.4	101	19.9	10.9
Halton Region Health Department	303	13.1	10.2	908	39.3	30.0	858	37.1	23.5
Hastings and Prince Edward Counties Health Unit	192	29.8	16.4	238	37.0	18.3	185	28.7	18.9
Huron County Health Unit	40	14.2	6.9	131	46.6	21.9	70	24.9	14.1
Kingston, Frontenac and Lennox & Addington Health Unit	197	21.7	11.1	365	40.2	18.8	210	23.1	12.3
Lambton Health Unit	112	25.2	14.1	201	45.1	24.4	177	39.7	24.9
Leeds, Grenville and Lanark District Health Unit	204	31.8	29.8	326	50.9	24.5	153	23.9	16.1

[‡‡] Study population, n = 652,118

Middlesex-London Health Unit	689	29.0	59.1	1173	49.4	27.1	952	40.1	111.3
Niagara Region Public Health Department	111	12.2	5.5	317	34.9	20.1	276	30.4	28.8
North Bay Parry Sound District Health Unit	46	13.1	7.2	74	21.0	8.6	61	17.3	18.0
Northwestern Health Unit	62	23.0	11.8	133	49.3	22.0	164	60.8	35.1
Ottawa Public Health	963	29.3	20.5	1170	35.6	56.6	1445	43.9	31.0
Oxford County Public Health & Emergency Services	111	19.9	11.3	269	48.3	26.5	158	28.4	16.7
Peel Public Health	927	12.3	23.9	2352	31.2	39.9	5294	70.1	129.3
Perth District Health Unit	55	13.8	8.3	145	36.5	20.0	98	24.6	11.8
Peterborough County-City Health Unit	156	35.9	14.9	87	20.0	11.7	83	19.1	9.1
Porcupine Health Unit	69	19.9	12.7	185	53.5	59.3	156	45.1	35.6
Region of Waterloo, Public Health	312	11.7	6.0	649	24.4	14.8	772	29.1	24.7
Renfrew County and District Health Unit	94	20.9	10.1	197	43.9	22.1	143	31.8	23.2
Simcoe Muskoka District Health Unit	507	29.4	14.2	1165	67.5	40.1	497	28.8	14.8
Sudbury and District Health Unit	185	20.3	10.8	328	36.0	20.0	228	25.0	17.2
Thunder Bay District Health Unit	203	28.4	68.8	440	61.5	48.0	343	47.9	26.9
Timiskaming Health Unit	4	20.8	20.4	15	78.1	29.4	5	26.0	14.4
Toronto Public Health	2105	15.3	68.5	3418	24.9	45.0	7173	52.3	70.9
Wellington-Dufferin-Guelph Health Unit	110	17.3	9.6	244	38.3	20.0	190	29.9	33.7
Windsor-Essex County Health Unit	95	4.3	2.1	992	45.4	23.6	1146	52.4	49.3
York Region Public Health Services	577	14.1	11.4	834	20.4	75.9	1937	47.3	29.1
Ontario	9,897	17.2	54.3	19,919	34.5	52.5	26,039	45.1	83.8

Figure 1. Age-standardized cumulative incidence of preeclampsia by Public Health Unit area in Ontario (2005-2009)

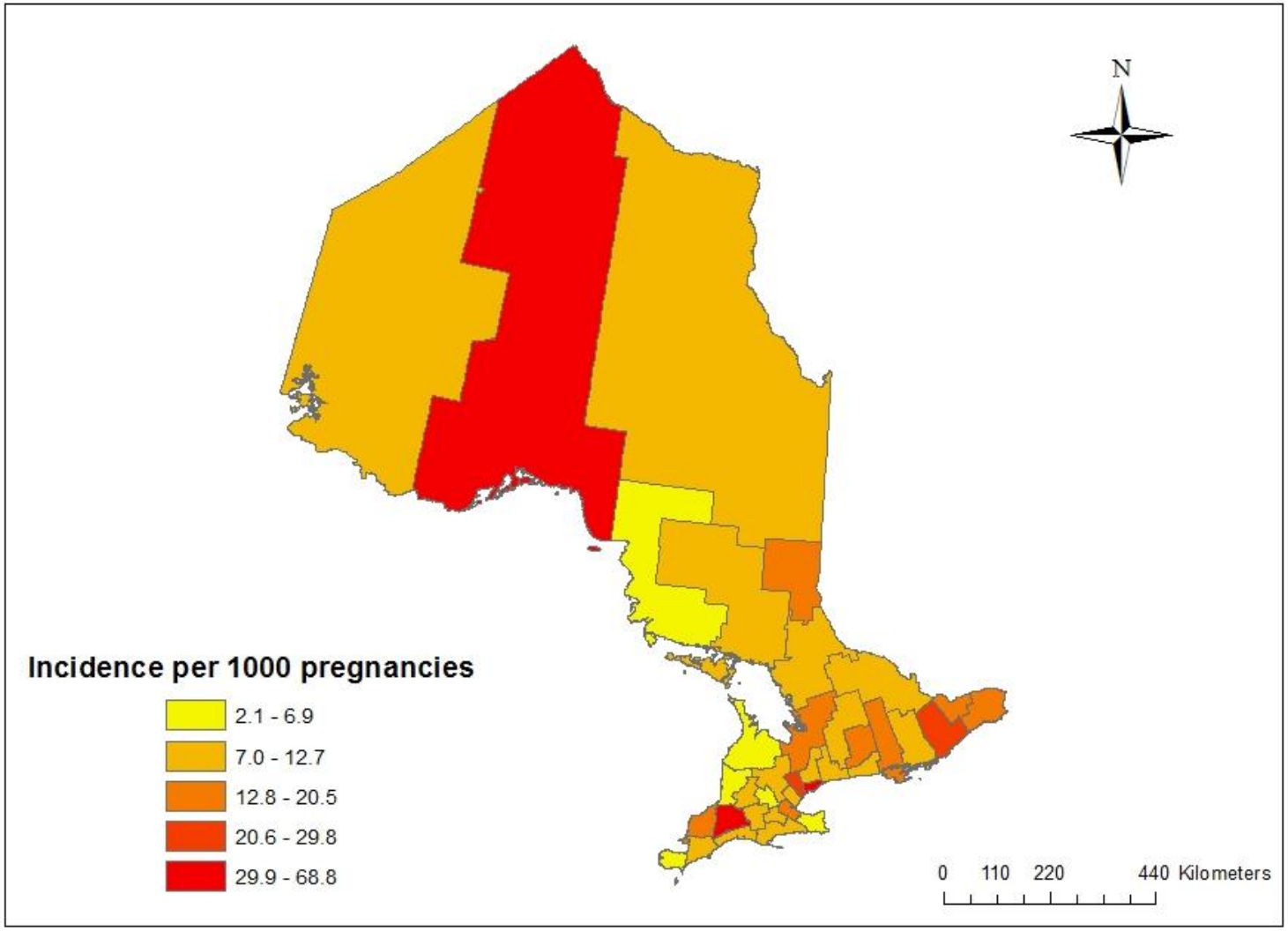


Figure 2. Age-standardized cumulative incidence of gestational hypertension by Public Health Unit area in Ontario (2005-2009)

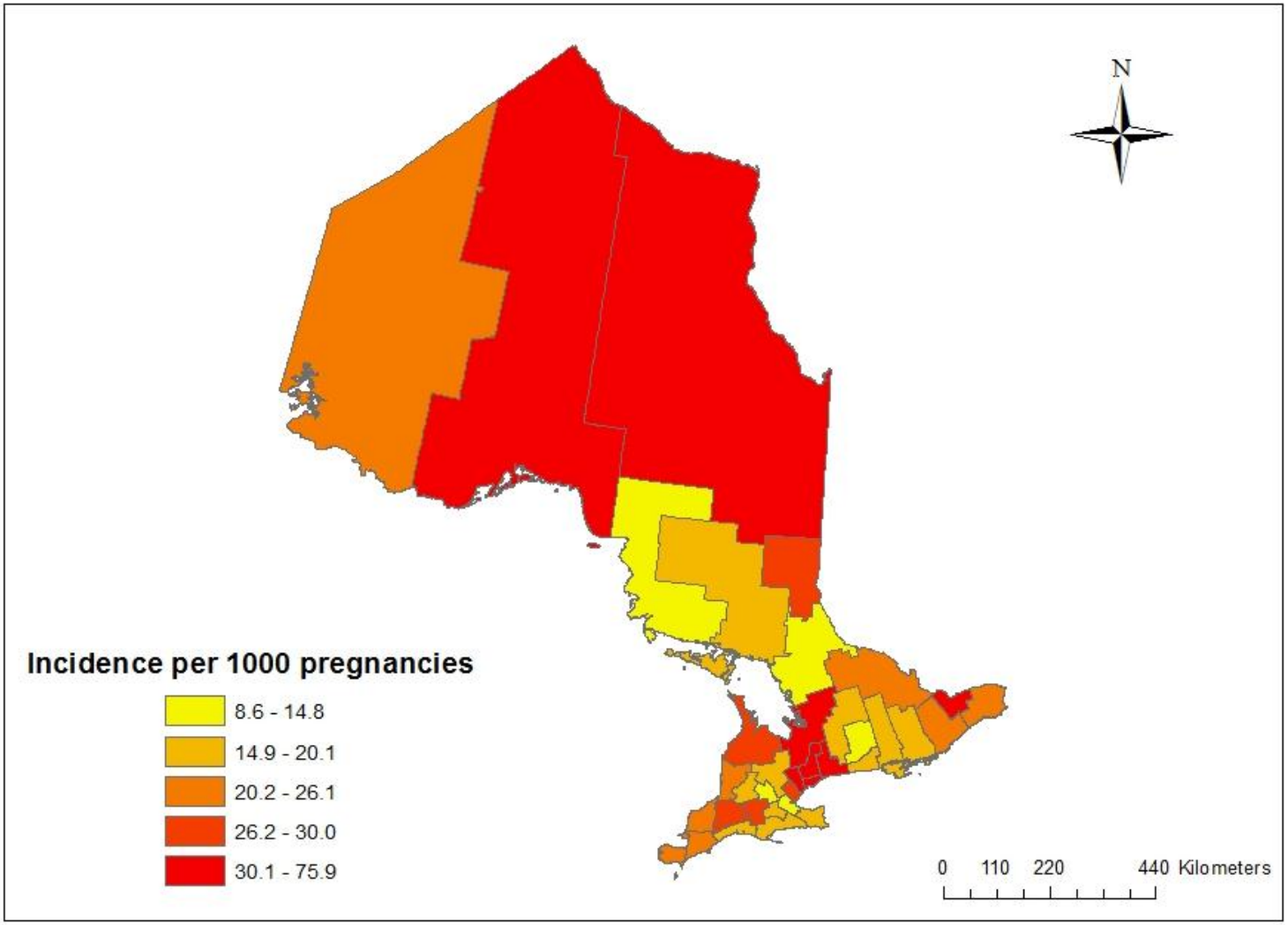


Figure 3. Age-standardized cumulative incidence of gestational diabetes by Public Health Unit area in Ontario (2005-2009)

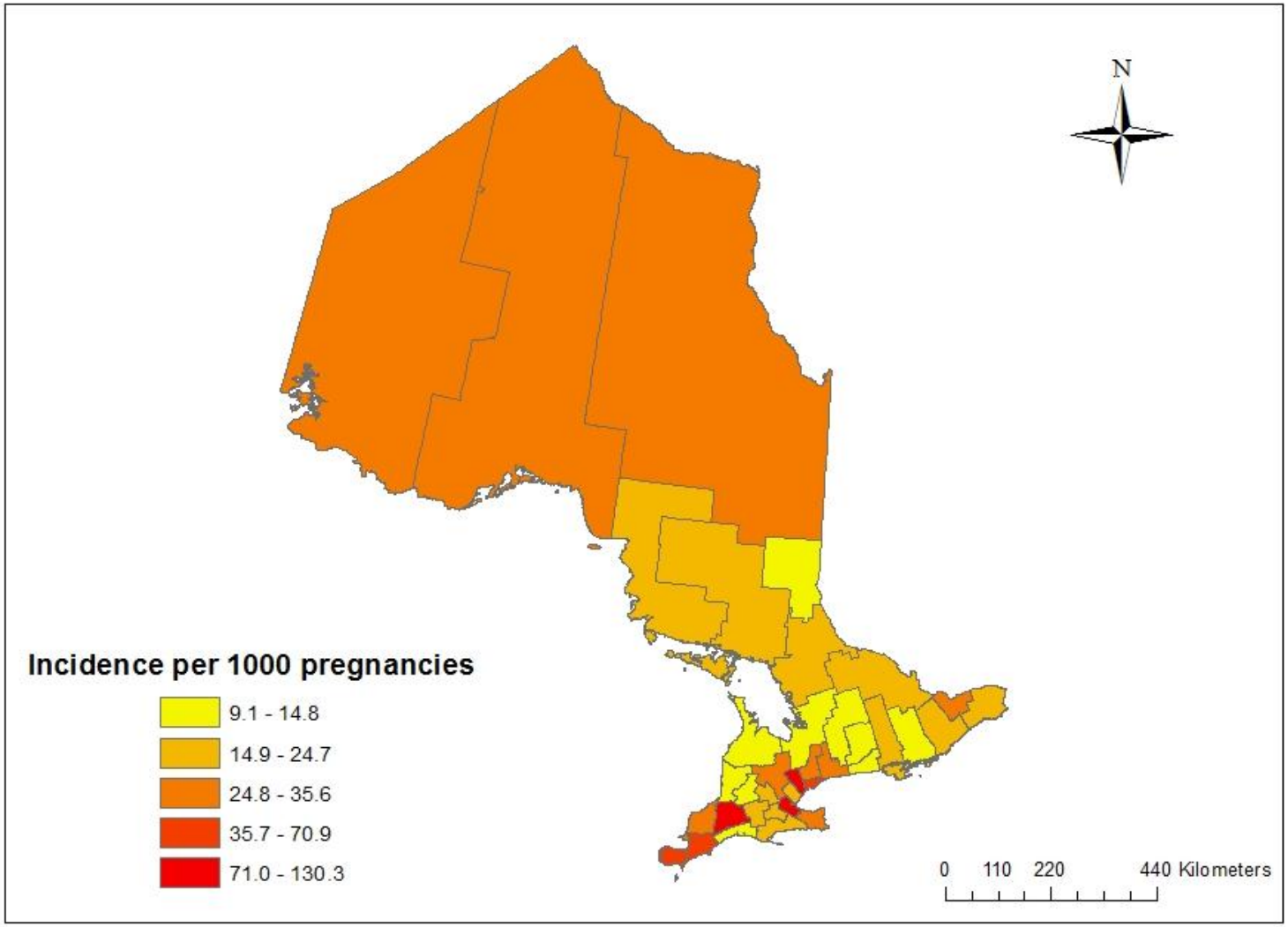


Table 7. Crude and age-standardized cumulative incidence (per 1000 pregnancies) of placental abruption, delivery of a small for gestational age infant, and preterm labour in Ontario (2005-2009)[§§]

Public health unit	Placental Abruption			Delivery of a SGA infant			Preterm Labour		
	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence
Algoma Public Health Unit	14	3.1	1.6	42	9.4	4.6	80	17.9	7.3
Brant County Health Unit	46	8.2	3.4	119	21.1	10.9	167	29.7	14.1
Chatham-Kent Health Unit	56	11.4	7.8	125	25.4	11.9	225	45.8	28.5
City of Hamilton - Public Health & Social Services	177	9.3	5.4	329	17.3	8.5	497	26.1	13.2
Durham Region Health Department	164	5.7	2.7	548	19.2	10.9	804	28.2	51.0
Eastern Ontario Health Unit	37	5.2	17.0	140	19.7	39.4	276	38.9	47.7
Elgin-St. Thomas Health Unit	30	7.4	5.0	71	17.6	10.0	173	42.9	20.8
Grey Bruce Health Unit	34	6.2	3.4	108	19.6	8.5	180	32.6	13.9
Haldimand-Norfolk Health Unit	28	8.3	3.3	60	17.9	11.5	98	29.2	16.8
Haliburton, Kawartha, Pine Ridge District Health Unit	34	6.7	2.9	45	8.9	4.8	179	35.3	20.2
Halton Region Health Department	115	5.0	2.9	302	13.1	7.3	606	26.2	13.0
Hastings and Prince Edward Counties Health Unit	46	7.1	4.3	238	37.0	17.1	179	27.8	16.0
Huron County Health Unit	20	7.1	5.3	62	22.0	15.3	111	39.5	19.7
Kingston, Frontenac and Lennox & Addington Health Unit	69	7.6	3.4	158	17.4	9.7	142	15.6	7.5
Lambton Health Unit	36	8.1	3.7	137	30.8	15.6	244	54.8	26.7
Leeds, Grenville and Lanark District Health Unit	32	5.0	2.0	102	15.9	9.3	208	32.5	19.0

[§§] Study population, n = 652,118

Middlesex-London Health Unit	276	11.6	6.4	689	29.0	21.7	1475	62.1	81.4
Niagara Region Public Health Department	60	6.6	3.9	154	16.9	49.4	271	29.8	44.9
North Bay Parry Sound District Health Unit	9	2.6	1.2	33	9.4	3.7	91	25.8	12.2
Northwestern Health Unit	18	6.7	2.6	29	10.8	6.2	49	18.2	8.6
Ottawa Public Health	138	4.2	2.8	1175	35.7	24.0	1169	35.6	21.0
Oxford County Public Health & Emergency Services	50	9.0	4.0	74	13.3	5.5	265	47.6	24.9
Peel Public Health	351	4.6	2.5	1296	17.2	9.8	1775	23.5	82.7
Perth District Health Unit	26	6.5	5.2	66	16.6	8.1	148	37.2	18.6
Peterborough County-City Health Unit	14	3.2	2.9	52	12.0	5.3	231	53.1	30.5
Porcupine Health Unit	13	3.8	6.4	61	17.6	6.7	70	20.2	12.6
Region of Waterloo, Public Health	153	5.8	5.1	422	15.9	10.6	613	23.1	20.7
Renfrew County and District Health Unit	34	7.6	5.6	145	32.3	14.8	144	32.1	14.6
Simcoe Muskoka District Health Unit	100	5.8	2.6	324	18.8	11.4	494	28.6	17.5
Sudbury and District Health Unit	29	3.2	2.0	96	10.5	4.5	200	21.9	10.1
Thunder Bay District Health Unit	33	4.6	3.0	208	29.1	14.4	166	23.2	11.9
Timiskaming Health Unit	3	15.6	8.4	8	41.7	17.7	13	67.7	25.3
Toronto Public Health	668	4.9	21.8	1876	13.7	18.1	4283	31.2	52.5
Wellington-Dufferin-Guelph Health Unit	49	7.7	4.3	122	19.2	79.7	204	32.1	16.3
Windsor-Essex County Health Unit	145	6.6	3.1	709	32.4	26.3	1009	46.1	26.0
York Region Public Health Services	174	4.2	2.6	653	15.9	13.1	1130	27.6	14.0
Ontario	3,296	5.7	12.1	10,800	18.7	25.8	18,021	31.2	47.6

Figure 4. Age-standardized cumulative incidence of placental abruption by Public Health Unit area in Ontario (2005-2009)

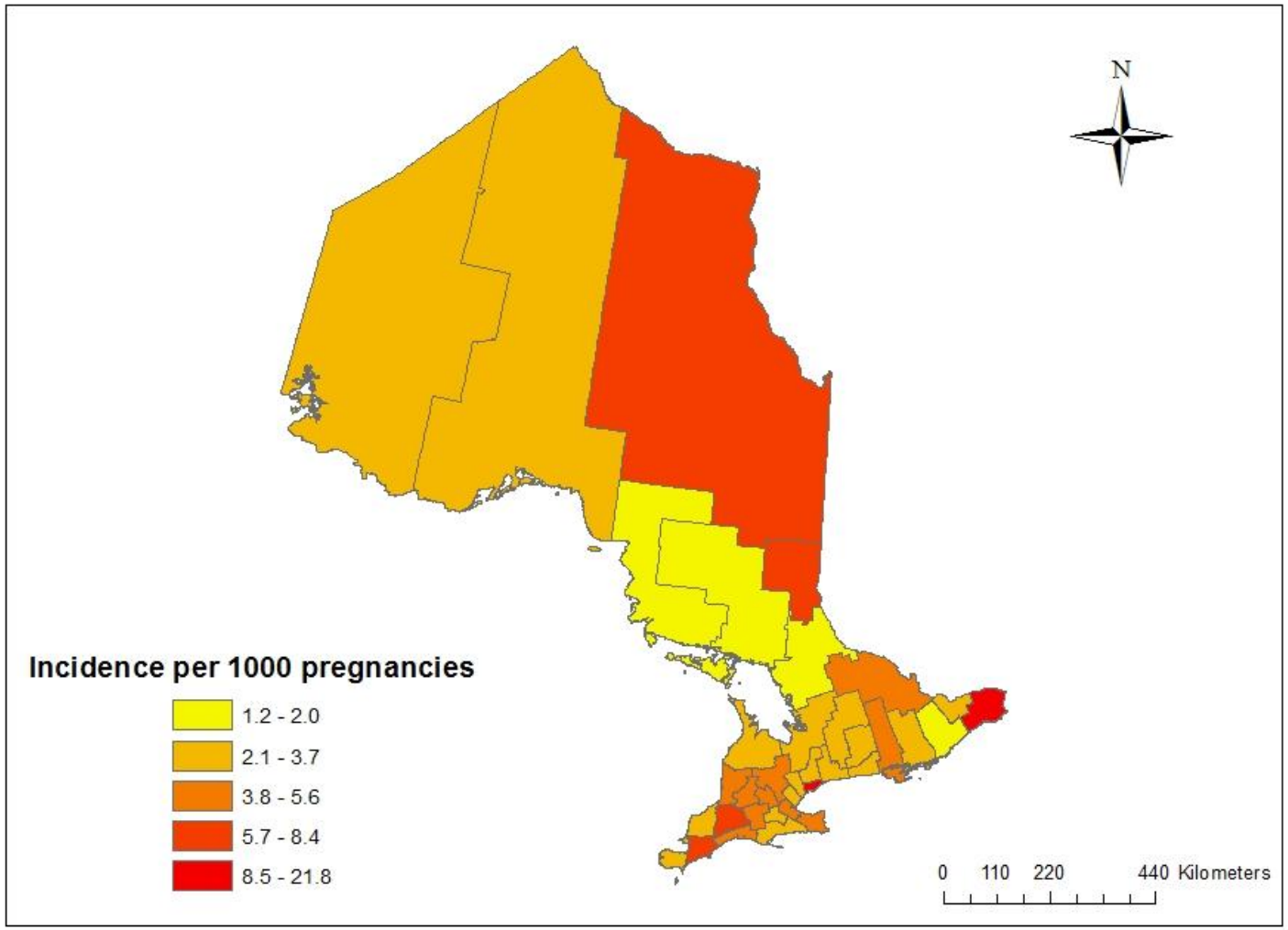


Figure 5. Age-standardized cumulative incidence of delivery of a small for gestational age infant by Public Health Unit area in Ontario (2005-2009)

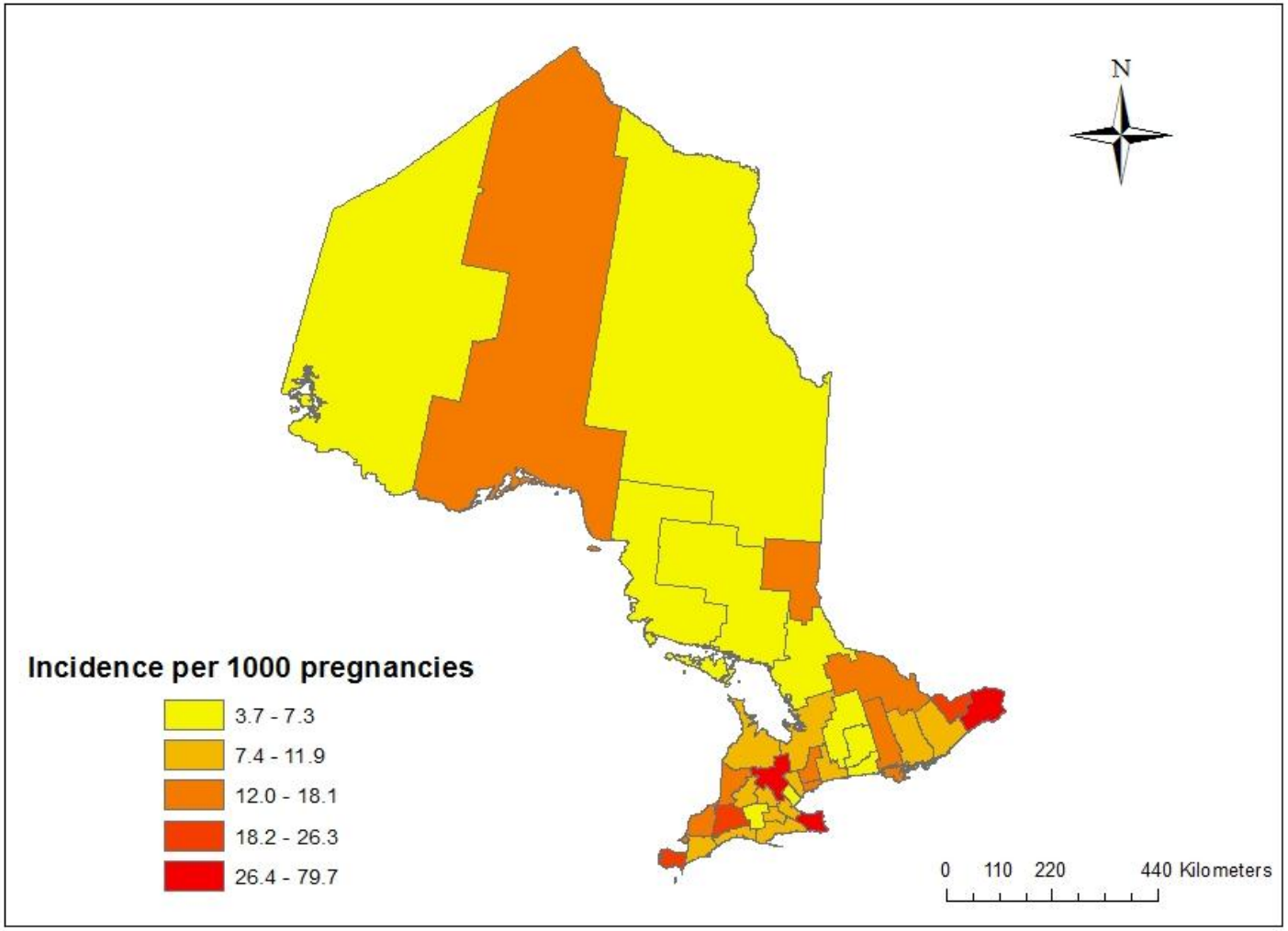


Figure 6. Age-standardized cumulative incidence of preterm labour by Public Health Unit area in Ontario (2005-2009)

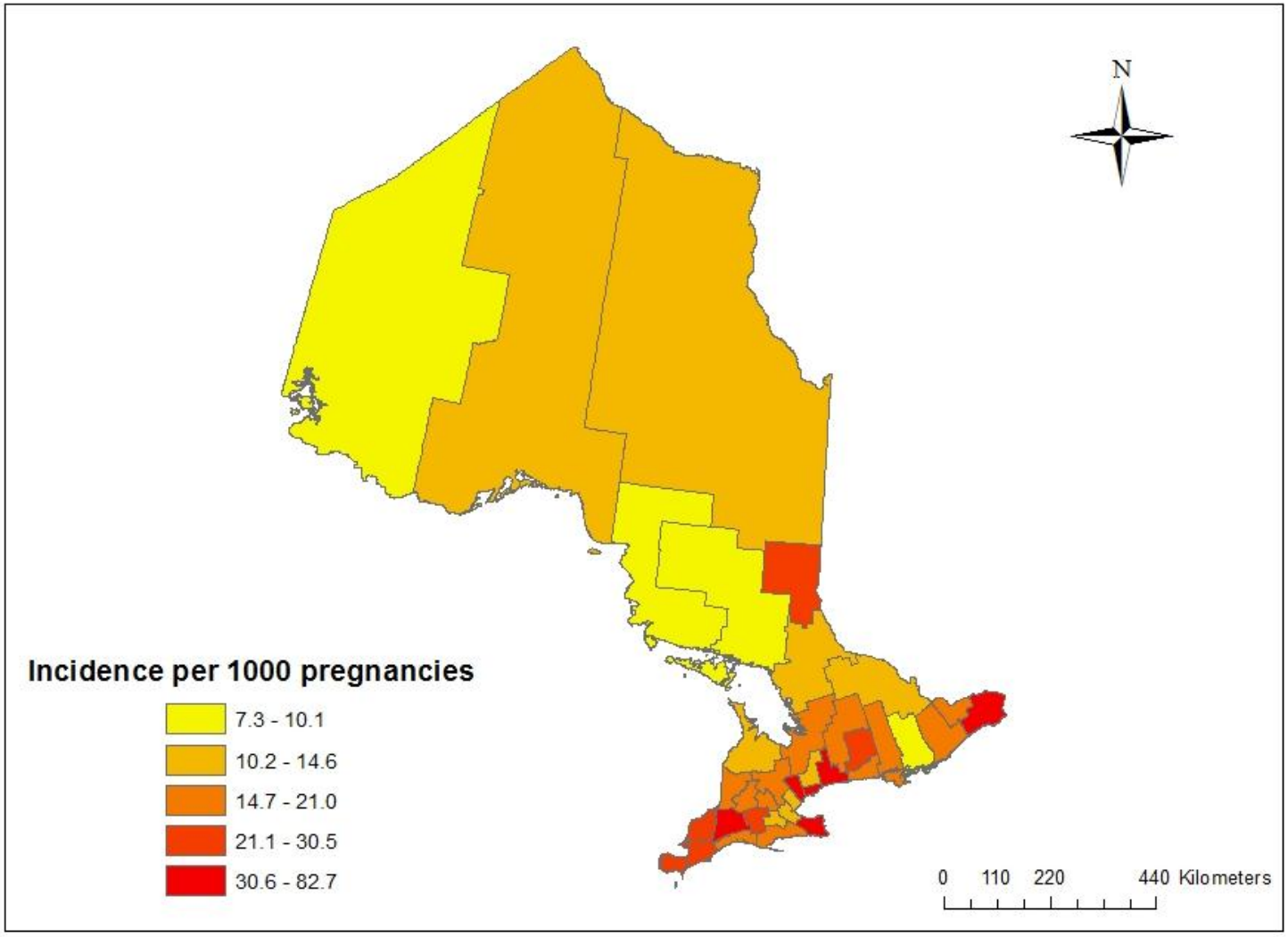
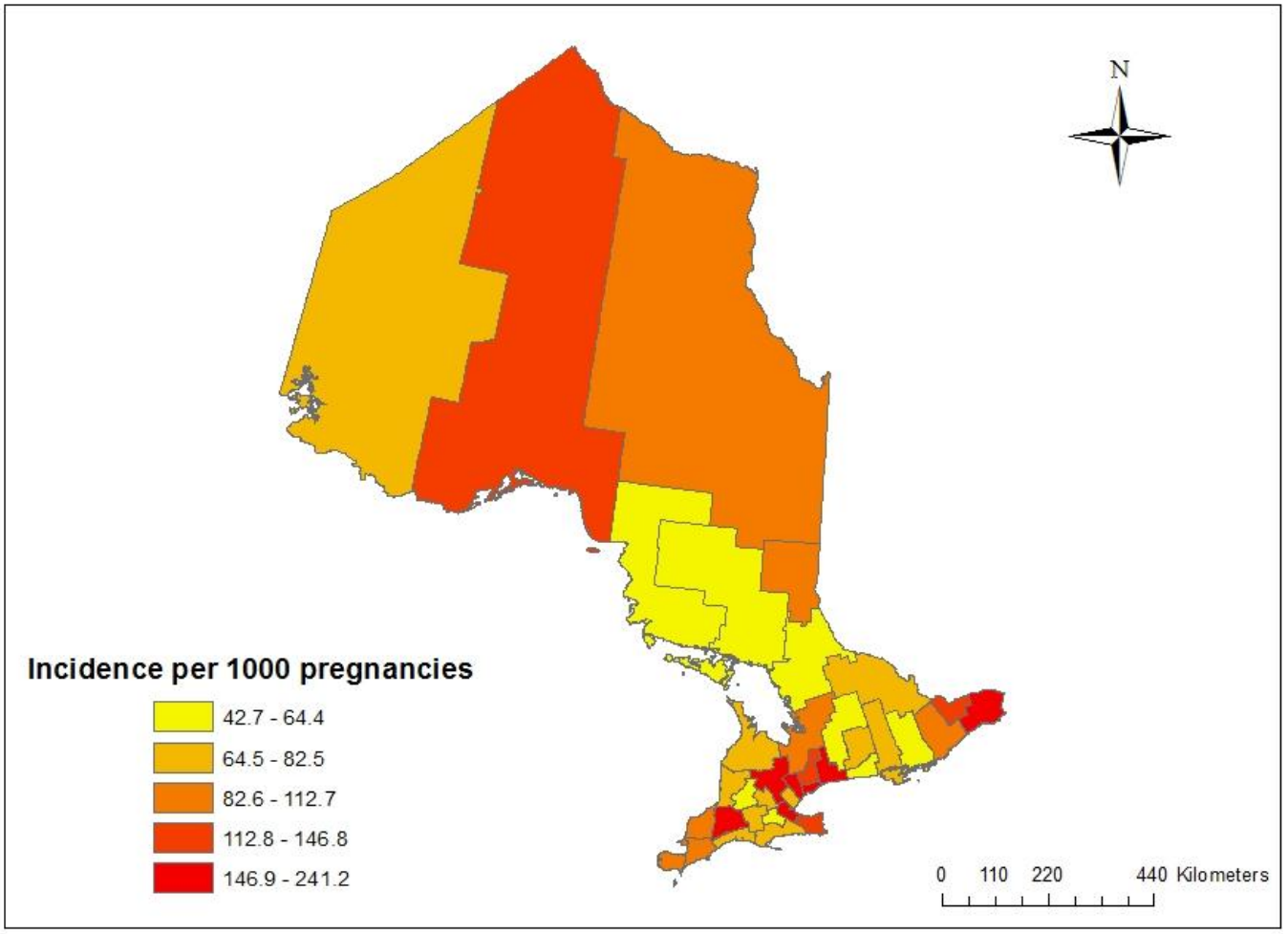


Table 8. Crude and age-standardized cumulative incidence (per 1000 pregnancies) of one or more pregnancy complications in Ontario (2005-2009)[***]

Public health unit	One or more complications		
	Number of cases	Crude cumulative incidence	Age-standardized cumulative incidence
Algoma Public Health Unit	330	74.0	42.7
Brant County Health Unit	715	127.1	63.9
Chatham-Kent Health Unit	944	192.2	109.7
City of Hamilton - Public Health & Social Services	2179	114.6	175.9
Durham Region Health Department	4276	149.9	164.6
Eastern Ontario Health Unit	1156	162.9	155.1
Elgin-St. Thomas Health Unit	503	124.7	67.0
Grey Bruce Health Unit	645	116.8	66.2
Haldimand-Norfolk Health Unit	416	123.9	73.4
Haliburton, Kawartha, Pine Ridge District Health Unit	562	110.8	60.0
Halton Region Health Department	2822	122.2	80.8
Hastings and Prince Edward Counties Health Unit	987	153.2	82.5
Huron County Health Unit	377	134.1	72.0
Kingston, Frontenac and Lennox & Addington Health Unit	1049	115.6	57.2
Lambton Health Unit	788	177.0	91.7
Leeds, Grenville and Lanark District Health Unit	921	143.7	91.9
Middlesex-London Health Unit	4571	192.4	240.6
Niagara Region Public Health Department	1081	118.9	146.8
North Bay Parry Sound District Health Unit	292	82.9	48.2
Northwestern Health Unit	401	148.7	76.2
Ottawa Public Health	5451	165.8	139.5
Oxford County Public Health & Emergency Services	819	147.0	80.3
Peel Public Health	10979	145.4	241.2
Perth District Health Unit	484	121.7	64.4
Peterborough County-City Health Unit	580	133.4	70.1
Porcupine Health Unit	499	144.2	112.7
Region of Waterloo, Public Health	2638	99.3	71.7
Renfrew County and District Health Unit	670	149.2	80.1
Simcoe Muskoka District Health Unit	2686	155.5	88.6
Sudbury and District Health Unit	956	104.9	57.9
Thunder Bay District Health Unit	1247	174.3	143.2
Timiskaming Health Unit	43	224.0	100.5
Toronto Public Health	17451	127.2	198.5
Wellington-Dufferin-Guelph Health Unit	808	127.0	154.3
Windsor-Essex County Health Unit	3650	166.9	110.3
York Region Public Health Services	4802	117.2	137.3
Ontario	78,904	136.8	216.2

[***] Study population, n = 652,118

Figure 7. Age-standardized cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by Public Health Unit area in Ontario (2005-2009)



4.2 Spatial Analysis

4.2.1 Public Health Unit area level

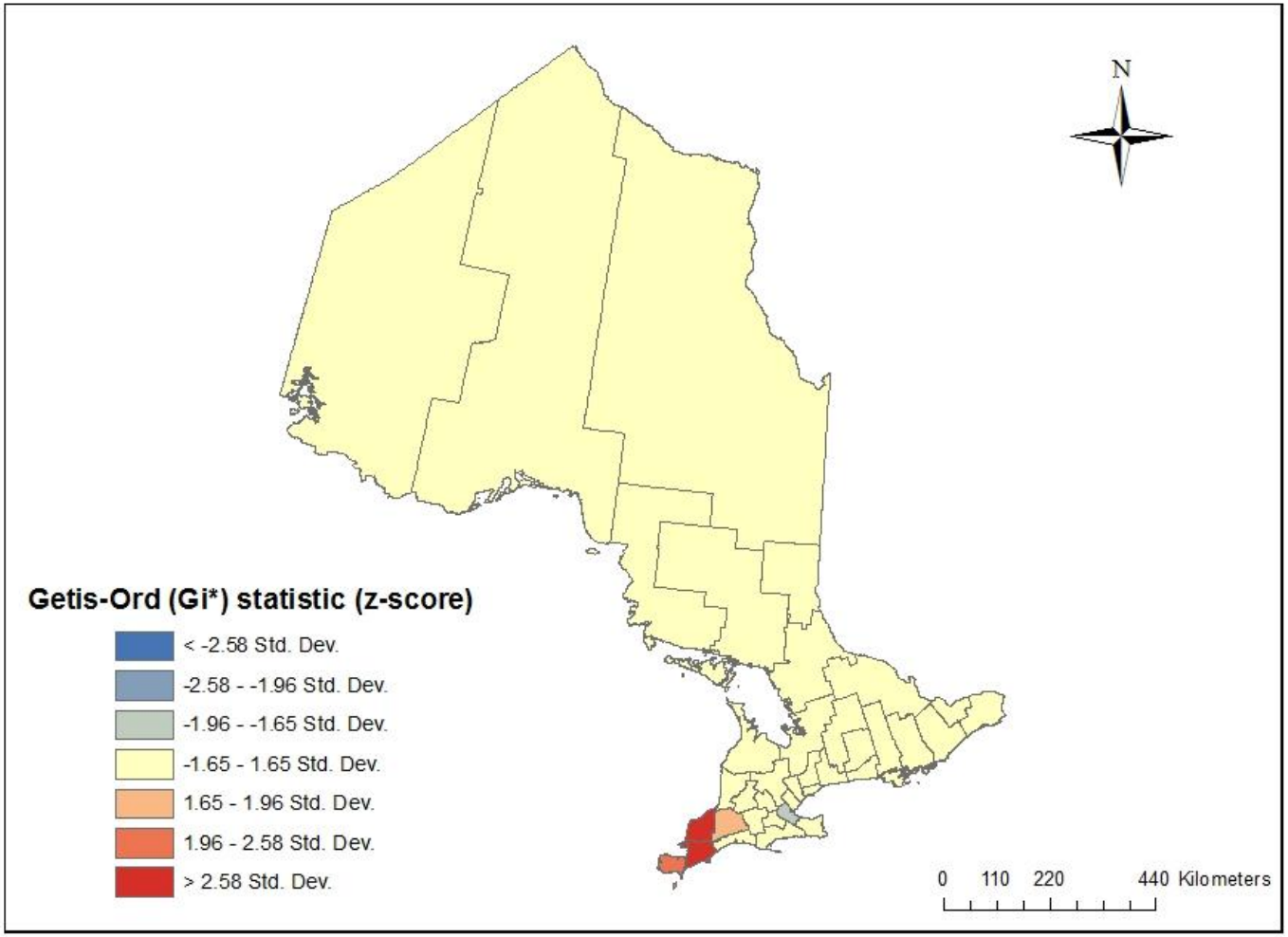
4.2.1.1 Global spatial pattern analysis

The test for spatial autocorrelation in the geographic distribution of the crude cumulative incidence of one or more pregnancy complications at the PHU area level estimated a global Moran's I value of 0.057 with a p-value of 0.42, suggesting that there was no spatial autocorrelation. Based on these results, the global spatial distribution of cumulative incidences of one or more pregnancy complications was random at the PHU area level across the entire province.

4.2.1.2 Detection and visualization of local clusters

Hot spot analysis was performed using the crude cumulative incidence of one or more pregnancy complications at the PHU area level and the map output is presented in Figure 8. Results of this analysis revealed one statistically significant cluster, involving three PHU areas. A statistically significant cluster of high cumulative incidence spanned Lambton, Chatham-Kent, and Windsor-Essex Health Unit areas. Middlesex-London PHU was identified as a possible cluster of high cumulative incidence, but with a p-value of 0.061, it was not statistically significant. Hamilton PHU area was identified as a possible cluster of low cumulative incidence with a p-value of 0.057, but this was not statistically significant.

Figure 8. Hot spot analysis of cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by Public Health Unit area in Ontario (2005-2009)



4.2.2 Census subdivision area level

4.2.2.1 Global spatial pattern analysis

In the test for spatial autocorrelation in the geographic distribution of the crude cumulative incidence of one or more pregnancy complications at the CSD level, the global Moran's I value was 0.33 with a p-value of 0.00. This indicated significant positive autocorrelation. Based on these results, the global spatial distribution of cumulative incidences was not random at the CSD area level in Southern Ontario, and overall, the distribution of cumulative incidences exhibited a clustered pattern.

4.2.2.2 Detection and visualization of local clusters

The map output of the hot spot analysis at the CSD level is display in Figure 9. Fourteen statistically significant clusters were identified: seven statistically significant clusters of high cumulative incidence and seven statistically significant clusters of low cumulative incidence. Statistically significant clusters of high cumulative incidence are displayed in Figure 10. Gi* statistic and p-values of CSDs within each significant cluster of high cumulative incidence are presented in Table 9. For a similar map and table for statistically significant clusters of low cumulative incidence, please see Appendix J.

The largest cluster of high cumulative incidence in terms of geographic area was located in the Chatham-Kent, Lambton, and Middlesex-London areas. The largest cluster of high cumulative incidence according to population size occurred in Ottawa, extending outwards to the Leeds, Grenville and Lanark region. Three clusters of high cumulative incidence were located in the Simcoe Muskoka and Grey Bruce regions, one was located in Renfrew County, and one was located within the Eastern Ontario health region.

Figure 9. Hot spot analysis of cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by census subdivision in Southern Ontario (2005-2009)

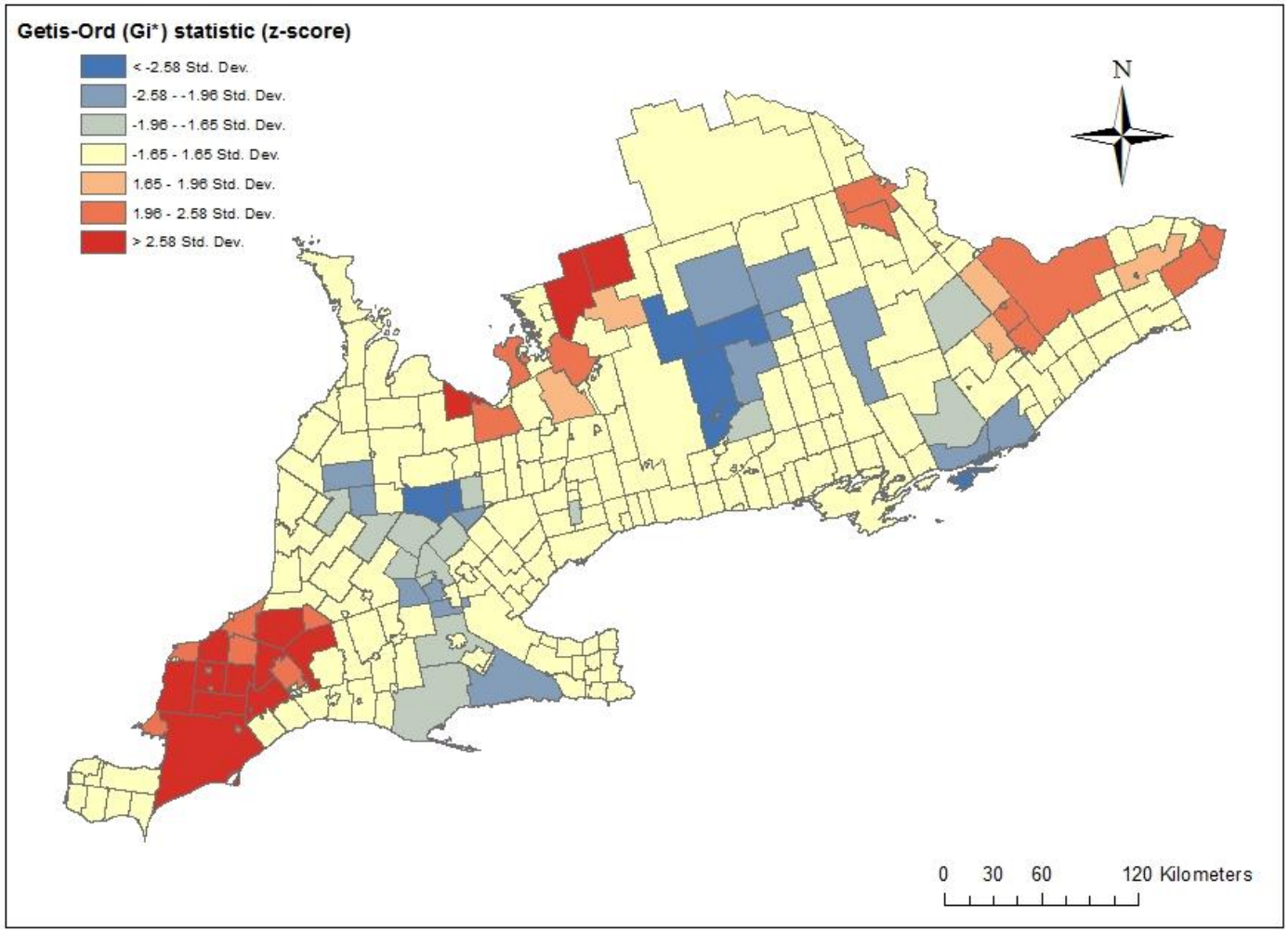


Figure 10. Statistically significant clusters of high cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by census subdivision in Southern Ontario (2005-2009)

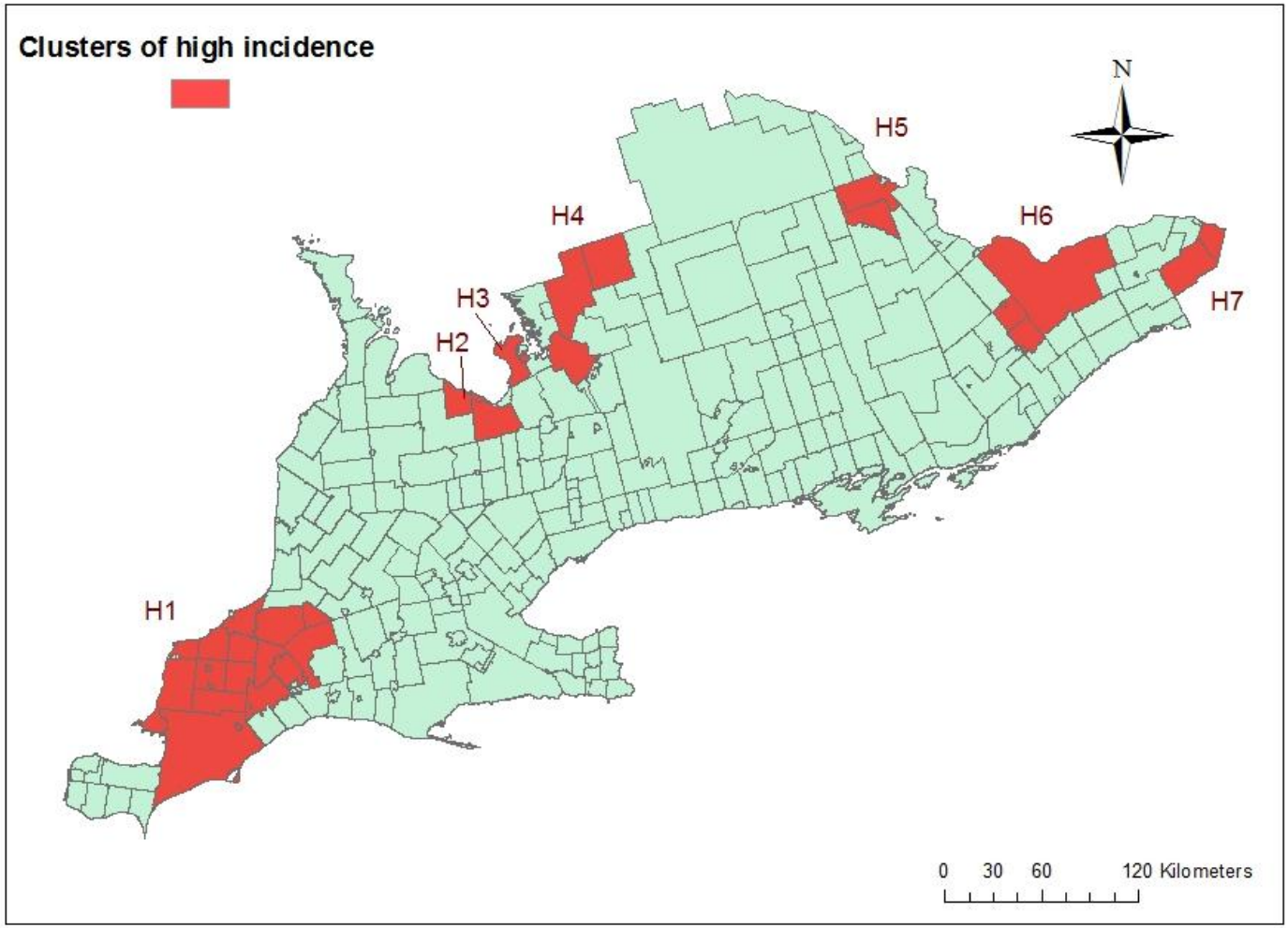


Table 9. Statistically significant clusters of high cumulative incidence from a hot spot analysis of cumulative incidence of one or more pregnancy complications at the census subdivision level in Ontario (2005-2009)¨

Cluster	Census Subdivision	Public Health Unit	n†††	Gi*	p-value
H1	St. Clair	Lambton Health Unit	561	4.65	0.000
H1	Dawn-Euphemia	Lambton Health Unit	51	3.87	0.000
H1	Chatham-Kent	Chatham-Kent Health Unit	3,691	3.76	0.000
H1	Brooke-Alvinston	Lambton Health Unit	67	3.74	0.000
H1	North Middlesex	Middlesex-London Health Unit	245	3.60	0.000
H1	Enniskillen	Lambton Health Unit	340	3.55	0.000
H1	Southwest Middlesex	Middlesex-London Health Unit	220	3.46	0.001
H1	Adelaide Metcalfe	Middlesex-London Health Unit	109	3.39	0.001
H1	Middlesex Centre	Middlesex-London Health Unit	768	2.93	0.003
H1	Plympton-Wyoming	Lambton Health Unit	222	2.65	0.008
H1	Walpole Island 46	Lambton Health Unit	94	2.42	0.016
H1	Warwick	Lambton Health Unit	202	2.42	0.016
H1	Strathroy-Caradoc	Middlesex-London Health Unit	883	2.36	0.018
H1	Oil Springs	Lambton Health Unit	*	2.28	0.023
H1	Petrolia	Lambton Health Unit	*	2.28	0.023
H1	Lucan Biddulph	Middlesex-London Health Unit	253	2.24	0.025
H1	Sarnia	Lambton Health Unit	2,380	2.09	0.036
H1	Moravian 47	Chatham-Kent Health Unit	*	2.09	0.037
H1	Lambton Shores	Lambton Health Unit	370	1.99	0.046
H2	Collingwood	Simcoe Muskoka District Health Unit	237	2.92	0.004

¨ Spatial analysis population, n = 470, 489, ††† n = number of women in the spatial analysis population in each census subdivision, * = less than 5 pregnancies recorded during the study period

H2	Blue Mountains	Grey Bruce Health Unit	6	2.87	0.004
H2	Clearview	Simcoe Muskoka District Health Unit	209	2.24	0.025
H3	Midland	Simcoe Muskoka District Health Unit	324	2.17	0.030
H3	Tiny	Simcoe Muskoka District Health Unit	194	2.09	0.037
H4	Huntsville	Simcoe Muskoka District Health Unit	113	3.14	0.002
H4	Muskoka Lakes	Simcoe Muskoka District Health Unit	48	2.73	0.006
H4	Severn	Simcoe Muskoka District Health Unit	319	2.01	0.045
H5	North Algona Wilberforce	Renfrew County and District Health Unit	30	2.25	0.025
H5	Laurentian Valley	Renfrew County and District Health Unit	308	1.99	0.047
H6	Carleton Place	Leeds, Grenville and Lanark District Health Unit	417	2.46	0.014
H6	Beckwith	Leeds, Grenville and Lanark District Health Unit	93	2.36	0.018
H6	Montague	Leeds, Grenville and Lanark District Health Unit	216	2.29	0.022
H6	Ottawa	Ottawa Public Health	42,145	2.14	0.032
H7	North Glengarry	Eastern Ontario Health Unit	201	1.97	0.049
H7	East Hawkesbury	Eastern Ontario Health Unit	55	2.07	0.038

Chapter 5

Discussion

This study has examined the distribution of pregnancy complications associated with CVD risk and identified clusters of high cumulative incidence within the province of Ontario. This chapter summarizes the main findings of the study and discusses limitations. The results are interpreted in the context of relevant literature, and implications of the research findings are described.

5.1 Summary of main findings

Cumulative incidences of each pregnancy complication and one or more pregnancy complications vary by PHU areas in Ontario, and variation in age distribution did not explain all variation in complications. For women with no history of cardiovascular complications or traditional cardiovascular risk factors, one statistically significant cluster of high cumulative incidence was identified at the PHU area level in Ontario. This cluster spanned the Lambton, Chatham-Kent, and Windsor-Essex Health Unit areas. For women with no history of cardiovascular complications or traditional cardiovascular risk factors, statistically significant clusters of high cumulative incidence were identified at the CSD level in Ontario. The largest cluster of high cumulative incidence, containing the greatest number of CSDs, was located in the Chatham-Kent, Lambton, and Middlesex-London areas. The largest cluster of high cumulative incidence, containing the greatest number of pregnancies, was located in the Ottawa and Leeds, Grenville and Lanark regions. Of all regions in Southern Ontario, these particular regions of high cumulative incidence, as well as the Windsor-Essex, Simcoe Muskoka, Grey Bruce, Renfrew County, and Eastern Ontario health regions, may receive the most benefit from post-partum screening clinics and programs to increase education and awareness about the association between pregnancy complications and maternal CVD risk.

5.2 Study Limitations

Some limitations which may have affected the results of this study include: 1) the quality of the data used; 2) the availability of data; 3) potential misclassification and 4) geographic areas used in analysis.

5.2.1 Data quality

Data quality was a limitation of this thesis, as quality measures for all variables used in this thesis have not been assessed. A quality audit of the Niday Perinatal Database, currently managed by BORN Ontario, was published in 2011 reporting on comprehensiveness, completeness, and reliability, using a data re-abstraction approach[97]. At the time the audit was conducted in 2008, 96% of births in the province were captured in the Niday Perinatal Database, with data from 95 delivering hospitals (including midwifery hospital births) and also on some home births. With respect to completeness of the database, 34% of all variables were missing more than 10% of data, and only data fields with less than 10% missing data were included in the re-abstraction procedure. Of the data fields analyzed, 44% showed substantial or perfect agreement and 17% had slight, fair, or moderate agreement based on Cohen's kappa or intraclass correlation coefficient scores. Variables included in the audit and relevant to this study were smoking, postal code, and maternal date of birth. Reliability measure values were as follows: Smoking: 78.9% (percent agreement), 50.7% (Cohen's kappa); Postal code: 93.0% (percent agreement); Maternal date of birth: 90.8% (percent agreement). The quality of pregnancy complication and maternal health complication data fields has not been published.

Although the percentage of missing data in each field for the overall study population was low, the geographic distribution of missing data varied across PHU areas. Of the three data fields with approximately 10% missing data (smoking, pregnancy complications, and maternal health complications), the percent missing data ranged from 0.1 to 57% across PHU areas. One potential explanation for the geographic variation in percent missing data is that during the study period data entry in these three fields was voluntary. It is possible that factors such as busyness of hospital, number of staff working on a given day, or the individuals responsible for inputting data for each centre may have influenced whether data

abstraction and data entry occurred for mandatory data fields only, or for both mandatory and voluntary fields. It is also possible that factors such as busyness of a hospital could be related to the level of hospital. For example, Level 3 hospitals which are responsible for care of women who experience significant complications during pregnancy may have been more likely to have a higher percentage of missing data than Level 1 hospitals which typically provide care for uncomplicated, full-term pregnancies. If this is true, cumulative incidences in locations serviced by Level 3 hospitals may have been underestimated. The full impact of geographic variation in percent missing data on results in this thesis is unknown, as the reasons underlying the presence or absence of data could not be determined. If percent missingness of data was related to maternal health or health behaviours, it may have introduced systematic error (bias) into the results of this study.

The Postal Code Conversion File (PCCF), a Statistics Canada digital file, was used to convert postal code into CSD information by BORN Ontario. One of the major limitations with this file is that postal codes, particularly in rural areas, may not represent the exact physical locations of individuals receiving mail for that postal code. For example, postal codes in some rural areas are associated with rural route service and post office pick-up. Some rural routes cross boundaries of multiple dissemination areas and also CSDs. There may also be postal code conversion inaccuracies with respect to representation of home address in urban areas which are served by community mailboxes covering multiple dissemination areas[98]. Despite these limitations with the PCCF, it has been used to provide geographic classification data for spatial analysis studies in Ontario[75,73].

5.2.2 Data availability

Data availability was also a limitation in this project. In terms of cardiovascular diagnoses and traditional cardiovascular risk factors, some variables of interest were unavailable. BORN Ontario does not collect information on all CVD risk factors unrelated to pregnancy for which women may already be undergoing CVD screening, such as chronic renal disease, atherosclerosis, and hyperlipidemia; however this likely was a very small percentage of the study population. The recommended ages for screening for these

conditions is well above the average age of women within the study population and screening is also recommended in the presence of other risk factors which were included in study, such as diabetes, smoking or hypertension[99,100,53]. Obesity is also a risk factor for CVD, and although BMI data is collected by BORN Ontario, there was a high percentage of missing data, and thus this variable was not included in this study. Data availability issues may have led to overestimation of the number of women who would benefit from screening based solely on the development of pregnancy complications because some women in the study population may already have been undergoing routine CVD screening.

Stability of clusters of pregnancy complications over time could not be assessed in this thesis due to data availability issues. Year of birth (delivery) was requested from BORN Ontario in the original data request (see Appendix A), but was inadvertently not included in the dataset generated for this study. Due to the late stage at which this was identified, year of delivery was not obtained for analysis in this thesis. Eclampsia, a severe form of preeclampsia, which has also been associated with increased maternal CVD risk, was not included in the dataset generated for this thesis. In the BORN record level data request form there was no field to request this variable, so it was assumed that preeclampsia and eclampsia were grouped together. It was later discovered that eclampsia was coded separately in the data dictionary, and thus was not included in the dataset. Although the eclampsia variable could not be requested in time for completion of this project, the incidence of eclampsia in the study population was approximately 0.02%, and is not expected to alter the results of this thesis.

No uniquely identifiable information was available for pregnant women in this study therefore it was not possible to determine how many pregnancies were contributed by the same women in the study population. It is possible that over the four year study period, multiple pregnancies from the same woman were captured. Women with a history of preeclampsia or gestational diabetes are more likely to develop these complications again in subsequent pregnancies[101-103]. This may be of concern in the CSD level analysis, as small fluctuations in numbers of events may have had a great impact on calculated incidence

rates. It is likely that the cumulative incidence of one or more pregnancy complications was artificially inflated (for the purposes of this project) for small CSDs in which women with a history of pregnancy complications gave birth more than once during the study period.

Due to a high percentage of suppressed CSD data, analysis at this level could not be completed for Northern Ontario and variation within PHU areas could not be investigated. In Southern Ontario, approximately 14% of CSDs had less than 5 pregnancies, and thus location data was suppressed for women within these CSDs. The spatial analysis methods used in this thesis require all units to have values in order to run in ArcGIS. For this reason, cumulative incidence of the PHU in which the CSD was located was input in place of the true cumulative incidence. It is unknown if the spatial analysis results would be different if data had not been suppressed and true cumulative incidence rates were available.

5.2.3 Misclassification

There is a possibility of misclassification of smoking status in this thesis. Smoking data contained within BORN Ontario is self-reported, and it is possible that some women who smoke during pregnancy may not report it, an effect known as the social desirability bias. There is however evidence that pregnant women accurately report whether or not they smoke, but under report the number of cigarettes smoked daily[104].

Preterm labour data was inadvertently requested in place of preterm delivery when the data request was submitted to BORN Ontario. Approximately 8-24% of women who experience preterm labour will proceed to deliver preterm[105], therefore some women classified as being at risk for CVD based on the development of pregnancy complications in this study may not be at risk. The rate of preterm labour in Ontario in 2006-2007 was approximately 5% lower than the rate of preterm delivery[91]. Despite not having access to preterm delivery data in this study, some women who delivered preterm during the study period may be captured in the one or more pregnancy complications variable field. Of all preterm births, approximately 45% are attributed to spontaneous preterm labour and 30% occur as a result of iatrogenic causes, specifically labour induction or Caesarian section for complications including preeclampsia and

SGA[106,107]. Of those with one or more pregnancy complications in this study, approximately 10% developed only preterm labour and no other complications associated with CVD measured in this study. Of these 10%, some may have gone on to deliver preterm, and may be at risk of CVD. Misclassification of preterm labour as preterm delivery may have altered cumulative incidence calculations at the PHU area and CSD levels, and the effect on the spatial analysis results is unknown as preterm delivery data was not accessible for this thesis.

To create the spatial analysis population for identification of areas in which women would benefit from post-partum cardiovascular screening, women with a history of CVD or traditional risk factors were excluded. It is likely that some women with these traditional risk factors may not have been undergoing screening even though it is recommended in Canadian guidelines[3,53] and may also benefit from post-partum screening. There may also have been misclassification of women with one or more cardiovascular complications or traditional cardiovascular risk factors. Women with a history of smoking during pregnancy, chronic hypertension, heart disease, diabetes, or over the age of 50 were excluded from the spatial analysis population to create a group likely not undergoing CVD screening prior to pregnancy. When any of the variables were missing, exclusion was based on the values of remaining variables. For example, if maternal health complication (chronic hypertension/heart disease/diabetes) data were missing, and a woman was under the age of 50 and a non-smoker, she was included in the study population. However, if the same woman was over the age of 50, she was not included in the spatial analysis study population. This approach assumed that women with missing data did not have the diagnosis or risk factor. This assumption is likely untrue for all women with missing data, and some of these women would have been included in the spatial analysis population had the data been available. Using this method, it is probable that a small number of the women included in the spatial analysis population would already be undergoing CVD screening and the need for post-partum CVD screening will be overestimated. The alternative method of excluding women with missing cardiovascular complication or traditional cardiovascular risk factor data would have underestimated the need for post-partum cardiovascular

screening in some areas, as women who were not undergoing screening would not have been represented in the spatial analysis population.

5.2.4 Geographic units of analysis

The results generated by the spatial analysis may be subject to the modifiable area unit problem[106]. It is possible that if different geographic units of analysis were used in this study, a different global spatial pattern and different local clusters would be detected. For example, if pregnancy complications were aggregated to the dissemination area level in Southern Ontario, a different clustering pattern may have been detected in the hot spot analysis. Aggregation of pregnancy complication data to the CSD level may hide patterns at a smaller regional level and it was impossible to investigate any clustering occurring within CSDs in this thesis. Despite this, it has also been argued that aggregation to larger geographic areas is warranted as it creates rates that are more statistically robust and less likely to be influenced by data errors or small random fluctuations in number of events[108]. It is likely that many dissemination areas in Southern Ontario would have small population numbers in this study, and more data would have been suppressed by BORN Ontario.

Due to a high percentage of suppressed CSD data because of small population counts, spatial analysis at the CSD level could not be performed in Northern regions of Ontario. Spatial analysis at the PHU area level was the lowest level of aggregation which could be used to assess the distribution of pregnancy complications in Northern Ontario in this study. As PHU areas in Northern Ontario span large geographic regions, analysis at this level may not be representative of the distribution of complications at a more local level.

5.3 Interpretation of findings

5.3.1 Descriptive analysis

The cumulative incidences of gestational diabetes and placental abruption for the study population were similar to rates reported in the literature[21,37,43,109]. The cumulative incidences of preeclampsia, gestational

hypertension, and delivery of a SGA infant were lower than those reported elsewhere, but the rates are similar to those previously published using data from BORN Ontario for the period between 2006-2007[91].

The provincial cumulative incidences of preeclampsia and gestational hypertension in the study population examined in thesis were 17.2 cases per 1000 pregnancies (1.7%), and 34.6 cases per 1000 pregnancies (3.5%), respectively. Rates for preeclampsia and gestational hypertension have been reported to range between 3-8%[22,28,29,34] and 4-6%[35,36], respectively. Although definite explanations for these differences cannot be determined, differences in the prevalence of risk factors for pregnancy complications may have contributed to lower rates observed in Ontario compared to other regions. In a population-based study capturing 99% of deliveries in Newfoundland between 1996 and 1997, 5.6% of pregnant women developed preeclampsia[27]. One potential explanation for the higher preeclampsia rate in Newfoundland is that Newfoundland has a higher obesity rate than Ontario[110], and obesity is a risk factor for the development of preeclampsia[101,102]. Across the United States, the cumulative incidence of gestational hypertension was 4%. Lower obesity rates in Canada compared to the United States may also partially explain differences in gestational hypertension rates[111], as obesity is also a risk factor for the development of gestational hypertension[112].

In this study, the cumulative incidence of delivery of SGA infants in Ontario (2005-2009) was 18.7 cases per 1000 pregnancies (1.9%). The percentage of pregnancies which result delivery of SGA infants has been estimated to be between 5 and 9%[25,45,46]. In Ontario, between 2009 and 2010, the SGA delivery rate was estimated at 9.3%, using data from the Hospital Morbidity Database from the Canadian Institute for Health Information (CIHI) [46]. It is unclear as to why the rate calculated using BORN data in this study, as well as the rate calculated using BORN data from 2006-2007[91], is low in comparison to other data reported for the province.

There was much variation observed for pregnancy complications across PHUs, even after adjusting for differences in age distribution of populations. Regional variation in the distribution of other known risk factors for these pregnancy complications may help explain some of the variation in the geographic distribution within the province. Many risk factors for the development of these pregnancy complications have been identified including ethnicity, genetic mutations, personal and family history of pregnancy complications, obesity, extremes of maternal age, chronic hypertension, smoking, diabetes, chronic kidney disease, high BMI, multifetal gestation, and nulliparity[101-103,113,114]. Variation in the number of traditional risk factors for CVD (smoking, hypertension, obesity, diabetes, sedentary lifestyle, and low income), some of which are also risk factors for pregnancy complications, with a prevalence above the Canadian average has been reported across PHUs in Ontario in the Institute for Clinical Evaluate Sciences (ICES) Canadian Cardiovascular Atlas[5]. In this report, individuals living in Sudbury, Algoma, Timiskaming, North Bay Parry Sound District, Elgin-St. Thomas and Windsor-Essex Health Unit regions had the highest prevalence of traditional risk factors in Ontario, with the prevalence of 5 risk factors exceeding the Canadian average (2000-2001). These findings differ from the distribution of pregnancy complications between 2005 and 2009 in this thesis, for which Sudbury, Algoma, and North Bay Parry Sound District had the lowest crude cumulative incidences of one or more pregnancy complications in comparison to other PHU areas. The findings for traditional CVD risk factors and pregnancy complications in Elgin-St. Thomas also do not agree, as this region had a crude cumulative incidence slightly below the provincial cumulative incidence. Findings for Windsor-Essex however, were similar as this region also had a higher crude cumulative incidence of pregnancy complications compared the provincial cumulative incidence. Differences in the distribution of risk factors and pregnancy complications could be due to the fact that the studies were conducted at different points in time, or other risk factors for pregnancy complications that were not included in the ICES Atlas, such as age or race, may have had a stronger influence on the development of pregnancy complications. It is also possible that better agreement between published information and findings in this thesis may have been observed if

prevalence of traditional CVD risk factors in the ICES Cardiovascular Disease Atlas was stratified by gender.

5.3.2 Spatial analysis

In the PHU area level analysis, the results of the test for global spatial autocorrelation suggested that the overall spatial distribution of cumulative incidences of one or more pregnancy complications was random. The hot spot analysis revealed statistically significant clustering in the data. These conflicting results are not completely surprising however, because global spatial autocorrelation tests for a systematic pattern in the spatial distribution over the entire study area and is a measure of the degree of similarity or dissimilarity of all cumulative incidence values overall, whereas the hot spot analysis measures clustering at the local level.

The results of the hot spot analyses at the PHU area and CSD level of analysis were different, illustrating the modifiable areal unit problem. Different levels of aggregation produced different spatial clustering patterns. The analysis at the CSD level allowed for investigation of variation within PHU areas and revealed more clusters of high and low cumulative incidence, as well as clustering in areas which were not identified in the PHU area level analysis. There was evidence of clustering of high cumulative incidence within Middlesex-London, Lambton, and Chatham-Kent health regions in both analyses, but only the PHU area level analysis identified Windsor-Essex as within a cluster of high cumulative incidence. Ottawa PHU and the City of Ottawa CSD have identical geographical boundaries, yet in the CSD level analysis, Ottawa was identified within a statistically significant cluster of high cumulative incidence, and was not identified within a cluster at the PHU area level hot spot analysis. Although the two units were identical in shape and size, the units sharing borders with Ottawa used to calculate the Gi* statistic were different in shape, size, and incidence rates, resulting in different z-scores and p-values in the hot spot analysis. Similarly, a cluster of low cumulative incidence approaching statistical significance was identified in Hamilton at the PHU area level, and although the PHU and CSD boundaries for the City of Hamilton are identical, it was not identified as a cluster in the CSD hot spot analysis. Again, this

disagreement can be explained by the different bordering units used to calculate the Gi* statistic for this area.

Taking both hot spot analyses into consideration, there is the most evidence to support clustering in the Middlesex-London, Lambton and Chatham-Kent health regions. Clusters appeared in these regions in both the PHU area and CSD level (Cluster H1 in Table 9) analyses. Within the H1 cluster, containing 19 CSDs, there were 3 CSDs with suppressed data (due to less than 5 pregnancies captured in the registry) for which the cumulative incidence of the PHU had to be substituted. All three of these CSDs are located within larger CSDs and share boundaries with only one or two other CSDs; thus Gi* calculations for other CSDs within the H1 cluster are not expected to be heavily impacted by these CSD units. Confidence in cluster H2 is lower, as it contains only 3 CSDs, one of which had only 6 pregnancies. In this CSD, the cumulative incidence may have been influenced by small random fluctuations in number of events or data entry errors.

5.4 Implications

The findings of this research have many implications for further research, prenatal and primary care practice, and public health.

5.4.1 Further Research

This analysis could be repeated with eclampsia and preterm delivery variables, in addition to the other pregnancy complications used in this thesis, to determine whether spatial analysis results differ from the results presented in this thesis. Variation at lower geographic levels of aggregation than examined in this thesis may be investigated within highly populated areas in Southern Ontario such as the Greater Toronto, Ottawa, Hamilton, London, Kitchener-Waterloo, and Windsor areas. In these regions, census tract or dissemination area level aggregation could allow for analysis at a more local level in comparison to CSDs used in this thesis. Using spatial regression techniques, future research could also investigate explanations for clustering of pregnancy complications such as ethnicity, measures of socioeconomic status, and age. This information would be informative for public health planning. As more recent data becomes available

from BORN Ontario, this analysis could be repeated to examine stability of the clusters observed within Southern Ontario. This may also highlight other areas within the province in which women may benefit from post-partum CVD screening. The cluster detection method implemented in this thesis was able to detect regions of high cumulative incidence, based on values of neighboring geographic units. It is possible that individual PHUs or CSDs with high cumulative incidence values were not identified as clusters if they shared boundaries with PHUs or CSDs of low cumulative incidence. These independent high incidence regions may also benefit from post-partum screening, and this is a possible area for further investigation. Other regions which may benefit from post-partum screening are areas with a high number of pregnancies in which women develop complications. In this thesis, cumulative incidence *rates* were used to assess need for screening, but future research could investigate the distribution of *cases* of pregnancy complications in women without a history of cardiovascular disease or traditional risk factors to determine where programs could have great impact based on number of affected individuals. The cumulative incidence of delivery of SGA infants in Ontario calculated using BORN data, and reported by CIHI, differ by approximately 7%. Reasons for this are unclear, and this is an area that future research could investigate.

5.4.2 Prenatal and primary care practice

5.4.2.1 Post-partum screening clinics

This research has identified a number of areas in which women are in need of post-partum cardiovascular screening. These regions would benefit from post-partum screening clinics, similar to the Maternal Health Clinic developed for the Mother's Health Education, Research and Screening (MotHER's) Program (www.themothersprogram.ca) by Dr. Graeme Smith in Kingston, Ontario[115]. This is the first clinic of its kind that targets women who develop pregnancy complications associated with CVD risk. Six months following delivery, women are invited to be screened for cardiovascular risk factors and prevention strategies are discussed. Afterwards, screening results are forwarded to the woman and her primary care provider for follow-up and management.

5.4.2.2 Practice guidelines

This research and related research in this field has implications for prenatal and postnatal care practice. The results of this thesis suggest that there are concentrated areas in the province of Ontario where women are at risk of CVD, based on the development of pregnancy complications, and many women in these areas may not be undergoing screening for CVD.

There are guidelines which exist to address care of women with pregnancy complications, including the Society of Obstetricians and Gynaecologists of Canada Clinical Practice Guidelines for Diagnosis, Evaluation, and Management of the Hypertensive Disorders of Pregnancy[116], Association of Ontario Midwives Clinical Practice Guidelines for Hypertensive Disorders of Pregnancy[117], and The Evidence-Based Guidelines for the Prevention of Cardiovascular Disease in Women 2011 Update: A Guideline From the American Heart Association[20], although not all describe details of appropriate follow-up required for women with a history of these complications. The most recent Canadian guidelines for prevention of CVD do not include pregnancy complications as risk factors for maternal CVD[53]. Research conducted in Ontario has shown that prenatal care providers may not be aware of the association between pregnancy complications and CVD risk, and if they are, increased risk is not always communicated to patients and primary care providers[56]. To date, there has been no research conducted on the knowledge of primary care providers with respect to pregnancy complications and maternal CVD risk. Canadian practice guidelines specific to management and follow-up of women who develop pregnancy complications associated with CVD risk, including hypertensive disorders of pregnancy and other complications, may be beneficial in increasing awareness among healthcare practitioners and reducing CVD incidence and mortality among Canadian women. As more evidence has become available to support the association between CVD and complications including delivery of a SGA infant, preterm delivery, and placental abruption, it is important to address these complications in guidelines for prevention and care. Recognizing these complications in guidelines for prenatal care providers as well as primary care providers is crucial to ensure appropriate care and prevention measures are employed post-partum.

5.4.3 Public Health

5.4.3.1 Education and awareness

The results of this study have the potential to inform public health planning. Educational campaigns to increase awareness about the association between pregnancy complications and maternal CVD risk could be developed and focused in regions where clusters of high cumulative incidence were identified. One possible component of such a program could involve posters encouraging women to speak to health care providers about CVD risk if they have experienced particular pregnancy complications. These posters could be placed in areas frequently visited by women during pregnancy, such as hospitals, physicians' offices, and Public Health Units. Areas identified as high cumulative incidence clusters may also benefit from programs that aid post-partum women in lifestyle modifications to decrease the risk of developing CVD later in life, including healthy eating and physical activity. Combining education about risk factors and screening programs that identify personal risk factors and methods to reduce these risks is an effective strategy in CVD prevention[3].

5.5 Conclusions

This study is the first to use spatial analysis methods to examine the geographic distribution of pregnancy complications and assess the need for post-partum cardiovascular screening in Canada. The results of this study suggest that there is regional variation in the distribution of pregnancy complications within the province of Ontario and that there are statistically significant clusters of women in Southern Ontario who would benefit from post-partum cardiovascular screening. There are many possible explanations for the observed variation in distribution of pregnancy complications across Ontario, including variation in the distribution of numerous demographic and health-related characteristics of pregnant women, and this is an area to consider in future research.

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Appendix A

Better Outcomes Registry and Network Record Level Data Request

a)

DATA REQUEST FORM - RECORD LEVEL DATA

December, 2010 v1

Please see instructions on the BORNOntario.ca website for information about the process of requesting BORN information.

To submit this **APPLICATION FORM**

1, Send electronically to both: science@bornontario.ca

Be sure to indicate in your email whether you are sending a signed copy, by mail or fax, to:

Research Requests
BORN Ontario
Suite 106, 1785 Alta Vista Drive,
Ottawa Ontario
K1G 3Y6

Or

Fax - 613-523-9057

b)

To contact BORN Ontario with any questions or concerns about

Application Form or privacy issues

Privacy Officer
BORN Ontario
Telephone: (613) 523-5341

E-mail: privacy@bornontario.ca

Data being requested

Ann Sprague
Scientific Manager,
BORN Ontario
Telephone: (613) 737-8579

E-Mail: asprague@ottawahospital.on.ca

c)

NOTE TO APPLICANT – This document is set up as a Microsoft Word form.

To unlock the form which allows you to type in the form where indicated – Go to View. Then choose toolbars, and forms. A small menubar will appear. There will be a small picture of a lock on the menubar. Click on the lock to unlock the form.

APPLICATION FORM FOR ACCESS TO HEALTH DATA FOR RESEARCH OR STATISTICAL PURPOSES

e)

f) Table of Contents

Definitions of terms used in this Application Form

Disclose, as per PHIPA s.2, in relation to health data or personal health information, means: to make the information available or to release it to another health information custodian or to another person, but does not include to use the information.

Individual, as per PHIPA s.2,means: in relation to personal health information, the individual, whether living or deceased, with respect to whom the information was or is being collected or created.

Information practices, in relation to a researcher, means the policy of the researcher for actions in relation to health data or personal health information, including the administrative, technical and physical safeguards and practices that the researcher maintains with respect to access, use, retention and disposal of the information.

Personal health information as per PHIPA s.4 means identifying information about an individual in oral or recorded form, if the information, (a) relates to the physical or mental health of the individual, including information that consists of the health history of the individual's family, or (b) relates to the providing of health care to the individual, including the identification of a person as a provider of health care to the individual.

PHIPA means the Personal Health Information Protection Act, 2004 S.O. 2004, c. 3, Schedule A

Research as per PHIPA s.2, means: a systematic investigation designed to develop or establish principles, facts or generalizable knowledge, or any combination of them, and includes the development, testing and evaluation of research. Research includes statistical analysis.

Research Ethics Board as per PHIPA s.2, means a board of persons that is established for the purpose of approving research plans under section 44 and that meets the prescribed requirements. The Research Ethics Board at CHEO will conduct reviews of research plans submitted under this Application Form.

Use, as per PHIPA s.2, in relation to health data or personal health information means to handle or deal with the information, including by researchers who are employees or are similarly affiliated with CHEO or BORN, but does not include to disclose the information. Use, as a noun, has a corresponding meaning.

g) Section 1: Researcher Contact Information and Affiliation

Please provide the name, contact information and affiliation of the principal investigator (researcher) who will be the project authority or main contact person for the research project

h)

i) RESEARCHER / RESEARCH BODY

Research Organization: Queen's University

Contact Person Name: Jessica Stortz

Address: 865 Johnson Street

Kingston, Ontario, Canada K7L 2B7

Telephone: 613 893 0727 Ext:

Fax:

Email: Jessica.stortz@queensu.ca

Please provide the following information if applicable:

Institutional Affiliation (include department if relevant) and position:

Queen's University, Department of Community Health and Epidemiology, Graduate Student (M.Sc. Candidate)

Supervisor Name and Contact Information (if applicant is student):

Dr. Duncan Hunter

Carruthers Hall, Room 202

Queen's University

Kingston, Ontario, Canada K7L 3N6

613 533 6000 x 74616

hunter@queensu.ca

Dr. Graeme Smith

Victory 4, Room 3-456

76 Stuart Street

Kingston General Hospital

Kingston, Ontario, Canada K7L 2V7

613 548 2405

gns@queensu.ca

Dr. Dongmei Chen

Mackintosh-Corry Hall, Room D125

Queen's University

Kingston, Ontario, Canada K7L 3N6

613 533 6045

chendm@queensu.ca

The Researcher requests access to health data, either as personal or non personal information, collected and maintained by BORN for the purposes of a research project described in Sections 2 and 3 and Appendix A. Section 4 asks the researcher to outline their plans for REB approval.

Access will be considered **only** to files and data elements identified and for the retention period specified in Section 2.

For BORN Ontario use only:

Project Title:_____

_____

Request Number:_____ Date of Receipt: _____

j) Section 2: Description of the Research Project

1. Project title: Spatial analysis of pregnancy complications associated with cardiovascular disease risk in Ontario

2. Project objectives summary

Please limit to a maximum of 10 lines: you may attach a full proposal, including methodology and research questions, if applicable):

Geographic variation in the prevalence of traditional risk factors for cardiovascular disease (CVD) has been observed between and within the provinces of Canada. This study aims to determine if the same can be said of pregnancy complications associated with CVD risk in Ontario. The goal of this study is to locate areas within Ontario in which women may benefit from CVD screening, programs to assist in post-partum lifestyle modifications, and increased CVD awareness, based on the development of specific pregnancy complications known to be associated with CVD risk. Cumulative incidences of each pregnancy complication and an aggregate measure, one or more pregnancy complications, will be calculated for public health unit areas. Spatial analysis tools will be used to investigate the spatial distribution of the incidence of one or more pregnancy complications across the province.

3. Methods summary

(Please limit to a maximum of 10 lines):

The study population for analysis will be comprised of women under the age of 50, without a history of CVD, smoking, chronic hypertension, or diabetes. Crude and age-standardized incidence rates will be calculated for each public health unit and visually displayed using maps. For the spatial analysis, cases of one or more pregnancy complications will be aggregated to the census subdivision level. Cumulative incidences will be calculated for each census subdivision and geographically assigned to the centroid, or central point, of each census subdivision. ArcGIS will be used to perform all spatial analyses in this project. A test for spatial autocorrelation will be performed to determine whether a global spatial pattern exists in the incidence of one of more pregnancy complications. A test to detect any significant spatial clusters of high or low incidence census subdivisions will also be performed.

4. Public interest value and benefits of the project

(Please limit to a maximum of 5 lines):

Regional distribution of risk factors for CVD is relevant to program planning, design, and implementation within public health units. This project will be of interest to public health units in Ontario. It will indicate areas in which women may benefit from interventions and education to decrease the risk of CVD later in life, based on the development of certain pregnancy complications.

5. Duration of the research and when the requirement for use of the health data will end – with any required retention period explained:

This project is a Master's thesis, expected to be completed by August 2012.

6. Where the research will be conducted, and, if a different location, where data will be held.

The research will be conducted and data will be held at Queen's University in Kingston, Ontario.

7. Please indicate if you or any of your colleagues on this project have requested, and whether you or they have obtained data from BORN (or its member data holdings) in the past.

k) Dr. Graeme Smith has previously requested and obtained data from BORN related to pregnancy complications associated with CVD risk.

l) Data Requested

m)

n) 3A. Cohort Definition

1. Year(s) of data (data range) requested (Note: Niday data is collected by Fiscal Year)

   2005-2009

2. Patient cohort requested (i.e. all women having an operative vaginal birth OR all women who had a particular complication OR all babies that had congenital anomalies)
   All women within the study period (2005-2009)

3. Any subset information – regional information or other criteria. (i.e. in LHIN 10 & 11 OR in a certain postal code sortation area)

o) Public health unit, census subdivision

p)

q) Section 3B: Specific Data Elements Requested

Record level data for almost all hospital births in Ontario are contained in the Niday Perinatal Database. Many researchers ask for datasets from the BORN Niday Perinatal Dataset.

BORN Ontario subjects every data request to the following assessments:

- Is the researcher asking for data the BORN can provide?
- Is the researcher asking for data that is potentially identifiable, alone or in combination with other data elements?
- Is the researcher requesting information deemed to be personal health information?

The form in Appendix A allows you to specify the specific data elements you want. The data elements in a shaded box or in red font are the ones considered to be variables that can lead to re-identification of an individual (baby or mother), especially when they are provided in combination with other elements. The reason(s) they are considered problematic is described in each of the respective boxes. ***Please be aware that in order to balance risk of inadvertent or intentional re-identification of individuals, if BORN provides more granular information in one type of identifier, it may only be able to provide less granular information in another.***

If you have ticked off that you want data in any of the shaded boxes in Appendix A, you must complete this section.

3C. Requirement for Personal Health Information

Is personal health information in individually identifiable form requested? (See page1 of this Application for a definition of 'personal health information' or see the shaded boxes on the

__x_ **No** (skip to next section)

___ If **Yes**, please complete the following information:

r) An explanation of how the personal health information will be used, including a description of any proposed linkages to be made between personal health information in the files requested and any other personal information and how this linkage will be done. Please include a statement of the benefits of the linkage, how this in the public interest, and any potential harms to the individuals.

s) An explanation of why the research project cannot reasonably be accomplished without access to personal health information in individually identifiable form.

t) BORN assumes that consent has not been sought for the use of this information (explain if this is not the case), but we are required to have researchers explain why consent to the disclosure of the personal health information is not being sought from the individuals to whom the information relates.

NOTE: Researchers will not be permitted to make direct contact with individuals to whom personal health information relates without the express written permission of BORN, including, if consent is sought, BORN approval of the proposed consent form.

u) A description of any reasonably foreseeable harms that may arise from the use of the personal health information and how the researchers intend to address those harms.

v) A statement of whether the researcher's interest in the disclosure of the personal health information or the performance of the research would likely result in an actual or perceived conflict of interest with other duties of the researcher.

w) Information as to how and when the personal health information will be disposed of or returned to BORN.

x)

Section 4: Research Ethics Board Approval

Before the use or disclosure of health data for research purposes, a researcher must submit a copy of the decision of a Research Ethics Board that approves the research plan.

Typically, the research plan will also be reviewed by the CHEO Research Ethics Board in addition to whatever REB the researcher must submit to as a condition of their institutional affiliation.

Details about the Project

Is the project being done under contract?

__x_**No**

___If **Yes**, specify the contracting organization's contact information:

Organization:

Name:

Telephone:

Is the project funded by a grant-funding agency?

_x__ **No**

___ If **Yes,** specify the name of the agency:

Is the project a thesis or dissertation?

___ **No**

_x__ If **Yes,** attach a letter from the REB committee chair from the academic institution

Research Ethics Board Review

Has the project been approved following a formal Research Ethics Board review?

___ **No**

x__ **Yes**

Proof of Research Ethics Board Approval:

___**Pending**

__x_**Copy Attached**

Approval Date: November 25, 2011

Period of Approval: November 25, 2011 – November 25, 2012

Section 4:

I certify that the above information is accurate to the best of my knowledge, and that any changes to this information will be conveyed to BORN in writing at the earliest possible opportunity.

_____

Signature of Researcher

_____

Signature of Witness

Witness Name:

Witness Position:

APPENDIX A

BORN Ontario
NIDAY PERINATAL DATABASE VARIABLES

PROJECT NAME:
PROJECT KEY CONTACT:
DATA PERIOD REQUESTED: FROM: (dd/mm/yyyy)
TO: (dd/mm/yyyy)

Data Element Required? (Click in box to insert check mark, and specify further where more info is requested)	**Data Element**	**SAS_Name**	**Field Details and Additional Definitions**
☒ **Specify:** ☐ Exact DOB ☒ Age at time of birth ☒ Year of birth ☐ Birth year in intervals (specify, e.g. 2 yrs, 5 yrs)	**Mother's Birth Date** **- This field can make the mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	MDOB	If age range <14 or >45, system will ask user to verify.
☐ **Specify:** ☐ Full PC ☐ First 3 characters only ☐ First 2 characters only	**Mother's Postal Code** **- This field can make the mother more unique in the population, and hence easier to re-identify, especially when combined with other variables. BORN is very UNLIKELY to give full postal code access**	PCODE	ANANAN format

☐ First character only			
☐	**City/Town** **- This field can make the mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	HL_SiteCityTown	Do not overwrite when City/Town auto-populates with the entry of a valid Postal Code. If the City/Town does not match the information in the maternal chart please verify the Postal Code
☐	**Province**	PROVINCE	
☐	**Language** **- This field can make the mother more unique in the population, and hence easier to re-identify, especially when combined with other variables** **- Currently this field has a lot of missingness in the database**	LANGUAGE	Per CIHI list plus others frequently spoken in ON
☐	**Aboriginal** **- This field can make the mother more unique in the population, and hence easier to re-identify, especially when combined with other variables** **- Currently, this field has a lot of missingness in the database**	ABORGST	Select one (default) • Unknown • Not applicable • 1st Nations • Metis • Inuit
☐	**Antenatal Care Provider**	ACP0-ACP5	• None • Family Physician • Midwife • Nurse Practitioner (APN/CNS)

			• Obstetrician • Other
☐	**First Trimester Visit**	FIRSTVIS	Select one (default) • Unknown • No • Yes
☐	**Prenatal Classes**	PRENCLAS	Select one (default) • < 20 weeks • > 20 weeks • < 20 and >20 weeks • None
☒	**Smoking**	SMOKING	Select one (default) • Unknown • < 20 weeks • > 20 weeks • < 20 and >20 weeks • No Smoking
☐	**Intention to Breastfeed**	INTBF	Select one (default) • Yes • No • Unknown • NA
☐	**Maternal Height**	MATHGTCM	1 inch = 2.54 cm

☐	**Maternal Weight**	MATWGTKG	10 lbs = 4.55 kg 1 kg = 2.2 lbs
☐	**Maternal BMI**	BMI	SI units – BMI = weight (KG) / height ^{2} (m^2)
☐	**Previous C/S**	PREVCS	Select one (default) • No • Yes • Unknown
☐	**# of previous C/S**	PCSNUM	Select one (default) • 1-10
☒ Information on highlighted conditions is requested	**Maternal Health Problems** **This contains very sensitive information and its inclusion will increase the invasion of privacy risk for the data set. You may be asked to indicate exactly which of these you need**	MATHP0-MATHP28 MATHP99	• None • Chronic Hypertension • Diabetes insulin dependant • Diabetes non-insulin dependant • Heart disease • Thyroid disease • Lupus • Alcohol dependance syndrome/Alcoholism • Asthma • HIV • Other • Hepatitis B **Substance Use** • Drug & Medication Use-Opioides • Drug & Medication Use-Narcotics • Drug & Medication Use-Cocaine • Drug & Medication Use-Halucinogens • Drug & Medication Use-Marijuana • Drug & Medication Use-Gas/Glue Sniffing • Drug & Medication Use-Prescription

			drugs • Drug & Medication Use-Naturopathic/Herbal remedies • Drug & Medication Use-Methadone treatment **Mental Health** • Psychiatric disorders-Previous history of depression • Psychiatric disorders-Depression during this pregnancy • Psychiatric disorders-Previous history of Anxiety • Psychiatric disorders-Previous history of post partum depression • Psychiatric disorders-Anxiety during this pregnancy • Psychiatric disorders-Other Mental Illness • Unknown
☒ Information on highlighted conditions is requested	**Obstetrical Complications**	OBCOMP0-OBCOMP15 OBCOMP99	• None • Gestational diabetes: carbohydrate intolerance of varying severity with onset of first recognition during present pregnancy (glucose tolerance test) • Hypertension (gestational, transient): No proteinuria. Rise in systolic pressure of at least 30 mmHg, rise in diastolic pressure of at least 15 mmHg or a diastolic pressure of at least 90 mmHg. A BP of 140/90 on at least 2 occasions at least 6 hours apart. Mean arterial pressure of 105. • IUGR/SGA: fetus/baby below 10 percentile of mean weight for gestation • LGA: fetus/baby above the 90 percentile of mean weight for gestation • Peridontal infection • Placenta previa: implantation of the

			placenta low in the uterus either overlying or reaching the vicinity of the cervical os • Placental abruption: premature separation of a normally implanted placenta that results in retroplacental bleeding after the 20th week of gestation and before the fetus is delivered • Pre-eclampsia: the development of hypertension with proteinuria, occuring after the 20th week of gestation (hypertension - see above; proteinuria in a concentration greater than 3g on 24 hr urine collection) • Premature rupture of membranes (PROM): rupture of membranes prior to onset of labour (diagnosed with nitrazine paper or ferning) • Preterm labour: initiation of labour when fetus < 37 weeks gestation and > 20 weeks • Preterm Premature rupture of membranes (PROM): rupture of membranes prior to onset of labour and fetus < 37 weeks gestation and > 20 weeks • UTI: urinary tract infection as evidenced by bacteria in the urine (may be asymptomatic or not) • Other cervical/vaginal infection • Other • Unknown
☐	**Group B Strep Screening**	GBSSCR	Select one (default) • No • Yes

			• Unknown
☐	**Group B Strep Results**	GBSRES	Select one (default) • Negative • Positive • Unknown
NOT GIVEN OUT	**Maternal Transfer From**		Select one (default) • No transfer • Planned home birth • Out of region • List of hospitals…(contact your Niday Manager if a transfer site is missing)
☐	**Reason for Maternal Transfer**	MATTRR	Select one (default) • Not applicable • Fetal health concern • Lack of physician coverage • Lack of nursing coverage • Maternal medical/obstetrical problem • No beds available • Other • Unknown
☐	**Number of Previous Term Babies**	PTERM	Select one (default) • Unknown • 0-15
☐	**Number of Previous Preterm Babies**	PPRETERM	Select one (default) • Unknown

			• 0-15
☐	**Reproductive Assistance**	REPASS	Select one (default) • Unknown • None • IUI: intrauterine insemination is a fertility procedure in which sperm are washed, concentrated, and injected directly into a woman's uterus • IVF (fresh or frozen): (fresh or frozen) – invitro fertilization is the uniting of egg and sperm in vitro (in the lab). Subsequently the embryos are transferred into the uterus through the cervix • IVF ICSI (fresh or frozen): (fresh or frozen) – Intracytoplasmic Sperm Injection (ICSI): is a procedure in which a single sperm is injected directly into an egg • Ovulation induction: induction of ovulation involves the use of medication to stimulate development of one or more mature follicles (e.g. clomiphene citrate, injectable gonadotropins, GnRH pump, and bromocriptine)
☐	**Multiple Gestation**	MULTGEST	Select one (default) • Singleton • Twin • Triplet • Quadruplet • Quintuplet • Sextuplet

			• Septuplet
NOT GIVEN OUT	**Maternal History Comment**		If "other" selected in a previous field please free text information
☐ **Specify:** ☐ Exact DOB ☐ Month of birth ☐ Year of birth ☐ Birth year in intervals (specify, e.g.. 2 yr, 5yr)	**Baby's Birth Date** **- This field can make the baby & mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	BDOB	
☐	**Labour Type**	LABTYPE	Select one (default) • Induced: Medical or surgical intervention to initiate uterine contractions prior to onset of spontaneous onset of labour. • Spontaneous – labour that initiated without intervention • No labour: cesarean section
☐	**Indication for Induction**	INDIND0- INDIND16 INDIND99	• Diabetes • Elective: non-urgent, non-emergency • IUGR/SGA: fetus/baby below 10 percentile of mean weight for gestation • LGA: fetus/baby above the 90 percentile of mean weight for

			gestation • Maternal obstetrical conditions • Multiple gestation: more than one fetus in this pregnancy • Abnormal NST • Oligohydramnios: amniotic fluid pocket < 2 cm • Poor biophysical score • Post dates: greater than 41 completed weeks gestation • PROM: rupture of membranes prior to onset of labour (diagnosed with nitrazine paper or ferning) • Pre-eclampsia: the development of hypertension with proteinuria, occuring after the 20th week of gestation. Evaluation and Management of Hypertensive Disorders of Pregnancy. http://www.sogc.org/guidelines/documents/gui206CPG0803_001.pdf • Pre-existing maternal medical conditions: other conditions which affect mother and/or fetus • Other – Maternal • Other – Fetal
☐	**Method of Induction**	INDMETH0- INDMETH7 INDMETH9	• Amniotomy • Cervidil • Cytotec / Misoprostol • Mechanical • Oxytocin • Other prostanglandin • Other

☐	**Number of induction attempts**	INDATT	Select one (default) • NA • 1-10
☐	**Augmentation**	AUGMENT0- AUGMENT4	• None • Amniotomy • Oxytocin • Prostaglandin • Other
☐	**Intrapartum complications**	IPCOMP0- IPCOMP11 IPCOMP99	• None • Cord prolapse: occurs when the umbilical cord descends alongside or beyond the fetal presenting part . • Intrapartum bleeding: more than show • Meconium: presence of meconium in the amniotic fluid • Non progressive labour/lack of descent/dystocia • Non-reassuring fetal status: included Atypical or abnormal fetal surveillance : including abnormal NST , poor biophysical profile • Post-partum hemorrhage: Blood loss in excess of 500 cc in a vaginal delivery and in excess of 1,000 cc in an abdominal delivery • Shoulder dystocia: baby is born but shoulders cannot be delivered by the usual means • Suspected chorioamnionitis: infection of chorion, amnion and amniotic fluid (considered suspected because confirmation requires lab results) – symptoms include premature labour < 34 weeks, maternal fever, tachycardia,

			increased fetal heart rate, uterine tenderness, purulent or malodorous discharge • Suspected sepsis (unexplained fever): maternal temp > 38 C • Uterine rupture/dehiscence • Other
☐	**Maternal Pain Management**	MATDR0- MATDR10	• None • Epidural • General • Local • Narcotics • Nitrous Oxide • Non-pharmacologic • Pudendal • Spinal • Spinal-Epidural combination (CSE) • Unknown
☐	**Fetal Surveillance**	FS1-FS6	• No Monitoring • Admission EFM strip: includes initial EFM strip done during triage or admission to labour & birth unit when woman ends up giving birth (i.e. exclude triage EFM strip if she is not admitted) • Auscultation • Intrapartum electronic (external) • Intrapartum electronic (internal) • Unknown
☐	**Group B Strep - Antibiotics**	GBSANT	Select one (default) • No • Yes

			• Unknown
☐	**Antenatal Steroids**	ANTESTER	Select one (default) • None • 1 dose < 24 hours (before the time of birth) • 2 doses: Last Dose < 24 hours (before the birth) • 2 doses: Last Dose > 24 hours (from the time of the last dose to the time of birth)
NOT GIVEN OUT	**Labour/Birth Comments**		
☐	**Forceps/Vacuum (operative Vaginal Delivery)**	ASSISTED	Select one (default) • Unknown • None • Forceps • Vacuum • Forceps and Vacuum
☐	**Episiotomy**	EPISIOT	Select one (default) • Unknown • None • Midline • Medio-lateral
☐	**Laceration**	LACERAT	Select one (default) • Unknown • None • 1st degree • 2nd degree • 3rd degree

			• 4th degree • Cervical Tear
☐	**Presentation**	PRESENT	Select one (default) • Unknown • Vertex (Vertex Occiput Anterior, Vertex Occiput Posterior, Vertex Occiput Transverse, Brow, Face) • Breech (Frank, Footling, Kneeling) • Compound • Other
☐	**Delivery Type**	DELTYPE	Select one (default) • Vaginal • Cesarean • Unknown
☐	**Indication for C/S**	CSIND0- CSIND19 CSIND99	• Breech • Cord prolapse: displacement of the umbilical cord to a position at or below the presenting part • Failed forceps / vacuum: forceps and/or vacuum unsuccessful in assisting delivery of baby • Non-progressive labour/descent/ (dystocia) • Fetal anomaly: any fetal anomaly which lead to decision to perform cesarean • Diabetes • IUGR/SGA: fetus/baby below 10 percentile of mean weight for gestation • LGA: fetus/baby above the 90 percentile of mean weight for gestation • Maternal request: cesarean at request

			of mother • Multiple gestation • Non-reassuring fetal status: non-reassuring fetal heart rate characteristics (by intermittent auscultation or EFM) or scalp sampling or other methods of surveillance • Placenta previa: implantation of the placenta low in the uterus either overlying or reaching the vicinity of the cervical os • Placental abruption: premature separation of a normally implanted placenta after the 20th week of gestation and before the fetus is delivered • Pre-eclampsia: the development of hypertension with proteinuria, occuring after the 20th week of gestation. Evaluation and Management of Hypertensive Disorders of Pregnancy. http://www.sogc.org/guidelines/documents/gui206CPG0803_001.pdf • Prematurity: fetus < 37 weeks gestation and > 20 weeks • Previous cesarean • PROM: Premature rupture of membranes – rupture of membranes prior to onset of labour (not usually indication on own for cesarean, indicate other problems • Other – fetal health problem • Other – Maternal health problem
☐	**Cesarean Type**	CSTYPE	Select one (default) • Unknown • Planned/elective: planned prior to onset of labour

			• Unplanned
☐	**Cervical dilation at C/S**	CSDILAT	Select the closest value from the drop down list.
☐	**Time fully dilated**	TDILAT	Use 24 hr format (ie. 08:35, 21:25, etc)
☐	**Time started pushing**	TSTPUSH	Use 24 hr format (ie. 08:35, 21:25, etc)
☐	**Time of Birth**	TOB	Use 24 hr format (ie. 08:35, 21:25, etc)
☐	**Delivered By**	DELBY	Select one (default) • Unknown • Family physician • Obstetrician • Nurse Practitioner (APN/CNS) • Other • MIdwifery Practice group: select appropriate group from the list - contact Regional Coordinator if a group is missing.
☐	**Newborn Resuscitation**	NBRES0- NBRES9	• Unknown • None • FF02 • PPV • Intubation • Chest Compression • Drugs
☐	**Baby's Sex** **- This field can be problematic if there was a rare sex-linked chromosomal disorder, and**	GENDER	• Male • Female • Ambiguous

	hence easier to re-identify the baby, especially when combined with other variables like postal code		• Unknown
☐	**Gestational Age**	GEST	Completed weeks should be entered (ie. if 36 weeks and 6 days, select 36 weeks).
☐	**Birth weight** **- parents often announce, post, and broadcast their baby's birth weight, so is arguably general knowledge useful for re-identification** **- This field can make the baby & mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	BWEIGHT	
☐	**Apgar 1**	APGAR1	
☐	**Apgar 5**	APGAR5	
☐	**Apgar 10**	APGAR10	
☐	**Arterial Cord pH**	ARTCPH	
☐	**Arterial Base Excess**	ARTBE	
☐	**Venous Cord pH**	VENCPH	
☐	**Venous Base Excess**	VENBE	
☐	**Congenital Anomalies** **- can be an issue for re-identification if the anomaly is rare, especially when combined with other data variables**	CONGAN0- CONGAN55 CONGAN99	Select one or more • None • Unknown **Central Nervous System** • Anencephalus/acrania • Spina bifida/myelomeningocele (spinal)

			• Hydrocephalus • Encephalocele/meningocele(cerebral) • Microcephalus • Other **Eye/Ear** • Eye • Ear **Orofacial** • Cleft palate • Cleft lip • Other • Cardiac • Transposition of great vessels • Tetralogy of fallot • Ventricular septal defect • Atrial septal defect • Coarctation of aorta • Congenital heart block • Other **Respiratory system** ▪ Choanal atresia ▪ Other **Gastrointestinal** ▪ Diaphragmatic hernia ▪ Esophageal atresia with tracheoesophageal fistula ▪ Esophageal atresia without tracheoesophageal fistula ▪ Pyloric stenosis ▪ Gastroschisis ▪ Omphalocele ▪ Other **Genitourinary** ▪ Renal agenesis ▪ Prune belly ▪ Posterior urethral valve ▪ Bladder exstrophy ▪ Hypospadius

			▪ Epispadius ▪ Indeterminate sex ▪ Other **Musculoskeletal** ▪ Achondroplasia ▪ Reduction deformity/upper limbs ▪ Reduction deformity/lower limbs ▪ Hip dislocation and or dysplasia ▪ Club foot/talipes ▪ Polydactyly ▪ Syndactyly ▪ Other **Chromosomal** ▪ Trisomy 13 ▪ Trisomy 18 ▪ Trisomy 21 (down syndrome) ▪ Turner syndrome (45 xo) ▪ Other trisomy ▪ Other chromosomal anomalies **Anomalies unclassified elsewhere** ▪ Conjoined twins ▪ Fetal alcohol syndrome ▪ Multisystem ▪ Other syndromes
☐	**Phototherapy**	PHOTOTH	Select one (default) • Unknown • No • Yes
NOT GIVEN OUT	**Newborn Comment**		
☐	**Infant Feeding in Hospital**	FEEDH	Select one (default) • Unknown • Breastmilk only (exclusively breastmilk) • Combination of formula and breastmilk • Formula only

			• Other • NA
☐	**Infant Feeding - Reason for Substitute**	BMSUBR0- BMSUBR11	• None • Breast reconstruction/surgery • Clinical evidence of severe dehydration: weight loss > 10%, dry mucosa, decreased skin turgor, flat or sunken fontanel, increasing tachycardia, irritability, lethargy, decreasing voiding or stools • Hypoglycemia unresponsive to feeding: glucose levels below accepted range (2.6mmol/L) 30 minutes after breastfeeding • Inborn errors of metabolism: e.g. PKU, maple syrup disease, galactosemia, G6PD etc • Infant unable to feed at breast: due to illness, prematurity, separation from mother • Mom taking contraindicated medication: very few meds are contraindicated (e.g. antineoplastics) • Separation of mom and baby • Severely ill mother • Other
☐	**Infant feeding - on discharge**	FEEDD	Select one (default) • Unknown • Breastmilk only (exclusively breastmilk) • Combination of formula and breastmilk • Formula only • Other

			• NA
☐	**Hearing Screening**	HEARSCR	Select one (default) • Pass (both ears) • Referral • Not done • Inconclusive / no result • Unknown
☐	**Parkyn Screen**	PARKYN	Select one (default) • Parkyn completed and sent to Health Unit • Parkyn completed but not sent to Health Unit • Not completed
☐	**Parkyn - if not done, why?**	NOPARK	Select one (default) • Unknown • Mother refused • Consent signed but left hospital before completing • Language barrier • Transferred • Other
☐	**Neonatal Death/Stillbirth**	NEODEATH	Select one (default) • Not applicable • Stillbirth (>20 weeks) • Neonatal death < 7 days • Neonatal death 7-28 days

☐	**Date of Infant discharge/transfer** **- can be an issue for re-identification because discharge date is strongly correlated with baby date of birth, and with birth date and infant discharge, length of stay can be calculated and this could lead to re-identification particularly in long stays.**	DISCHDAT	All babies transferred to NICU/SCN in same hospital must be entered as such. If the baby is returned to the mother/baby unit before discharge then this field is overwritten in at discharge “Home” with mother
☐	**Time of Infant Discharge/transfer**	DISCHTIM	All babies transferred to NICU/SCN in same hospital must be entered as such. If the baby is returned to the mother/baby unit before discharge then this field is overwritten in at discharge “Home” with mother
☐	**Baby Weight at Discharge** **This variable is strongly correlated with birth weight and therefore has the same re-identification tisks**	DISCHWGT	
☐	**Discharged / Transferred to**	DISCHTO	Select one (default) • Unknown • Home • Other unit in same hospital • NICU/SCN in same hospital • NICU/SCN in other hospital • From Home to Hospital • Other
☐	**Reason for Transfer**	NEOTRR	Select one (default) • Unknown • Bed required for sicker baby • Lack of physician coverage • Lack of nursing coverage • No bed available

			• Requires further investigation • Requires higher level of care • Condition improved • Other
NOT GIVEN OUT	**Neonatal Transfer Hospital**		Contact your Regional Coordinator if a transfer site is missing from your drop down list.
☐	**Parity**	PARITY	
☒ Also requesting census subdivision information	**Health Unit Region** **- This field can make the baby & mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	RESPHUNO	
☐	**LHIN** **- This field can make the baby & mother more unique in the population, and hence easier to re-identify, especially when combined with other variables**	MOHLHINNO	

Appendix B

De-identification report provided by the Better Outcomes Registry and Network

Ann Sprague
Scientific Manager - BORN Ontario
Box 241, The Ottawa Hospital - General Campus

22nd February 2012

Re: De-identification Report for Project "Spatial analysis of pregnancy complications associated with cardiovascular disease risk in Ontario"

Dear Ann,

This is to confirm that the final de-identification for the above project has been accepted by the principal investigator Jessica Stortz and does meet the risk threshold criteria. The following is the final de-identification report:

Requested Cohort

The definition of the requested cohort is as follows:

- All births in calendar years 2005-2009
- For the "Maternal Health Problems" field, only the following values will be provided:
  - - Chronic Hypertension
  - - Diabetes insulin dependant
  - - Diabetes non-insulin dependant
  - - Heart disease

The cohort has 658,744 births.

Requested Quasi-identifiers

The following are the variables that have been determined to represent a risk of re-identification within the cohort (the quasi-identifiers):

Quasi-identifier
C_MATAGE
RESPHUNO
SUBDIVISION

Electronic Health Information Laboratory
CHEO Research Institute, 401 Smyth Road, Ottawa, Ontario K1H 8L1, Canada
Tel: +1 (613) 737 7600 x.4147 --- Fax: +1 (613) 731 1374 --- info@ehealthinformation.ca
www.ehealthinformation.ca

The requested generalizations for this data set are as follows:

Quasi-identifier	Requested Generalization
C_MATAGE	unchanged
RESPHUNO	unchanged
SUBDIVISION	unchanged

Calculated Variables

Census Subdivision (SUBDIVISION) has been calculated from the GEOGRAPHY column in the BORN database by using the CSDUID column from the Statistics Canada Dissemination Area Boundary Files for Canada, 2006 Census, where GEOGRAPHY = DAUID
(available here:
http://geodepot.statcan.gc.ca/2006/040120011618150421032019/021521140401182506 09120519/0401-0104_05-eng.jsp - the .dbf file from the ArcInfo format can be opened using Excel)

Final De-identification Results

De-identification Parameter	Value
Threshold	0.2
Percentage of records with some missingness due to original missingness or suppression during de-identification	3.53%

Variable Name	Generalization	Total Missingness (%)
C_MATAGE	Top/Bottom Code <15 and >=50 (1 year age intervals)	997 (0.151%)
RESPHUNO	Unchanged	2,179 (0.330%)
SUBDIVISION	Unchanged	22,189 (3.368%)

Please let me know if you have any questions.

Sincerely,

Khaled El Emam

Electronic Health Information Laboratory
CHEO Research Institute, 401 Smyth Road, Ottawa, Ontario K1H 8L1, Canada
Tel: +1 (613) 737 7600 x.4147 --- Fax: +1 (613) 731 1374 --- info@ehealthinformation.ca
www.ehealthinformation.ca

Appendix C

Queen's University Research Ethics Approval

QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW
November 25, 2011

Ms. Jessica Stortz
Department of Community Health and Epidemiology
Queen's University

Dear Dr. Stortz
Study Title: EPID-368-11 Spatial analysis of pregnancy complications associated with cardiovascular disease risk in Ontario
File # 6006440
Co-Investigators: Dr. D. Hunter and Dr. G. Smith

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol and the data request form – record level data – December , 2010 V1 for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # **6006440** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file **6006440** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Allan L. Clark

Appendix D

Children's Hospital of Eastern Ontario Research Ethics Approval

Children's Hospital of Eastern Ontario
Centre hospitalier pour enfants de l'est de l'Ontario

CHEO Research Ethics Board
Approval for Record Level Information from the BORN Dataset

Principal Investigator	Jessica Stoetz
REB Protocol Number	12/39X
BORN Reference Number	N/A
Protocol Title	Spatial Analysis of Pregnancy Complications Associated with Cardiovascular Disease Risk in Ontario
Primary Affiliation	Queen's University
Approval Date	March 8, 2012
Valid Until	February 15, 2013
Documents Reviewed & Approved	• BORN Ontario Application Form and Approval letter

The Better Outcomes Registry & Network Ontario (BORN Ontario - previously the Ontario Perinatal Surveillance System - OPSS) houses data from its five founding members (Ontario Maternal Multiple Marker Screening, Fetal Alert Network, Ontario Midwifery Program, Niday Perinatal Database and Ontario Newborn Screening). These data can be used secondarily to answer research questions. The Children's Hospital of Eastern Ontario has governance over the BORN program. The hospital provides the founding support and sponsorship of BORN. Accordingly, the CHEO REB has jurisdiction over the human research conducted on BORN data that is record – specific, meaning that the information is specific to an individual and drawn from their record.

This letter provides notification that the Children's Hospital of Eastern Ontario Research Ethics Board has granted approval for the above named research study. Your project was reviewed under the expedited stream, which is reserved for projects that involve no more than minimal risk to human subjects.

Investigators are asked to report the following to the CHEO REB:

- Any breach of confidentiality or security
- BORN Audit Results

Unless otherwise indicated by the investigator, the CHEO REB will assume that the study will be concluded within a year of this approval date. If a longer activation period is required by the investigator, an annual renewal report should be filed with the Board prior to the date referenced above.

Regards,

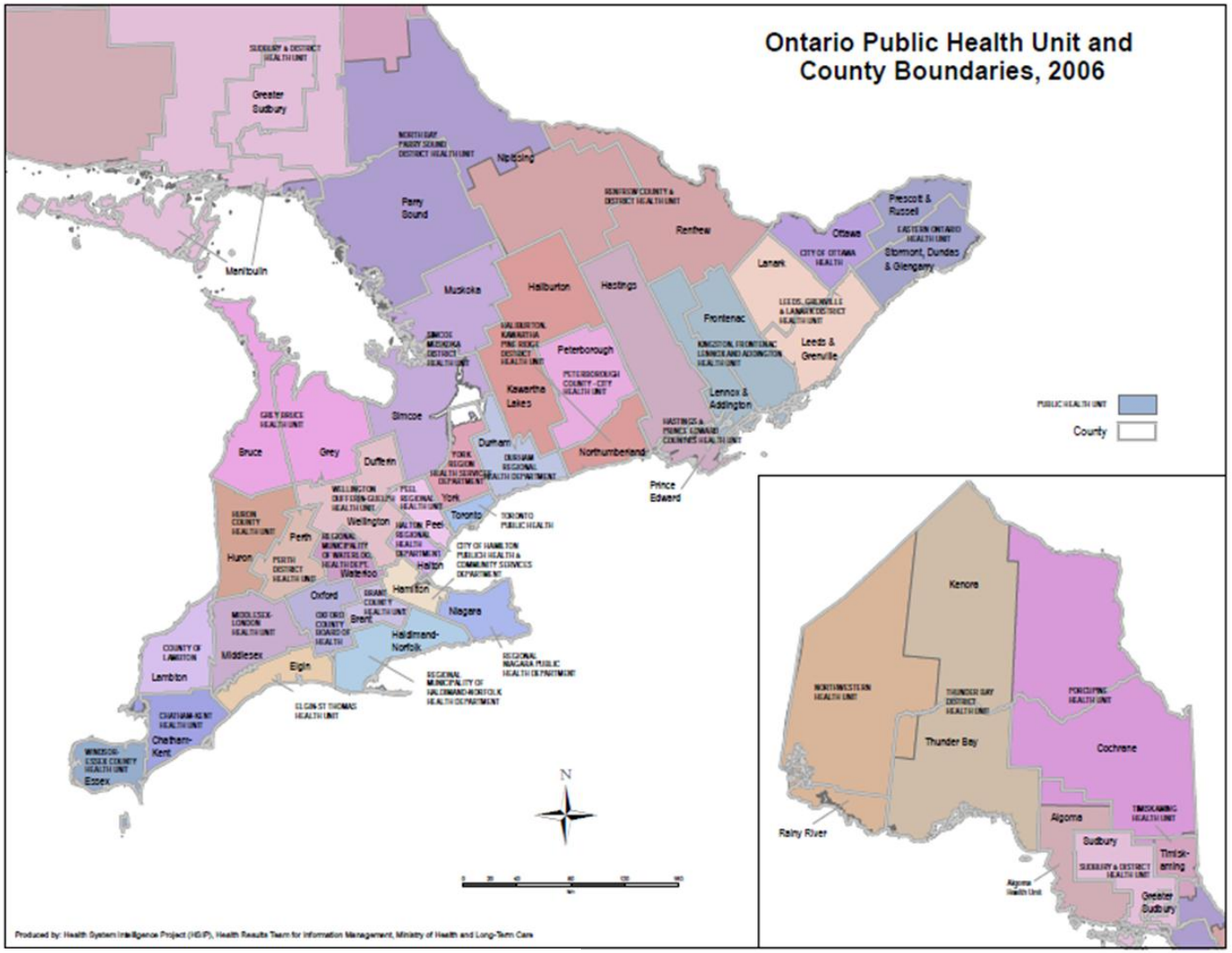
Dr. Carlo Gentile, C.Psych.
Chair, Research Ethics Board

c.c.:

- Ann Sprague, Scientific Manager, BORN
- CHEO Research Institute Administration

Appendix E

Map of Public Health Unit Areas in Ontario

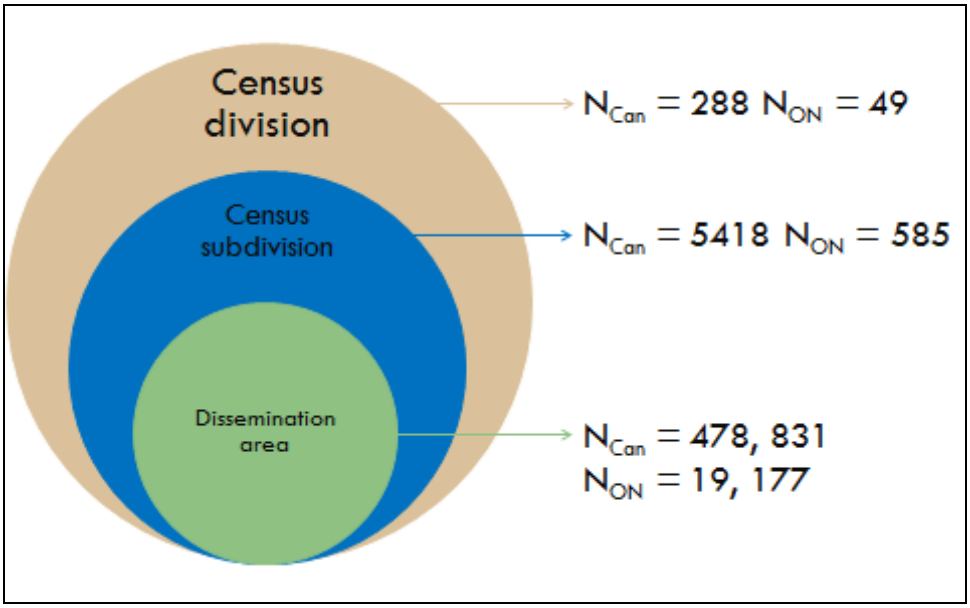


Source: Association of Public Health Epidemiologists in Ontario website[118]

Appendix F

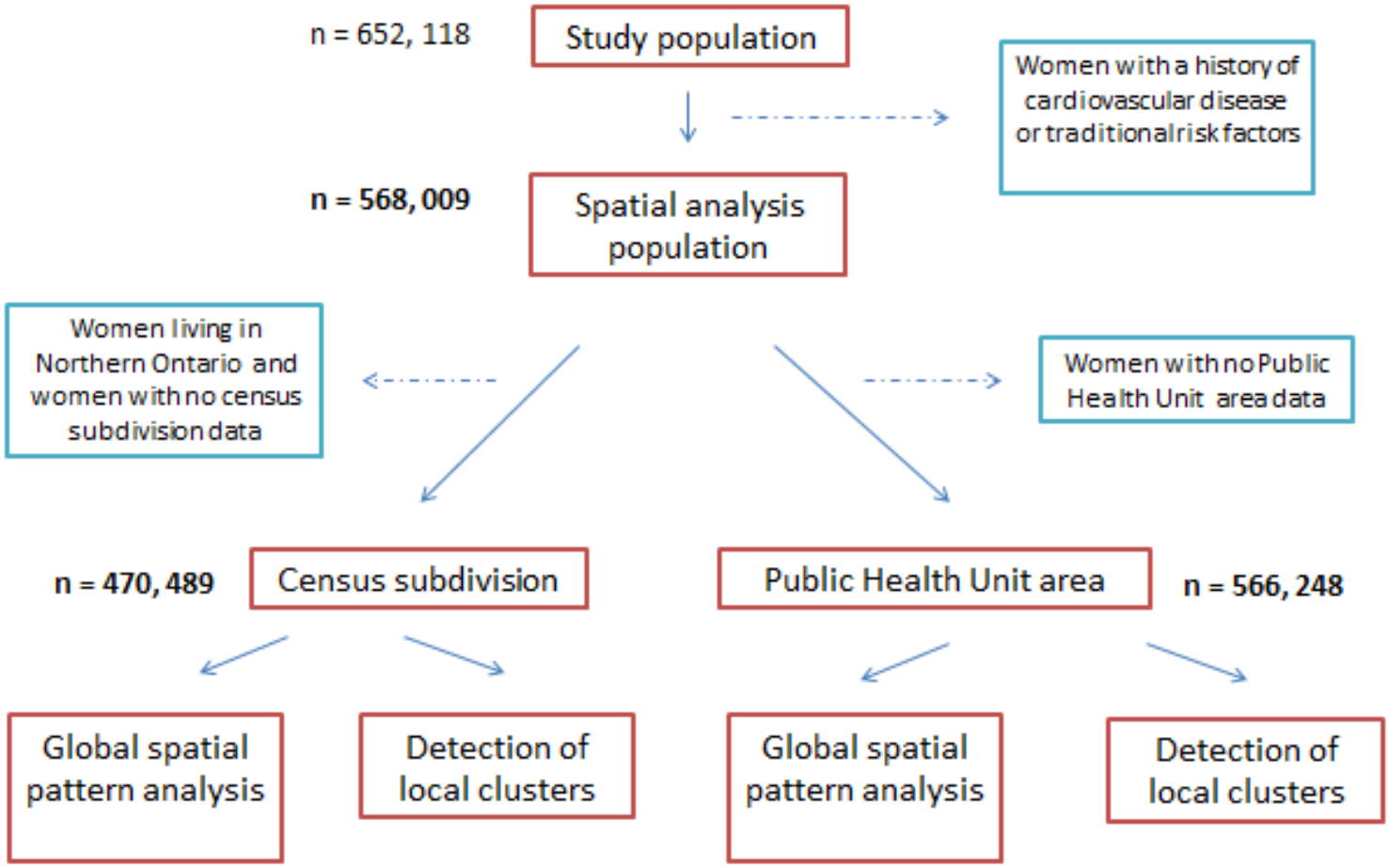
Standard Geographic Classification of Canada

Statistics Canada has divided provinces and territories into census units for the purpose of surveying demographic characteristics of Canadians and producing statistics by geographical area. The Standard Geographic Classification of provinces and territories divides each province/territory into census divisions, census subdivisions, and dissemination areas. A schematic of the Standard Geographic Classification units of Canada is displayed below, including number of units in Canada (N_{Can}) and number of units in Ontario (N_{ON}).



Appendix G

Schematic of Spatial Analysis Objective


n = 652, 118
Study population
Women with a history of cardiovascular disease or traditional risk factors
n = 568, 009
Spatial analysis population
Women living in Northern Ontario and women with no census subdivision data
Women with no Public Health Unit area data
n = 470, 489
Census subdivision
Public Health Unit area
n = 566, 248
Global spatial pattern analysis
Detection of local clusters
Global spatial pattern analysis
Detection of local clusters

Appendix H

Mathematical Formula for Calculation of Moran's I Statistic

The Moran's I statistic for spatial autocorrelation is given as:

$$I = \frac{n}{S_0} \frac{\sum_{i=1}^{n} \sum_{j=1}^{n} w_{i,j} z_i z_j}{\sum_{i=1}^{n} z_i^2} \quad (1)$$

where z_i is the deviation of an attribute for feature i from its mean $(x_i - \bar{X})$, $w_{i,j}$ is the spatial weight between feature i and j, n is equal to the total number of features, and S_0 is the aggregate of all the spatial weights:

$$S_0 = \sum_{i=1}^{n} \sum_{j=1}^{n} w_{i,j} \quad (2)$$

The z_I-score for the statistic is computed as:

$$z_I = \frac{I - \mathrm{E}[I]}{\sqrt{\mathrm{V}[I]}} \quad (3)$$

where:

$$\mathrm{E}[I] = -1/(n-1) \quad (4)$$

$$\mathrm{V}[I] = \mathrm{E}[I^2] - \mathrm{E}[I]^2 \quad (5)$$

Source: Esri's ArcGIS 10 website[119]

Appendix I

Mathematical Formula for Calculation of Gi* Statistic

The Getis-Ord local statistic is given as:

$$G_i^* = \frac{\sum_{j=1}^{n} w_{i,j}x_j - \bar{X}\sum_{j=1}^{n} w_{i,j}}{S\sqrt{\frac{\left[n\sum_{j=1}^{n} w_{i,j}^2 - \left(\sum_{j=1}^{n} w_{i,j}\right)^2\right]}{n-1}}} \quad (1)$$

where x_j is the attribute value for feature j, $w_{i,j}$ is the spatial weight between feature i and j, n is equal to the total number of features and:

$$\bar{X} = \frac{\sum_{j=1}^{n} x_j}{n} \quad (2)$$

$$S = \sqrt{\frac{\sum_{j=1}^{n} x_j^2}{n} - \left(\bar{X}\right)^2} \quad (3)$$

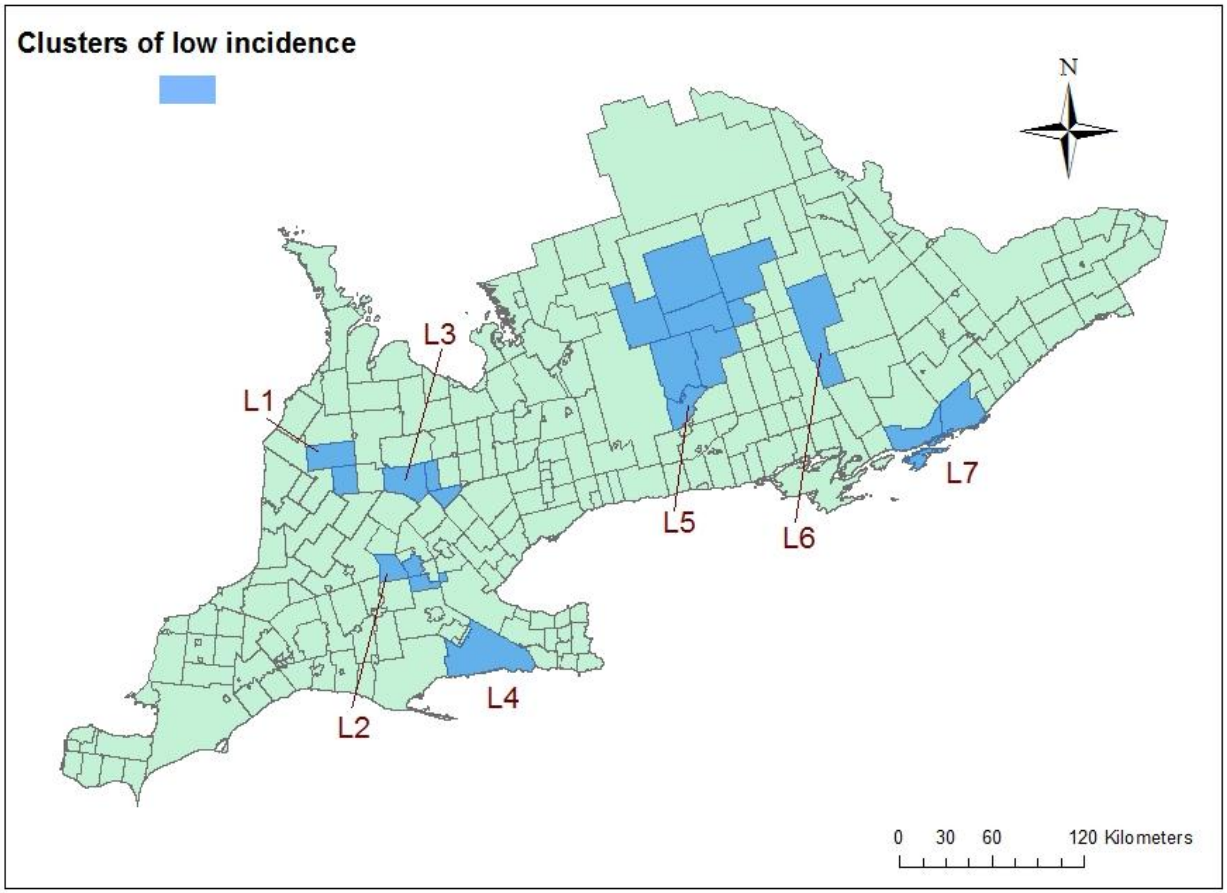
The G_i^* statistic is a z-score so no further calculations are required.

Source: Esri's ArcGIS 10 website[120]

Appendix J

Statistically significant clusters of low cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by census subdivision in Southern Ontario (2005-2009)

Statistically significant clusters of low cumulative incidence of one or more pregnancy complications associated with cardiovascular disease risk by census subdivision in Southern Ontario (2005-2009)



Statistically significant clusters of low cumulative incidence from a hot spot analysis of cumulative incidence of one or more pregnancy complications at the census subdivision level in Southern Ontario (2005-2009)[◊◊]

Cluster	Census Subdivision	Public Health Unit	n[‡‡‡]	Gi*	p-value
L1	South Bruce	Grey Bruce Health Unit	230	-2.22	0.027
L1	Howick	Huron County Health Unit	242	-2.17	0.030
L2	Wilmot	Region of Waterloo, Public Health	753	-2.54	0.011
L2	Kitchener	Region of Waterloo, Public Health	10,400	-2.39	0.017
L2	North Dumfries	Region of Waterloo, Public Health	356	-2.24	0.025
L3	Wellington North	Wellington-Dufferin-Guelph Health Unit	250	-2.88	0.004
L3	East Luther Grand Valley	Wellington-Dufferin-Guelph Health Unit	87	-2.84	0.005
L3	East Garafraxa	Wellington-Dufferin-Guelph Health Unit	39	-2.60	0.009
L4	Haldimand County	Haldimand-Norfolk Health Unit	1,295	-2.06	0.039
L5	Highlands East	Haliburton, Kawartha, Pine Ridge District Health Unit	18	-4.10	0.000
L5	Galway-Cavendish and Harvey	Peterborough County-City Health Unit	24	-4.09	0.000
L5	Smith-Ennismore-Lakefield	Peterborough County-City Health Unit	726	-3.65	0.000
L5	Minden Hills	Haliburton, Kawartha, Pine Ridge District Health Unit	79	-2.68	0.007
L5	Hastings Highlands	Hastings and Prince Edward Counties Health Unit	270	-2.53	0.011
L5	North Kawartha	Peterborough County-City Health Unit	20	-2.45	0.014
L5	Dysart and Others	Haliburton, Kawartha, Pine Ridge District Health Unit	117	-2.42	0.016
L5	Faraday	Hastings and Prince Edward Counties Health Unit	*	-2.24	0.025
L5	Curve Lake First Nation 35	Peterborough County-City Health Unit	11	-2.20	0.028
L6	Addington Highlands	Kingston, Frontenac and Lennox & Addington Health Unit	11	-2.62	0.009
L7	Leeds and the Thousand Islands	Leeds, Grenville and Lanark District Health Unit	416	-2.30	0.021
L7	Gananoque	Leeds, Grenville and Lanark District Health Unit	148	-2.13	0.033
L7	Kingston	Kingston, Frontenac and Lennox & Addington Health Unit	4,736	-2.06	0.040

[◊◊] Spatial analysis population, n = 470, 489, [‡‡‡]n = number of women from spatial analysis population in each census subdivision, * = less than 5 pregnancies recorded during the study period

VITA

Name:	Jessica N. Stortz
Place and year of birth:	Scarborough, Ontario, 1987
Education:	University of Guelph, Guelph, Ontario Bachelor of Science (Biomedical Toxicology, Co-op) 2005-2010
Experience:	Teaching Assistant – Infectious Diseases Queen's University Kingston, Ontario 2012
	Research Assistant Queen's University Kingston, Ontario 2011-2012
	Research Assistant (Co-op) Agriculture and Agri-Food Canada Guelph, Ontario 2008
	GLP Study Personnel (Co-op) Chemtura Canada Guelph, Ontario 2007
	Product Development Assistant (Co-op) Campbell Company of Canada Toronto, Ontario 2007
Awards:	Queen's University Graduate Award 2010-2012
	Natural Sciences and Engineering Research Council of Canada Undergraduate Student Research Award 2007