Accounting for the Distribution of Adverse Birth Outcomes in Ontario: A Hierarchical Analysis of Provincial and Local Outcomes

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Abstract

Background: Adverse birth outcomes present a difficult and chronic challenge in Ontario, in Canada and in developed countries in general. Increasing proportions of preterm births, significant regional disparities and the high cost of treating all adverse birth outcomes have focused attention on explaining them and developing effective treatments.

Methods: Birth outcomes and maternal characteristics for approximately 626,000 births, about 90% of births in 2005–2009, were linked to small geographic areas throughout Ontario. For each of four adverse outcomes: late preterm, moderate to very preterm, small for gestation age and still births, proportions of total births were calculated for the full province and for each small geographic area. Geographic hotspots of elevated rates were identified for each of the different adverse birth outcomes using the local Moran's I statistic.

Data for nine known ecologic and individual risk factors were then linked to the areas. Hierarchical regression analysis was used to model each of the outcomes for the full province and for dispersed local areas. The resulting models for the different outcomes were contrasted.

Results: Significant geographic hotspots exist for each of the four outcomes. Hotspots for the different outcomes were found to be largely spatially exclusive. For like outcomes, predictive models differed markedly between local areas (i.e. local groups of hotspots) as well as between full-province and local areas. Ecologic level variables played a strong role in all models; the influence of individual level risk factors was consistently modified by ecologic risk factors except for small for gestational births.

Conclusions: The finding of significant hotspots for different adverse birth outcomes indicates that certain geographic areas have aetiologies or patterns of predictors sufficient to create significantly elevated levels of particular outcomes. The finding that hotspots for the different

adverse outcomes are largely exclusive implies that the aetiologies are specific; i.e., those that are sufficient to create significantly higher levels for one outcome do not also create significantly higher levels of others.

The consistently strong role of ecologic level risk factors in modifying individual level risk factors implies that contextual characteristics are an important part of the aetiology of adverse birth outcomes. Differences in local area models suggest the existence of location-specific (rather than universal) aetiologies. The findings support the need for more careful attention to local context when explaining birth outcomes.

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Last I give credit to my mother, Serene, who taught me to be quietly tenacious.

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List of Abbreviations and Acronyms

Italicized abbreviations and acronyms refer specifically to birth outcome or predictor variables that have been statistically created for use in this analysis.

- *%Asian:* the proportion of immigrants from South and East Asia living in a DA
- *%HigherEd*: the proportion of women in a DA, ≥20 years of age, who have had education beyond a bachelor's degree
- *%NoDip*: the proportion of women in a DA, ≥20 years of age, that did not obtain a high school diploma or the equivalent
- BORN Ontario: Better Outcomes Registry & Network Ontario
- DA: census dissemination area, varying size with full population counts between 500–700 people
- *HlthProb*: whether a woman had a pre-existing health problem at the time of her child's birth
- hotDAs: census dissemination areas (DAs) that are designated as part of a hotspot
- Hotspot: two or more contiguous DAs which have adverse birth outcome values significantly higher than surrounding DAs
- IQR: inter-quartile range represented by the values of the upper boundary of the first and lower boundary of the fourth quartiles of the data distribution
- *LateP*: births with a gestational age of less than 37 weeks and equal to or greater than 35 weeks
- *MedInc*: the median household income for a DA
- *Midage*: women aged >19 but <35 years
- *ModVeryP or ModVP*: births with a gestational age of less than 35 weeks
- *Olderage*: the mother was ≥35 years of age at the time of the birth
- *SGA*: births where birthweight is <0.90% of births of same gestational age and sex
- SGA: small for gestational age birth
- *Smoked*: whether a woman smoked at any time during her pregnancy

- *Stillbirth*: stillbirth mortality
- *Teenage*: the mother was <20 years of age at the time of the birth
- *Urban*: a DA within a metropolis with a population of ≥10,0

Chapter 1. Introduction

1.1 The Research Problem

Adverse birth outcomes present a complex, evolving and growing health issue for Ontario. While often grouped together under a single label such as preterm (also called premature) (1-5) or low birthweight outcomes (6,7), adverse birth outcomes present a multi-faceted issue; the three most common ones (premature, small for gestational age and stillbirths) each present distinctly different risk profiles (8) and entail different short- and long-term health implications (9). Recent research suggests that each of these three outcomes also presents a set of different outcomes (8).

Ontario is committed to reducing overall rates of adverse outcomes (10). In 2010 the province made reproductive health one of the 36 mandatory health programs and services offered by the Ministry of Health and Long Term Care. This commitment has been reconfirmed by actions taken centrally as well as by mandated reporting by local healthcare networks (11).

The proportion of premature births, defined as births at less than 37 weeks' gestational age, has steadily increased in Canada since about 1990, from 6% in the early 1980s (12) to 8.1% (95% CI, 8.0–8.2) in 2006–7 (13). Ontario figures rose from 7.1% in 2003 (6.9–7.2)[1] to 8.3% (8.1–8.4) in 2007 (9). Although some of the identified risk factors have been reduced, such as smoking and teenage births (9,10), other factors are increasing, notably fertility assistance and multi-gestational births to women over 40 (14,15), obstetric interventions (preterm caesarean births and inductions due to fetal distress) (15), and mothers living in low socioeconomic status

[1] All confidence intervals from this point forward will be at 95% and presented in this simplified format.

(SES) environments (9). The impact of the increase in these risk factors has been sufficient to offset the reductions (16,17).

Proportions of small for gestational age (SGA) births, defined as a newborn with a birthweight lower (that is in the lowest tenth percentile) than expected for the given gestational age and sex (9) have been decreasing across Canada (and Ontario) for the past decade. The Canadian figure was 8.3% (8.2–8.4) in 2006–7; Ontario had the highest provincial SGA rate, at 8.9% (8.7–9.0) in 2006–7 (9). Ontario has high levels of known risk factors for SGA: higher levels of older maternal age, high counts of South and East Asian first-generation immigrants as well as large urban-dwelling populations that are linked with low SES and high rates of smoking (9).

Rates of stillbirth, defined as a newborn with greater than 20 weeks' gestational age and no signs of life on delivery, have decreased in Ontario over the past two decades, from five per thousand births in 1995 to less than four per thousand in 2004 (18). This decrease was perplexing given the increase in premature births, which is one of the most important predictors of stillbirth (19-22). One explanation is that obstetric interventions, such as caesarean sections and induced labour at less than 37 weeks, are being used more often in response to indicators of foetal distress such as foetal growth restriction and risk of stillbirth; their use reduces SGA and still births while increasing rates of preterm birth (9,15). Although overall rates of SGA and still births have been decreasing in Ontario, significant regional disparities remain in these (as well as preterm birth outcomes (10,23,24).

Adverse outcome births have a higher cost, substantially more in initial hospital expenses as well as in long-term social expenses, than normal births (9,18,25). Initial mean hospital expenses for a premature birth (<37 weeks gestation) in Ontario were nine times higher than for a full-term infant (9). Preterm births, which accounted for 8.3% of births in 2006, used 45% of

the total hospital expenditures for all births (9,26,27). Research has shown that both direct and indirect costs of adverse birth outcomes continue across the life of the individual (26,28-32). Costs of adverse birth outcomes are discussed further in Section 2.4.

The goal of this research is to add to the understanding of the complex issue of adverse birth outcomes by concurrently modeling four different adverse birth outcomes in diverse geographic areas. An important part of this investigation will be to explore the complex and dynamic relationships that contextual factors (and their interaction effects with individual level factors) have with different adverse outcomes; the concurrent study of four outcomes in diverse areas will allow for this.

1.2 Research Context

This research applies a population health approach to the analysis of adverse birth outcomes. Population health is defined as the study of the health outcomes of a group of individuals (i.e. a population) including the distribution of such outcomes, patterns of health determinants and the phenomena that link the two (33). Three research questions are posed:

- Are there geographic hotspots[2] for the different adverse birth outcomes? If so, where are they?
- What are the significant predictors for the different adverse outcomes for local groups of hotspots (i.e., local areas) and for the full province?
- For each adverse outcome, do predictors differ between models for diverse local areas and between local models and the full province model; and do predictors differ across different adverse outcome models?

An observational cross-sectional research design involving geographic information systems (GIS) spatial cluster analyses and hierarchical regression analyses were used to answer these

[2] "Hotspot" is defined as a group of contiguous DAs where the risk of an adverse birth outcome is significantly different (at the 95% level of confidence) from surrounding areas (300).

questions. A database representing about 90% of births in Ontario for a five-year period (2004–9) was linked with Canadian census information for use in this analysis.

1.3. Research Contribution

Extensive research has sought to explain the different adverse birth outcomes; yet few studies have analyzed more than one outcome with the goal of contrasting risk factors (8,9). GIS spatial cluster analysis has been used extensively in epidemiological studies of rare diseases (34,35) but infrequently in studying adverse birth outcomes (36-40). The current study complements previous research by concurrently exploring four commonly studied adverse outcomes at different geographic scales and in diverse areas. This approach allows for a more granular understanding of the role of different ecologic and individual level risk factors in different outcomes.

This study has broken new ground by attempting to identify geographic hotspots (comprised of relatively small spatial areas) for four different adverse outcomes within the context of a very large area. Unlike previous studies that have analyzed small areas (40-43), geographic cluster analysis was used as a rigorous and methodical approach to identify areas (i.e., hotspots) for further exploration. Identification of multiple hotspots for each of the four different adverse outcomes allowed for the comparison of regression models representing diverse geographic areas and scales. It also allowed for the comparison of regression models across different adverse outcomes also for diverse geographic areas and scales.

It has been widely recognized that contextual effects have an important role in explaining adverse birth outcomes (8,9,41-43). There is also strong evidence that interaction effects between contextual and individual level variables play an integral part in this explanation and account for at least some of their complex and dynamic nature (3,9,38,44-50). By understanding

if (and how) key risk factors behave differently in different places, public health policy and decision makers may be better able to respond to regional disparities in adverse outcomes and design interventions suited to local populations.

1.4. Research methods

This research was conducted in two distinct phases:

1. Identification of hotspots. This phase involved the grooming the birth outcome database and creation of adverse outcome variables. Birth outcome data were linked with census dissemination area boundary files which served to link births to relatively small geographic areas. This linkage allowed for geographic cluster analysis and the identification of hotspots for each of the four different adverse outcomes.
2. Creation of regression models for each adverse outcome. This phase involved linking census data and maternal information (for each birth) to the small geographic areas. Variables representing nine individual and ecologic level risk factors were created. Diverse local groups of hotspots for each outcome were identified. This identification allowed for regression models to be created and significant predictors identified for each of the four different adverse outcomes for dispersed local areas as well as for the full province. Within this study, the term "risk factor" will refer to individual variables, such as smoking or maternal age that have not been shown to be significant; the term "predictor" will refer to either individual variables or interaction effects that have been found to be significant in the regression analysis. The final step in this phase involved a comparison of the resulting models within each adverse outcome as well across the different outcomes.

1.5. Limitations of the Study

There were five principal limitations to this research which were identified and are discussed in section 5.10. None is likely to affect the main conclusions. Each limitation is discussed at greater length in Section 5.10. First, the current research is an observational cross-sectional study that, as such, faced the possibility of selection bias (our sample represented about 90% of Ontario births for the 2004–9 time frame). Second, the risk factors included in regression analysis were limited to individual level variables available from the BORN database and to ecologic variables available from the 2006 Statistics Canada census. These data permitted the analysis of nine factors that have been consistently found to be significantly associated with the different outcomes but did not allow inclusions of several others also shown to be significant. Third, spatial cluster identification tools vary slightly in the size and location of clusters each is capable of detecting; the hotspots identified in this study may be slightly different from those that could have been found using a different analytic approach. Fourth, local hotspot groups used in the analysis were selected empirically for hypothesis generation purposes; they were not statistically representational. Fifth, relatively small local geographic areas, DAs, were used. While this permitted finely-grained analysis, it also increased the risk of the small number problem (i.e., that small area populations increase the possibility of statistical instability, such as in birth outcomes, as well as bias analyses through small event counts). The small number problem represents a trade-off with geographic resolution; geographic resolution was favored in order to best answer the research questions. As noted, this choice should not substantially affect the conclusions of the current research.

The nature of our research questions should, in part, limit the affects of these five principal limitations. We are more interested in comparing the regression models that result

from our analyses across diverse spatial areas, and across the four different adverse birth outcomes, than in their specific accuracy or exhaustiveness. In terms of identifying hotspots, our goal was to compare locations of the 'hotspot' clusters of DAs for the different outcomes. We can assume that much of the bias introduced by sampling and/or by the analysis tool, in this case local Moran's I, would have been equally shared across findings for the four outcomes and thus the hotspots identified would be comparable. In carrying out regression analysis our interest again lay in contrasting the predictive models for the different adverse outcomes rather than in their predictive strength or accuracy. While the small-number trade-off is an important consideration, research by Theall (51) found that when the number of groups is large (>459), small group sizes (<5 adverse birth outcomes) did not affect regression analysis outcomes.

CHAPTER 2. LITERATURE REVIEW

This research seeks to explore disparities in adverse birth outcome rates across Ontario and to explore explanatory factors for those disparities. It was carried out within a population health framework, whereas most previous research into adverse outcomes has focused on clinical- and/or individual level observations. The population health framework explores not only the individual characteristics and behaviors of mothers but also the contextual characteristics of the places where they live and the interactions between these levels of factors in predicting birth outcomes.

This chapter opens with a brief description of the study area and its characteristics that are important to the current research, followed by a discussion of research context and a summary review of relevant previous research. This review covers relatively recent research into predictors of adverse outcomes in Canada as well as key literature that describes and explores the key research methods used (i.e., geographic cluster analysis and hierarchical regression analysis).

2.1. Study Area: Ontario, Canada

2.1.1. Population: Ontario is the most populous province in Canada with a 2012 population of approximately 13,506,000 spread unevenly across its 917,741 square kilometers. The majority of Ontarians, 94%, live in the southern portion of the province. Between 2006 and 2011 the population increased by 5.7%, a decline from 6.6% growth in 2000–5 (52). Declines in immigration and increases in the number of emigrants moving to other provinces were the main contributors to this slight decrease (53).

Figure 2.1 The Study Area: Ontario, Canada

With a birth rate below replacement level, Ontario relies on immigration for demographic stability and growth. The true fertility rate (the ratio of total births to the total female population of childbearing age, between 15 and 45 years) for Ontario during 2008 was 1.58, well below the 2.1 level needed for generational replacement (54). Ontario receives the largest proportion of immigrants of all the Canadian provinces. In 2006 Ontario received about 50% of Canada's immigrants while representing less than 40% of the country's population. This proportion has been decreasing; in 2011 Ontario received about 40% of Canada's immigrants (55,56).

Ontario's population is aging. In the decade between 1998 and 2008 the median age of Ontarians increased from about 36 years to 39 years. The median age of the working-age population (15–64 years) increased from 38 years to 40.2 years. The number of children between 0 and 14 years fell from 20% to about 17.2% of the population (57). The aging of the population is relevant to the current study because older maternal age has been found to be predictive of adverse birth outcomes.

In 2006, about 85% of the Ontario population lived in urban areas. Approximately 74% lived within the 10 largest urban areas, all located in the South of the province (58). The majority of immigrants likewise settle in urban areas (53). Population location is relevant to the current study because Asian immigration and population density (or urban vs. rural location) are two of the explanatory factors reported in previous studies.

2.1.2. Social and Economic Well-Being: Canada ranks eighth in the United Nations Human Development index, a composite indicator of income, life expectancy and education. It ranks first among Organization for Economic Development and Cooperation (OECD) countries for the proportion of adults with a college degree, third-highest in dollar spending per tertiary student per year, and first in percentage of women with tertiary education (59). Canadian average per-person income earnings lie approximately one standard deviation above the mean for OECD member states, although the OECD report cites a "considerable gap" between the richest and poorest portions of the Canadian population (60). More than 72% of Canadians between the ages of 15 and 64 are employed; the OECD average is 66% (60). Ontario's scores in these areas are approximately equivalent to those of Canada (61).

In 2010 Ontario's economy was based primarily on services which account for about 77% of the province's gross domestic product (GDP). Goods make up the remaining 23%, of which 12.4% were manufactured (vs. agriculture, logging, mineral extraction, etc.). Ontario accounted for 52% of Canada's total manufacturing shipments in 2004 (57). Motor vehicles and parts accounted for about 31% of all exports; precious metals and stones were the second-largest. Export of services is expected to replace export of manufactured goods before 2030 (57). Ontario's GDP is expected to slow over the decade between 2010 and 2020. Whereas the aging labor supply could account for this by itself, slowing U.S. and global markets in the near term are expected to amplify this trend (57). Neighbourhood SES is an important risk factor in adverse birth outcomes and is included in the current study as a predictive factor.

2.1.3. Ethnic Make-up: In 2006 Ontario's population included about 2.7 million people from visible minorities, about 23% of Ontario's population and 54% of Canada's total visible minority population. This represents a 27.5% increase between 2001 and 2006. Most lived in major urban centres. A large portion of that growth was due to immigration, particularly from South and East Asia. South Asians (primarily from India) represented about 29% of visible minorities and were the fastest-growing group over the past decade. East Asian people (primarily from China) represent the second-largest visible minority group, about 21% of visible minorities. Blacks were the third-largest visible minority, about 15.2% of visible minority peoples. Other groups with more than 100,000 people included Filipinos, Latin Americans, Arabs and Southeast Asians (53,62). East and South Asian immigrants have been found to have significantly higher rates of SGA births than the

population as a whole; the percentage of each DA population that is made up of these immigrants is included as an ecologic variable in our research.

Ontario has one of Canada's largest provincial populations of Aboriginal peoples, comprised of North American Indian (First Nations people), Métis and Inuit. As of 2006 about 300,000 Aboriginal people lived in Ontario; 21% of all Canadian Aboriginal peoples (63). Between 2001 and 2006 the Aboriginal population grew by 29%, with the Métis population growing the fastest (63-65). Aboriginal origin is of interest in local area birth outcomes and is considered in secondary analyses.

2.1.4. Healthcare: Ontario has a universal, publicly funded healthcare system, delivered through the Ontario Health Insurance Plan (OHIP). The Ministry of Health and Long-Term Care is required to pay for a wide range of services that are considered to be medical necessities, including primary care; emergency care; neonatal, birth and pediatric care; and long-term home-care. But it does not pay for services that are not considered to be medically necessary, such as cosmetic surgery, dental care, and eye care. It also does not pay for pharmaceutical drugs (11,66).

The Ontario health system is under strain from increasing costs, the aging population and government budget constraints. Three key areas have been identified (and draw criticism) as being most in need of improvement: chronic disease management and avoidable hospitalizations, wait times and hospital safety. The Ministry has directed substantial resources to addressing these issues (66).

One chronic challenge is the quality of health services delivered to people who live in rural Ontario. Populations in rural areas have been shown to have worse health than urban according to a number of indicators, including mortality and birth outcomes, as well

as presence of morbidities (67,68). Geographic remoteness, long distances to healthcare facilities, low population densities, fewer providers and inclement weather conditions all add to this challenge. Local Health Integration Networks (LHINs) were introduced in 2006, and a Rural and Northern Health Care Panel in 2009, to help to address these challenges (67). Population density (i.e. urban vs. rural) has been found to be predictive of adverse birth outcomes and is included as a risk factor in the present study.

2.1.5. Social Welfare: Ontario offers social assistance to any individual or head of family who has shown that he or she is unable to provide for self and/or family. Assistance includes basic income support which helps recipients prepare for, gain and keep employment, and support for people with disabilities which includes both financial as well as employment assistance.

A number of mandated health benefits are included within basic income support; these include dental and vision care for children as well as pharmaceutical coverage. Discretionary benefits include dental and vision care for adults. Other benefits include expenses related to gaining and maintaining employment (69). Social welfare has been proposed as an important explanatory factor in adverse birth outcomes; this factor is included in the current study through an area SES variable.

2.2. Research Context

This research was carried out using a population health perspective which holds that the linkages among different factors and different levels of factors explain much of the variation in birth outcomes. In an effort to interpret the variety of statistical relationships produced from the current study's regression analyses (70) I used the social ecologic paradigm. This perspective widens the focus from the individual characteristics and

behaviour of prenatal women to include the broader physical and social context that surrounds and influences their decisions and actions (71,72). Choices are not made in a vacuum; while women may act individually, their actions are strongly affected by complex, dynamic, interdependent "mutually influential" (72) contextual characteristics such as neighbourhood SES, education levels, familial and social role models (71,73-76). Individual and area-level factors are mutually influential in that women work individually or in groups to modify their environmental conditions (72). Working with small geographic areas allowed for these contextual influences to be more effectively recognized and addressed.

To more effectively explain the statistical relationships uncovered in my analysis I required a more detailed model, one specifically applied to adverse birth outcomes. Figure 2.2 presents a high-level conceptual model put forward by Schempf (43), which represents those linkages as well as the interactive and reciprocal nature of the different factors and pathways that influence birth outcomes. This is a simplified version of a more complex model created by Culhane and Elo. The four categories of factors as well as their links were based on a review of adverse birth outcome research (77).

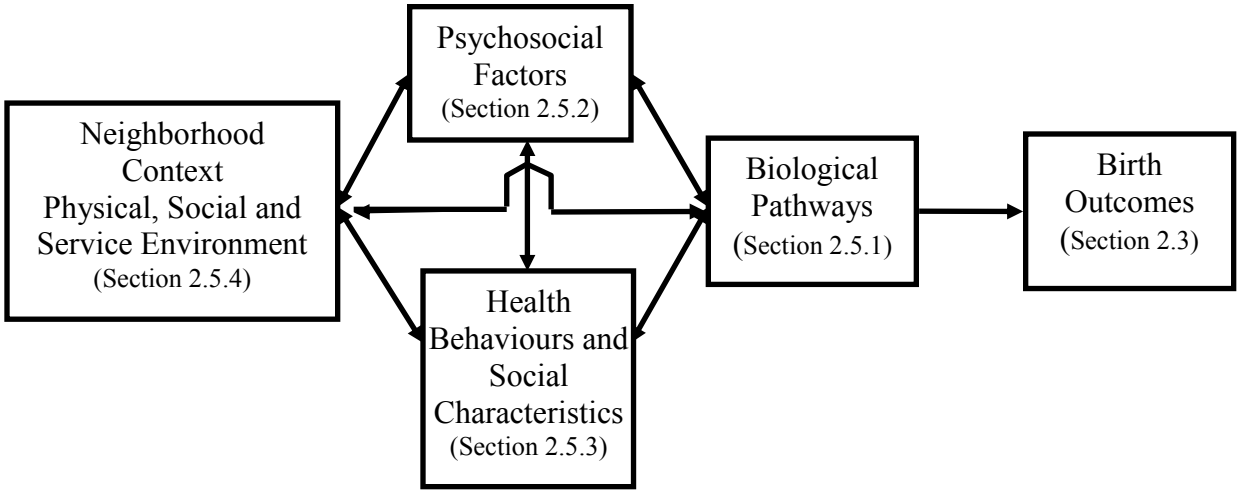


Figure 2.2 A Biopsychosocial Multilevel Conceptual Model of Birth Outcomes

Schempf simplified the model based on research by O'Campo (41,78,79) to the version shown here and again showed support for the various links except for the psychosocial factors (43). This model suggests that adverse birth outcomes are predicted by factors that reside within four contexts:

1. **Neighbourhood Context:** These include the physical (built and natural), social and service characteristics of the DA within which the mother lived at the time of the pregnancy and birth. These include economic status, racial makeup, population density, crime rates, pollution and other aspects of the built environment, social groups and norms, as well as the service environment, such as availability and quality of food and other goods necessary for healthy living (e.g., trash pick-up, police services, etc). Shempf conceptualized neighbourhood characteristics as having both direct and indirect pathways that may influence the biological production of adverse birth outcomes (43).

2. **Psychosocial factors:** Mothers living in low socioeconomic neighbourhoods will be exposed to stress-causing life events, ranging from major incidents to daily hassles (80,81). Hassles include stressors, both chronic and short-term, such as crime, noise and built environment (82,83). A link between stress of different kinds and adverse birth outcomes has been consistently shown (84-92).
3. **Health behaviours and social characteristics:** These may include smoking, diet, prenatal care, alcohol intake and exercise as well as individual education and income. Neighbourhood characteristics including social groups and shared norms and values have been linked to the adoption and/or retention of health behaviours associated with adverse birth outcomes (80,93).
4. **Biological pathways:** The individual biological pathways that lead to adverse birth outcomes are multifactorial and vary according to the characteristics of the foetus as well as the mother. These pathways include maternal health issues as well as physical attributes such as obesity and weight gain during pregnancy, placental ischemia or vascular lesions and uterine over-distension (8). Shempf conceptualizes neighbourhood characteristics as having both direct and indirect pathways that may influence the biological pathways that determine adverse birth outcomes (43).

The model also stresses the importance of the links between these four contexts.

I modified Shempf's model by making the linking arrows between neighbourhood, psychosocial, health behaviour and biological factors bidirectional in order to reflect the interactive and reciprocal relationship between the different factors. A one-way arrow remains between the factors and birth outcomes to reflect the predictive nature of those relationships.

This framework fits well within the social ecology perspective; in order to understand perinatal outcomes we need to broaden our focus from the individual, micro level, characteristics and behaviour of prenatal women to the broader physical and social context that surrounds and influences her decisions, behaviours, and actions (and is in turn influenced by these). This concept of "broader" needs to deal with micro, i.e. the individual and the individual's interactions with both social and physical surroundings, meso, i.e. the joint influence of multiple "life domains" such as work and home, and macro, i.e. social influences that lie beyond local community, such as government policies (71,73). While women may appear to act individually, what they do is strongly affected by complex, dynamic, interdependent, yet "mutually influential" (73) contextual characteristics such as neighbourhood SES, education levels, familial and social norms, mores, and role models (71,73,74,94,95). The social ecology theory also recognizes that the influences on prenatal women by their social and physical environment can and will have different effects in different places (71-73,96,97).

Drawing on that theory, I recognize that neighbourhood context should represent a set of factors that reflect local, meso and macro levels of influence (71,73,74,94,95). The social ecology theory also recognizes that social and physical environmental influences on prenatal women can and will have different effects in different places (71-73,96,97).

The following literature review is structured around the Schempf model. Adverse birth outcomes are discussed first, individual level biologic pathways second, health behaviours third, psychosocial factors fourth and neighbourhood context and interaction effects last. The numbers presented in Figure 2.2 identify the sections where each model step is discussed.

2.3. Adverse Outcomes: Review of Previous Research

This review covers four outcomes: premature (divided into late and moderate to very premature), small for gestational age (SGA) and still births. These four are commonly used in analyses by CIHI (9), the Public Health Agency of Canada (18) and Statistics Canada (98). Low birthweight is not included as an adverse outcome as it overlaps with prematurity and SGA outcomes (8). Findings for low-weight births are included in this literature review where that research informs the discussion of preterm and SGA outcomes. Multi-gestational births are not included as they have not been widely recognized or studied as an adverse outcome in the bulk of previous research.

2.3.1. Preterm births occur at less than 37 weeks' gestation (8,9). Estimating gestational age has been problematic in the past. Most commonly based on the estimated date of the beginning of the woman's last menstrual cycle, estimates were often biased due to poor memory recall, irregular menstrual cycle, stress and other causes (99-105). More recent estimations of gestational age based on foetal ultrasound techniques have been found to be more accurate (106,107). Use of prenatal ultrasound has been increasing rapidly; in 2005-6 69% percent of Ontario pregnant women had two ultrasounds; in 2009-10, approximately 96% had two or more (108). This suggests that the gestational age variable used in this research is likely to be of consistently higher accuracy than available for previous observational research.

Until the late 1900s, preterm birth was most often viewed as a single adverse outcome for research and decision making purposes (9). This view assumed a single biologic pathway which could be managed with a single treatment or approach; it met with limited success and rates of preterm birth continued to increase in most Western,

industrialized countries. More recent research has shown that the pathologic processes for preterm labour at different gestational ages are complex, multifactorial and dynamic (9).

While 37 weeks of gestation is generally considered the cut-off for premature birth (1,2,9,109), subdivisions of the preterm period are encouraged to better understand the distinctly different profiles for different gestational ages and to separate out those births that have a significantly greater impact on overall perinatal health (110,111), as well as to better understand the direct and indirect healthcare costs (112). Sub-division cut-off points and the labels applied to these periods, such as 'extremely', 'very', 'moderately' and 'late premature' (as well as others) have not been consistent in past research (1,6,7). While late premature is commonly defined as 34 to 36 weeks (8,113), recent studies have strongly suggested that 35 weeks is a more meaningful cut-off point (114-118).

Preterm births may be spontaneous or medically induced through Caesarean section (C-section) or induction. About 30% of preterm births in Canada are medically induced (9). They are most often performed in response to complications that are likely to increase the risk of a further adverse outcome, such as hypertensive disorders, preeclampsia, maternal bleeding, foetal distress and intrauterine growth restriction. These same complications may also cause spontaneous preterm births (2,3,9,119,120). While labour induction and C-section were not included in the risk factors for this research, all C-section and induced births were retained for analysis, classified as pre-term (and/or another adverse outcome – if they were) or as a normal birth. As noted, most inductions/C-section observations are due to complications which we suggest will be represented by one of the other risk factors used, such as pre-existing health problem or maternal older age. Also observations regarding induction and C-sections were not consistently available from BORN Ontario across the analysis period.

Pathways that lead to spontaneous preterm birth are thought to vary according to gestational age. In addition to the factors noted above, others that have been found to affect the risk of spontaneous preterm birth include ethnicity, stress, genital tract infections, substance use, poor prenatal care, placental disorders, multi-gestational pregnancy, vascular lesions, uterine over-distension (2,3,119,120) and a history of preterm delivery (8,9). Research reviews suggest that biological factors such as health problems and smoking play a stronger role in preterm births than in SGA outcomes (9,36,109).

Behrman proposed that preterm births represent a cluster of adverse outcomes, each with its own predictive model that also overlaps with the others (8). This perspective may help to explain the wide array of predictors identified in previous research; a number of different adverse outcomes categorized as preterm births (i.e. all births with less than 37 weeks gestational age) have been explored and explained as if they were a single outcome. This perspective suggests that a large amount of research to date is not very meaningful. It also suggests that by breaking the preterm birth cluster into smaller groups (such as by different degrees of gestational age) we should see different models for each group.

2.3.2. Small for gestational age (SGA)[3] births are those with greater than 22 weeks' gestational age and birthweight lower than the tenth percentile for gestational age, adjusted by sex of the child (9). This cut-off is generally used as the current standard in Canadian research (18). No standard or meaningful sub-categorization of SGA births has yet been developed (8) but recent research has suggested that degrees of SGA, such as births between the second and tenth percentiles and those below the second percentile, have different explanatory factors (121).

[3] For confidentiality purposes, the sex of the child for these births was not released. BORN staff created the *SGA* variable for each birth.

The Public Health Agency of Canada established the tenth percentile standard (bifurcated between male and female) for identifying SGA births in Canada. Other, more stringent definitions of SGA births, such as two or more standard deviations below the mean, are not commonly used (122,123). The accuracy of the Public Health Agency standard has been questioned. Race has been shown to be associated with the size of new-borns; women from East and South Asia have smaller babies at full gestational age possibly due to biological or nutritional reasons (8,123,124); yet no tables adjusted for race have been made widely available.

Pathways that lead to SGA births have not been studied as extensively as those for preterm births, but a review of previous research has suggested that ecologic level variables play a stronger explanatory role in this adverse outcome (9). SGA births have also been shown to have a more complex aetiology than any of the other three adverse outcomes reviewed here (8,12,36,125).

Intrauterine growth restriction (IUGR), which results in SGA births, is thought to arise primarily because of placental insufficiency: the placenta is unable to transfer sufficient vital nutrients such as oxygen or glucose to and from the foetus (126,127). Causes of IUGR can be subdivided into foetal and maternal etiologies (127). Important causes attributed to the foetus are genetic diseases, congenital malformations, infections, multiple gestations and placental cord abnormalities (8,127). Categories of maternal causes are decreased uteroplacental blood flow, reduced blood volume, decreased oxygen carrying capacity, nutrition status and teratogens (127). Other important factors include short inter-pregnancy intervals, ethnicity, age, low socioeconomic status and poor nutrition during pregnancy (16,128-130), low education (12,16,131), substance abuse, maternal age, primiparity and maternal comorbidities such as hypertension and infection (8,9,132).

Maternal smoking stands out as arguably the most influential single risk factor in SGA births (8,128,133-137); it has been estimated to account for about one-third of growth-restricted births in economically developed countries (138). A number of studies have found that stopping smoking by 15 weeks' gestational age reduces the impact on the foetus; rates of SGA births among this group did not differ from rates for non-smokers (139-142).

The Canadian in-hospital rate for SGA births was 8.3% in 2006–7. Ontario demonstrated the highest SGA rate among the provinces at 9.3%, significantly higher than the 2006–7 Canadian average (9)[4].

SGA may represent an array or cluster of problems (34) commonly indicated by restricted growth. The finding that SGA may have a more complex aetiology than other outcomes (8,12,36,125) suggests these possibilities. Therefore, I expected that SGA will have relatively complex explanatory models.

2.3.3. Stillbirths are defined in Canada as those births occurring at greater than 20 weeks' gestational age or where the foetus weighed greater than 500 gm without signs of life at delivery (10). Rates of *Stillbirth* have decreased in Ontario over the past two decades, from five per thousand in 1995 to less than four per thousand in 2004 (143). Yet, as will be discussed later in this section, there are substantial disparities in rates found across ethnic groups.

Causes of stillbirth can be subdivided into:

- obstetric conditions which include cervical insufficiency, placental abruption or preterm labor, and abnormalities of the placenta, and

[4] Recent reports have shown the Canadian SGA birth rate to be 8.7% among singleton births in 2010–2011(426).

- genetic or structural abnormalities of the foetus including umbilical cord abnormalities and maternal medical conditions such as infection and blood pressure disorders (144).

Research has consistently shown different rates of stillbirth across racial and ethnic groups. In Canada stillbirth rates among First Nations, Inuit and Métis populations have been about double that of the non-Aboriginal population for the past century (18). Among African-American women in the U.S. the rate has been more than double those of White, non-Hispanic women (267). While these rate differences have been widely recognized, widely accepted explanations have not been found. Low SES-related factors have been put forward; however, these factors are not consistently accepted (8).

Stillbirth is perhaps the least well explained of the adverse outcomes presented in the current study. Infrequent events and bias in vital statistics (9) may help to explain this shortcoming in Ontario. The BORN Ontario Niday database does not share that bias, which may allow for more accurate modeling.

2.4. The Costs of Adverse Birth Outcomes in Canada

Compared with normal births, adverse birth outcomes are expensive to the social insurance system in Ontario and to society as a whole (9,13). While accounting for about 8.3% of the approximately 135,000 Ontario live births in 2006, initial hospital expenses for all premature births were approximately $104 million, close to the $128 million spent on the 91.7% of remaining births (9,26,29). This excess cost has been growing with the increasing rate of preterm births over the past several decades (8,9,18,25,145). In Canada, the United States and indeed most Western countries, initial costs increase inversely to gestational age for babies <37 weeks (8,32,146). Preterm, SGA and low birthweight babies

are more likely to die shortly after birth or suffer adverse health problems throughout childhood and adulthood (147,148). Long-term costs have also been found to include family financial burden, stress and dysfunction (147,149-154). SGA babies have initial average hospital costs of about twice those of non-SGA babies, at $2,297 versus $1,050 (9), which represented an excess cost to Ontario of about $14.2 million in 2006–7. SGA infants also face a higher risk of morbidity and mortality at all stages of life including hypertension, diabetes and cardiovascular disease (155-158). Due to its relatively recent inclusion as a category of adverse birth outcome, the long-term effects of SGA births have not been studied as extensively as those for preterm or low birthweight births (8).

My review of the literature found no estimation of the costs of stillbirths. While the cost of a post-mortem assessment of a stillbirth has been estimated at about $1500 USD, evaluation of other costs such as funeral expenses and non-monetary costs were not found in this review. The importance of non-monetary outcomes such as maternal and familial grieving, depression and other aspects of bereavement are well recognized and standard procedures for supporting and assisting mothers and families have been established (159), yet financial costs have not been estimated. It is generally recognized that such costs would be difficult to estimate (160,161).

2.5. Predictive Factors for Preterm, SGA and Still Births

The following review of the most important risk factors considers biological pathways, psychosocial factors, health behaviours, social characteristics and neighbourhood contextual factors (i.e., the components specified in the theoretical model). It is important to note that these are loose groupings for discussion purposes only; factors could often be placed under several headings. Moreover, some factors placed under different headings,

such as individual race/ethnicity and neighbourhood race/ethnicity, may not be meaningfully separated.

Past research has identified different risk profiles for the different adverse outcomes (8,9,15,36,162). While the risk factors are reviewed individually here, it is recognized that each of the adverse outcomes is most effectively explained by models made up of multiple factors, including individual and ecologic factors as well as interactions between them (2,8,9,12,162). Research findings for interaction effects are discussed later in this section.

Substantial research has gone into explaining adverse birth outcomes using both individual and ecologic level variables (8). The large majority of the studies discussed here have focused on explaining a single adverse birth outcome such as preterm (3,94,109,163) or low-weight births (164-166). Comparative analysis of several outcomes, their risk factors and the relationships between them remains relatively uncharted.

Capturing accurate risk factor data is difficult for several reasons. Behavioural data are particularly susceptible to recall error (common in observational research); recall of behaviours during pregnancy may be even more problematic due to the stigma of adverse health behaviours such as smoking or drinking as well as denial after the birth has occurred (8). Attribute data, such as race, first language or morbidities, are affected by unwillingness to supply information seemingly unrelated to the event, sensitivity to giving the information and unwillingness to volunteer or to collect information that may reflect negatively on the mother (167). Nonetheless, a number of these risk factors are clinically important as possible indicators of higher-risk patients. Whether they are statistically significant as risk factors in a large observational study is an open question.

2.5.1. Biologic Pathways

Biologic pathways are direct physical characteristics of the mother; they include health issues as well as physical attributes such as age, obesity and weight gain during pregnancy, placental ischemia or vascular lesions and uterine over-distension (8). Past research has shown the following individual level biologic factors to be related with adverse birth outcomes; although it is important to recognize that the specific pathway(s) may not be clear. For example race and ethnicity are given as biologic characteristics but the link to an adverse outcome may be, at least in part, through social factors such as racism or segregation.

2.5.1.1. Maternal Age: Older (>35 years) and younger (<20 years) mothers are more likely to have poor birth outcomes. In most of the previous research reviewed for the current study, older women have been found to be at greater risk of multiple, preterm (9,12,15,145,163,168,169) and SGA births (12). The risk was particularly striking among primiparae over 35 years of age (170). These findings are not universally sustained; Bianco and colleagues found that older age (>40 years) was not associated with risk of adverse outcomes when other risk factors such as economic status and health issues were adjusted for (17).

Women less than 20 years of age at the time of giving birth are more likely to have an elevated percentage of SGA and preterm births (6,9,36,171,172). The risk is higher among those aged less than 16 years (171,173-178). Research using small population areas in Calgary found that teenagers under the age of 18 were at greatest risk of stillbirth and women over 40 were at second- greatest risk (36). A body of research has suggested that much of the elevated risk of adverse birth outcomes among teenagers may be due more to

contextual characteristics than to maternal age *per se* (9,179,180). Researchers who have adjusted for contextual characteristics have found that older teenage women are fully capable of bearing healthy babies (171).

Maternal age clearly represents two distinctly different risk factors, young and old age, each possibly with its own set of individual and contextual risk factors. Past research has also been contradictory, suggesting that women at both ends of the continuum (except for very young) are (at least theoretically) capable of having healthy babies; adverse outcomes are explained by other mediating factors. This suggests that the key question in the current study is not whether young or old maternal ages are risk factors but in which interaction effects (e.g., with which individual or ecologic risk factors) will each be significant?

2.5.1.2. Race and Ethnicity: Preterm and SGA birth rates vary significantly by race and ethnicity (7,181-185) as well as by the extent of segregation and racism experienced by the mother (43,163). The relationship between race/ethnicity, lower SES, poor health behaviours and adverse birth outcome is a complex and classic example of confounding (432). While some researchers have hypothesized that the links between race or ethnicity and adverse birth outcomes are due, in part, to an associated lower SES background as well as poor health behaviours such as smoking and alcohol or drug abuse during pregnancy; other studies have shown that these differences persist after socioeconomic differences and health behaviours were adjusted for (100,185-189). Stress and infections during pregnancy have been proposed as at least partial explanations for these differences. African-American women have been shown to have a higher risk of a range of infections, including bacterial vaginosis and sexually transmitted infections, than White women (190-194). While the causal pathways for higher infection levels are unknown (and the risk of confounding is

high), higher levels of stress among minority groups have been hypothesized as being moderated by segregation and racism (192,195). Immigrants from South and East Asia have been found to have a significantly higher rate of SGA babies, although it is not clear whether this association is due to nutritional and/or health behaviours or the biological characteristics of these women (47,124,196-200).

Race and ethnicity appear to represent a different risk in Canada than in the United States. Racism and segregation (and resulting stress) appear to be the principal explanatory pathways linking these individual characteristics to high rates of adverse outcomes in the United States. In Canada the pathways appear to be more strongly related to immigrant status and country of origin (in the case of SGA births).

2.5.1.3. Maternal Health Issues: Babies born to mothers with pre-existing morbidities are significantly more likely to be born premature, SGA or still; the outcome varies with type of morbidity (2,9,134,191,201-203). Approximately 20% of births in Ontario are to mothers with pre-existing health problems (143). Diabetes and hypertension are the two most common conditions; both increase the chances of preterm and SGA births (9). Appendix 1 lists the health conditions captured in the BORN Ontario Niday database used for analysis in the current study.

Individual health issues, taken as a single risk factor, represent a broad indicator of the health of the mother. Diabetes and hypertension are the most common maternal health issues (9,143) and the biologic pathways linking these risks to adverse outcomes are relatively well researched. But other health issues, such as mental health, have been studied much less.

2.5.1.4. Infertility Treatments: The use of infertility treatments has risen dramatically over the past two to three decades and has been associated with older maternal age and the trend towards delayed childbearing. Different infertility treatments have been associated with increased risk of preterm birth as well as multi-gestational births, which in turn are associated with SGA, preterm and stillbirths. The strong association between infertility treatments and older maternal age represents a challenge to birth outcome research because of a variety of possible mediating and confounding factors, as noted in Section 2.5.1.1 above (204-206).

2.5.1.5. Pre-Pregnancy Weight and Weight Gain During Pregnancy: Pre-pregnancy weight and weight gain during pregnancy are closely aligned with patterns of diet and nutrition. Evidence suggests that a low pre-pregnancy weight is associated with an increased risk of SGA birth (111,207-210). Yet a meta-analysis of research on this topic found that pre-pregnancy body mass index had little or no relationship with the risk of preterm birth overall (211). A low level of weight gain during pregnancy has been found to be associated with an increased risk of preterm birth (111,210), particularly for women who are not overweight or obese (208). Obesity during pregnancy has been found to be associated with increased risk of SGA birth (212-216). Weight and weight gain, similar to maternal age, poorly represent risk factors that exist at the two extremes; too little or too much present increased risk, but each one represents a different pathway.

2.5.2. Psychosocial Factors

Psychosocial factors may mediate the influence of neighbourhood conditions on biological processes affecting birth outcomes via neuroendocrine, immune and vascular mechanisms.

These have been found to influence the timing of delivery directly and secondarily through susceptibility to infection and hypertensive disorders (43). A common mediator is stress.

2.5.2.1. Stress is defined as the effects of environmental demands, the emotional and cognitive responses to those demands and the biological process of stress responses, including cardiovascular and immune responses. Maternal stress has been linked to an increased risk of preterm delivery (84-87). These studies outline possible biological pathways that could link maternal stress exposures and emotional states to preterm delivery and SGA births (although with less support for SGA births). Behrman and colleagues (8) found that about half of the studies in their review showed a significant effect of stress on preterm birth.

Different sources and types of stress have been studied. Stressful life events such as divorce, loss of job (88), catastrophic events such as the 2001 bombing of the World Trade Center (89) or earthquakes (90) were found to increase the risk of preterm pregnancy but did not predict SGA births (112,217,218). Several American case-control studies of African-American women indicated that three or more life events during pregnancy were significantly associated with very low birthweight and preterm births (91,187). Chronic stress has been the subject of a number of large population based studies. These have evaluated a wide range of chronic stress sources, from German-occupied Holland in World War II and homelessness to low-income and minority status, and have found that experiencing chronic stress between 16 and 30 weeks of pregnancy was significantly associated with a risk of preterm delivery (219-221).

This body of research suggests that stress is difficult to measure, yet even with that challenge in chronic doses it has been found to be significant as a risk factor in preterm

births. While important, finding an individual (or contextual) variable that effectively captures it is beyond the scope of the current study.

2.5.2.2. Maternal anxiety is an individual coping reaction to stressful situations and behaviours (222). Although the effects of maternal anxiety during pregnancy have been evaluated in a number of studies, findings are inconsistent (172,209,210). Defining and measuring anxiety has shown itself to be a major challenge, especially in retrospective observational studies (8) and when working with different ethnic and cultural groups which appear to perceive and deal with anxiety differently from White Americans (217,223). Reviews of research by Behrman (8) and Dunkel Schetter (224) both found that when various results are considered, those studies that focus on anxiety specific to the pregnancy itself have shown that anxiety is predictive of preterm birth.

Anxiety, like stress, may be an important risk factor in predicting adverse outcomes, but effectively measuring it to the extent where inconsistencies are corrected for represents a major challenge. This is especially true in an observational study such as mine, where it is highly likely that mothers represent a wide range of cultural and ethnic groups living in wide range of settings.

2.5.3. Health Behaviours and Social Characteristics

Individual level maternal health behaviours (e.g., smoking, alcohol consumption and prenatal checkups) and social characteristics (e.g., education level, economic status and marital status) have been shown to be strongly associated with birth outcomes. This broad range of factors represents positive, protective factors such as social support as well as risk factors such as smoking.

2.5.3.1. Maternal Education: Most commonly defined as the number of years of education completed; lower levels of maternal education have been consistently linked to preterm, SGA, and stillbirth outcomes (8,9,15,16). In most Western countries women with less than a high school diploma have been found to have significantly greater risk of SGA (9,16,94,121,225) preterm and still births (9,54,226-228). There is reason for optimism, however: between 2001 and 2005, the proportion of all Canadian mothers with less than a high school diploma decreased from 13.4% to 8.4% (9).

At the other extreme, levels of higher education, usually indicated by post-graduate degrees, have been shown to be associated with adverse birth outcomes. Extended university studies and career building have been suggested to be important explanatory factors in delayed motherhood and, in turn, older age childbearing (9,14,169).

Research results have been inconsistent regarding the relative importance of education versus income in association with adverse birth outcomes. A substantial body of research has suggested that income is the strongest predictor (8,9,16,229) and that individual education is modified by income (79), whereas other studies have suggested that education is equal to or more important than income levels (94,95,128). Blumenshine and colleagues found in a 2010 systematic review of socioeconomic disparities and adverse outcomes that individual measures of maternal education were more consistently predictive of adverse outcomes than income. Yet area based measures of income were more consistently associated with adverse outcomes than individual measures (16).

Like age, lower levels and higher levels of education appear to represent two different risk factors. Low levels of education have been consistently linked to all three of the adverse outcomes included in the current study. Because each adverse outcome has a unique risk profile, the consistent linking of low education levels to all three suggests an

attribute that is remarkably effective at mediating the "right" risk factors which, in turn, lead to adverse outcomes. I surmise that low education will be more commonly found in significant interaction effects than as a significant individual predictor. Higher levels of education seem to be of interest primarily as an indicator of an older maternal age; that association will be of interest in our evaluation of our results.

2.5.3.2. Economic Status: Most usually defined in terms of household income, disparities in preterm, SGA and still birth rates by economic status have been consistently and repeatedly documented in Canada and in many other countries (9,128,130,131,187,230-232). While universal access to high-quality prenatal and other medical care have been found to have a moderating effect, significant differences persist (8,9,130,233,234). The moderating effects of income status on all adverse birth outcomes are most commonly thought to be through higher levels of damaging health behaviours such as smoking, alcohol and illicit drug use, poor diet and nutrition as well as higher levels of existing morbidities and poor living conditions. Another possible pathway is stress, likely due to a variety of causes such as unemployment (43,48,97,109,163,235), higher neighbourhood crime rates (109,236,237) and poor housing conditions (42,100,238-240).

According to the body of research reviewed, household income is one of the most consistently supported risk factors for all adverse outcomes. Yet if low income (i.e. low SES) is a significant risk factor for all adverse outcomes, then identifying the risk factors that differentiate between the outcomes within the population of low income women is even more important.

2.5.3.3. Employment and Physical Exertion: Employment during pregnancy has been the subject of considerable research. Work that is physically demanding and/or stressful has been hypothesized to increase the risk of both preterm and SGA births (241). But the concept of employment has been inconsistently defined and measured across studies (8). A large study across 16 European countries found no association between working during pregnancy and preterm births overall; yet increased levels of risk were found for women who worked more than 42 hours per week, women who stood for more than 6 hours per day and women with low levels of job satisfaction (242). In general employment and moderate physical exercise reduced the risk of adverse outcomes compared to unemployment and no exercise (208,241). This variable, like weight gain, represents two different risk factors representing the two ends of the extreme and, again, the two extremes are quite different. Over worked versus unemployed are different enough that they likely should not be considered as two ends of a continuous variable.

2.5.3.4. Intendedness of Pregnancy: Studies of unwanted pregnancies have shown that only about half of them result in a live birth (243). These women are less likely to seek early prenatal care (243-246), are more likely have poor health behaviors as well as heightened levels of stress and depression (247) and to be either younger or older mothers (243,244).

Whether an unintended pregnancy represents an unwanted pregnancy would seemingly determine the degree of anxiety as well as poor health behaviours that accompany it. This body of research suggests a commonality between older and younger maternal age, specifically that a pregnancy in either age group may be more likely to be unwanted (and carry with it higher levels of anxiety and poor health behaviours). An

important extension of this body of knowledge would include a better understanding of the proportion of pregnancies in the different age groups that are wanted versus not and the different behaviours or coping mechanisms that come into play.

2.5.3.5. Marital Status and Cohabitation: Extramarital pregnancy has been found to be associated with a higher risk of preterm birth (248,249), most commonly explained in terms of reduced social support and resources (249,250). The protective effects of marriage differ across racial, ethnic and age groups (8,251). A study of Quebec births found the rate of preterm births was highest among single mothers living alone and lowest in traditional marriages; rates for common-law unions were about midway between those two (252).

2.5.3.6. Social Support and Social Capital: The effects of social support on birth outcomes have been researched to a much greater extent than the effects of social capital but for much of the research the definitions and measurements of social support and social capital have not only been unclear but also overlap extensively, making differentiation difficult (8). Several systematic reviews of research have found no consistently significant association between social support and preterm delivery (224,253-255). Yet social support has been positively associated with a variety of other outcomes, such as reduced anxiety and a more positive overall perception of the pregnancy (256).

2.5.3.7. Sexual Activity: Sexual activity during pregnancy was of particular interest to researchers in the 1980s; the principal concern was that the direct effects of semen or alteration of vaginal microflora otherwise might raise the risk of preterm birth. Research from this time period presented consistent evidence that sexual activity during pregnancy did not increase risk of preterm birth (257). In fact, more recent studies have suggested a

reduced risk of preterm birth when sexual activity continues through pregnancy (258). These findings may reflect the benefits of support from an intimate partner (8).

The previous three factors all suggest the importance of individual level social support as a factor in predicting adverse outcomes. Intimate partners (indicated both by sexual activity as well as marriage and/or long-standing partnering) and social support represent a complex array of factors that suggest a healthy birth outcome results, at least in part, from individual level social support as much as any individual behaviour or characteristic.

2.5.3.8. Tobacco: Smoking during pregnancy has been shown to be one of the most prevalent and preventable (8) cause of preterm (9,135,225,259), SGA and still births (9,133). Fifteen percent of Ontario mothers reported in 2008 that they had smoked during their last pregnancy (23). Nonetheless, the relationship of cigarette smoking to preterm birth is not strong and not entirely consistent (8,139,260). For SGA and still births, tobacco use has been consistently shown to increase risk (9,261,262). Smoking during later pregnancy (i.e., after 15 weeks' gestational age) appears to be the period of greatest risk; conversely, smoking during the first 15 weeks of pregnancy has not been shown to have a significant effect on the developing foetus (142). Between 2000 and 2007, estimated "smoked-during-pregnancy" percentages decreased in Ontario from 12.5 % to 11.6% (22,23,263).

Exposure to second-hand smoke has a significant association (and probably a causal relationship with) SGA births, preterm births and neonatal mortality (9,135,264,265) as well as a reduced likelihood of quitting during pregnancy (266-269). About 11% of women

in Ontario in 2005 reported exposure to second-hand smoke during pregnancy, compared to 14% in Canada as a whole (18).

Smoking represents the most consistent predictor of SGA births but has only inconsistent links to other adverse outcomes. This suggests possible mediating or confounding effects with other risk factors such as age, health, education or income. I expect smoking to be strongly represented as an important factor in the SGA models but less so in others. The nature of its relationship with SGA and other adverse birth outcomes, whether it is significant as an individual predictor or only through interaction effects, will tell a great deal about the pathway(s) between smoking and SGA births.

2.5.3.9. Alcohol Use: any alcohol consumption during pregnancy has generally been found to adversely affect foetal growth (8,238,270). Findings from studies that have attempted to differentiate between moderate and excessive alcohol consumption have suggested that moderate consumption, e.g. less than one glass of wine per day, does not significantly affect the health of the foetus (8,193). Research on excessive alcohol use during pregnancy is generally limited by the quality of exposure data, self reported or otherwise. Recall bias affects the representational quality of the observations (8,9,23).

2.5.3.10. Illicit Drug Use: Cocaine and marijuana are the two most commonly studied drugs for their potential effects of adverse birth outcomes (8). There is little evidence to suggest that marijuana use is linked to adverse birth outcomes (188). Research has consistently shown an association between cocaine use and adverse birth outcomes, particularly preterm birth (8), but there are evident challenges in the accurate measurement of the use of an illicit substance. In addition, other lifestyle factors that are often linked to

cocaine usage may form confounding factors in the association with adverse birth outcomes (208,271,272). These challenges have complicated effective causal analysis.

Alcohol and illicit drug use appear to underscore a theme that seems consistent in the research reviewed here: extremes are a risk factor. Extreme older age, younger age, low income, low education, excessive alcohol and drug usage within the context of Canadian society are predictive of an adverse birth outcome.

2.5.4. Neighbourhood Contextual /Ecological Factors: Clinical and interventional research that focused on individual level factors to explain adverse outcomes made up the large majority of this research until the 1980s (8,273). But these factors were found to explain outcome rates neither consistently nor effectively (8,41,79,274). While contextual factors had been recognized as important, their inclusion in birth outcome research was not common until the 1990s (8).

Ecologic level factors are different from individual level variables in several ways that are important to research design and analysis. Most ecologic variables, with a few exceptions (e.g. population density), are compositional rather than contextual. Factors representing education, income and proportion of immigrants are aggregated from individual characteristics. Aggregating individual data points such that they represent an area potentially distorts the estimates within each region if one assumes that every unit within that region has a characteristic equal to the aggregate value (e.g., income). This effect is also known as an ecologic fallacy. Critical to avoiding the ecologic fallacy is recognizing that an aggregate variable describes the environment of the area not the individual characteristics of residents. Hence, for example, median household income

describes the context of the area within which its residents live day-to-day, not the income of a given individual household.

A challenge in each of the studies discussed below has been to link ecologic level variables to adverse birth outcomes. This link must inherently work through the biological pathways that create birth outcomes. Figure 2.2 represents this; all links to birth outcomes are moderated by biologic pathways.

Ecologic level variables also introduce the need for a defined spatial unit, such as a census block, city, county, and so forth. These units or areas are a critical part of geographic clustering; other important considerations in different geographic analysis tools include their size, how their size is determined, differences in size, the populations that live within those units and the heterogeneity of those populations. These units are also important to comparisons between studies; findings based on analyses using relatively small areas may not be comparable to analyses using large areas. These variations are discussed at greater length in chapters 4 and 5.

The following neighbourhood factors have been found to be predictive of adverse birth outcomes:

2.5.4.1. Neighbourhood Social Environment: Level of neighbourhood cohesion and organization, civic engagement and involvement, crime and residential stability (including home ownership vs. rental) are hypothesized to influence birth outcomes through pathways such as the availability of social support, effectiveness of coping strategies and exposure to chronic stress. They have been widely studied (2,110,163,187,275,276). Yet a review of the research evaluating contextual social support variables found no consistent association between these factors and adverse birth outcomes (8).

Indicators of individual level social support, such as marriage or longer term partnering, were found to be have significant risk reducing effects (see Section 2.5.3.6). Neighborhood social environment assumes that neighbourhood level's of cohesion and organization will "trickle down" to the individual mother. Based on the review noted above this assumption does not seem supported.

2.5.4.2. Neighbourhood Income Levels: Neighbourhood economic status has been consistently shown to be one of the strongest predictors of birthweight as well as preterm, SGA and still births (9,95,128,130,277-279). A wide variety of explanatory variables including poor access to healthy foods and healthcare facilities, poor housing quality and high crime rates have been cited (8,9). Residents of disadvantaged areas, in turn, are not only at a greater risk of physical injury (ranging from domestic accidents to assaults) but are also exposed to higher levels of everyday life stressors. Neighbourhood income context also influences shared behavioural norms such as smoking, poor diet, physical activity, prenatal care and substance abuse. Neighbourhood effects and their association with health behaviours have been shown in studies by Boardman and others (80,93).

Neighbourhood socioeconomic conditions are closely linked to racial and ethnic composition and may have different effects on birth outcomes for different ethnic groups (7,91,186,280). Several of these studies, most clearly that of Pearl (280), also showed that foreign-born mothers were less affected by neighbourhood income effects (i.e., that living in a low-income neighbourhood did not increase their likelihood of an adverse birth outcome).

Neighbourhood income has been cited as perhaps the most influential ecologic factor in predicting each of the four adverse birth outcomes. If this finding holds true,

hotspots for all four outcomes should be found in close geographic proximity (i.e. in low income areas) and area income should also have a strong presence in regression models for each outcome. Whether the other risk factors can effectively differentiate between the different adverse outcomes will be of key interest.

2.5.4.3. Neighbourhood Education Levels: Neighbourhood education level (such as the percentage of the population over 20 years of age without a high school diploma or equivalent) is commonly used as an indicator of neighbourhood socioeconomic status (8,9,94,128). Even with inconsistent measures of area levels of education (8), research findings have been consistent: lower levels of neighbourhood education are significantly associated with preterm, SGA and still births (6,12,16,42,94).

The ecologic level of education for a given area presents a part of a picture, of the context, within which residents of that place live. It informs us of the possible social norms and behaviours of a given place; it does not suggest an education level for any given individual living in that area. As noted, it is commonly used almost interchangeably with neighbourhood income to describe area socioeconomic status; the two are strongly associated. An important part of this analysis will be to examine this relationship between the two SES indicators and to critically evaluate if they represent different risk factors.

2.5.4.4. Racial and Ethnic Composition: O'Campo and others found that, in general, women living in areas with higher concentrations of people from minority ethnic backgrounds experience higher levels of stress-causing factors including crime, under-employment, unemployment and poor housing conditions (40,99,185). Outcomes have been shown to differ by different ethnic backgrounds. For example, White non-Hispanic women living in such areas have higher rates of adverse outcomes than African or Hispanic

women (47,185,281). Yet the healthy immigrant effect, whereby recently immigrated women are less likely than their peers to have adverse birth outcomes, seemingly contradicts these findings (8,194,282,283). The healthy immigrant effect suggests that living in areas where higher concentrations of minorities or large proportions of recent immigrants also live (276) may be modified by other, possibly cultural, factors which have not yet been made clear. Social capital, cultural perceptions of health and self-selection (i.e., the belief that healthier people immigrate) have all been proposed as possible explanations of this effect (47,196,284). It is important to note, however, that the healthy immigrant effect decreases with years lived in Canada and/or the United States (194,196,282). Whether this decrease is due to long-term wear of segregation (and the possible stress-causing factors associated with it) or to other factors has not yet been discerned.

Clearly the racial and ethnic characteristics of a population living within a given area have been shown to have an association with adverse birth outcomes. Yet their inherent confounding with other culturally defined contextual variables such as social support, stress, and racism, limits understanding these important variables. The differences between the United States and Canada are illustrative culturally defined variables; race and ethnic attributes appear to be more strongly associated with size of the foetus and healthy immigrant effects rather than levels of stress.

2.5.4.5. Neighbourhood Physical Environment: Examples of factors in the physical environment to which a pregnant woman may be chronically exposed include toxicants, noise, air pollution, condition of housing, road and sidewalk repair, existence and condition of parks (109,237). Reviews of research evaluating the impact of such factors on birth

outcomes are inconsistent in their conclusions. For example, three different meta-analyses have reached different conclusions regarding the association between pollution and preterm births; one found sufficient evidence (285) and two did not (21,278). Behrman and colleagues concluded that the execution of these studies has strongly influenced their findings (8); studies using measures of ecologic pollution and toxicant exposure are limited by differences in levels of exposures, timing of exposure (during pregnancy) and individual maternal characteristics, as well as high levels of association between explanatory factors (187,286-289).

Neighbourhood environment commonly refers to human-made physical surroundings that provide the context for human activities (e.g., living, working and playing). It is more often applied to urban settings where human-made systems and infrastructure may have a stronger day-to-day effect and where a greater number of people are affected by the built environment than in less densely populated areas. Characteristics of the neighbourhood environment and how they are measured, like all ecologic variables, are greatly influenced by how "area" is defined. Use of smaller spatial areas will allow for greater resolution and a better understanding of differences between places; the use of census dissemination areas as geographic units in the current study should allow for this.

2.5.4.6. Population Density: The links between population density and adverse outcomes are complex. In Canada, both low-density (rural) and high-density (urban) areas have risk factors for adverse birth outcomes. Rural factors include isolation from health care (9) and higher rates of smoking (350). Urban factors include higher stress levels from contextual characteristics such as higher crime rates and greater concentrations of poverty (9). They also include greater concentrations of immigrant populations (East and South Asian are the

two most common) which have been found to be highly associated with SGA births (378). Urban versus rural residence of mother is the most common proxy measure of population density in birth studies. Inconsistent findings have been reported for preterm births in Canada and in Ontario but for SGA births the findings were consistent: SGA births are significantly more common in urban than in rural areas (9,290). But the interplay of other factors cannot be ruled out. For example, research has consistently shown that East and South Asian women, who tend to favour urban areas, have smaller babies (378). The differences between urban and rural SGA rates have been shown to be greater in Ontario than for Canada as a whole (9). In areas that are relatively isolated from cities (relative isolation reflects road, air and water transportation connections) and with rural/low density, low socioeconomic characteristics have been found to be associated with higher levels of adverse outcomes (68,120,277).

Population density potentially represents a greater range of attributes than the distance to the nearest hospital. While the effects of urban versus rural have been studied in past research, the use of relatively small geographic areas in the current study should allow the opportunity to improve on the current level of understanding. We expect urban (vs. rural) to act primarily as a mediating factor; important insights will be gained from the interaction effects between this and other risk factors.

2.6. GIS Analysis in Adverse Birth Outcome Research

Epidemiology, medical geography and geography have used the identification of spatial disease clusters as an important step in analysis of both infectious (34,291-293) and non-infectious diseases since, arguably, the founding of each discipline (78,185,294-296). GIS analysis techniques have been applied more and more to analyses of adverse birth outcomes

at national (36,280,286,288,290), provincial and state levels (226,297,298), and at the level of health regions (143,145), cities (78) and subsections of cities, such as neighbourhoods and groups of neighbourhoods (36,50,95,299).

To date, small-area spatial analysis of Canadian adverse birth outcomes has been limited. A Sault Ste. Marie study found neighbourhood-level smoking behaviours to be spatially associated with low birth-weight outcomes (37). Research by the Calgary Health Region found "meaningful" associations within sub-areas between adverse birth outcomes[5] and maternal age (young and older), and maternal smoking (36). Small-area level SES measures have consistently been found to form independent predictors of individual level birth outcomes (7,79,130,252).

2.6.1. Local Cluster Analysis

Spatial analysis of epidemiological data, such as adverse birth outcomes, has been noted as strong in hypothesis development but relatively weak in hypothesis testing through rigorous methods and falsification (293,300). Since 1995 GIS analysis tools have been increasingly developed that can investigate and identify spatial clusters of disease and other adverse health outcomes (293). Global autocorrelation tools for aggregated data, which were developed first, generally offer a formal measure of Tobler's First Law of Geography: "Everything is related to everything else, but near things are more related than distant things" (301). These tools estimate the degree of spatial similarity, or association, observed among neighbouring values of an attribute over a study area. But tools that estimate global autocorrelation, such as Moran's I, Ripley's *k* and Geary's *c*, do not identify the location of local clusters, only the general likelihood of their existence. When very large geographic

[5] Preterm, SGA and low birth-weight births and perinatal mortalities.

areas are analyzed, global tools risk missing local autocorrelation (302). The focus in the current study is on local cluster identification.

2.6.2. Local Cluster Identification

Local spatial cluster analysis avoids loss of autocorrelation information in large databases. It does so by measuring spatial dependence in relatively small portions of the study area; portion dimensions are specified by the researcher (such as radius from a centroid, adjacent neighbours only or within *x* kilometres). Local clustering tools are able to detect hotspots within a limited area in a large place.

2.6.3. Local Cluster Analysis Methods

Several local cluster detection tools are in common use in epidemiological research. Local Moran's I (LISA), Kulldorf's spatial scan and Besag-Newell were the three most commonly cited in a review of epidemiological research (303). Others were considered but these three were found relevant to the research questions of the current study and were reviewed and evaluated most carefully for use within it.[6] The findings of the review are summarized below.

The Besag-Newell method is favoured among epidemiology researchers because of its relatively high power for tests on rare diseases (304). However, this statistic has been found to be inaccurate in its identification of disease clusters in rural areas and also tends to detect clusters larger than "their real size" (305). In addition, the requirement (in Besag-Newell's R) that the user must define the distance radius centered at each cell (306,307) made the test unsuitable for the purposes of the current study given the size of Ontario, the

[6] The decision to focus on these three was based on applicability to the current study's research population, available reference material for evaluation and access to an application with adequate documentation.

large number of DAs within it, and the great heterogeneity in their size. A radius distance sufficient to cover multiple (34) DAs in a rural area would easily include hundreds (possibly thousands) of DAs in an urban area.

Kulldorf's spatial scan statistic is also recommended in epidemiology (and rare disease research) because it can adjust for multiple testing and heterogeneous background population densities (303) as well as because of its relatively high power for tests on rare diseases (304). However, this scan statistic assumes that a circle will most effectively capture the centroids of adjacent regions (34,305,306), which does not necessarily reflect the wide diversity in shapes and sizes of DAs in Ontario (306,307). The test's default circular shaping of regions also results in a relatively high rate of false positives and false negatives within clusters, given the tool's likelihood calculation method (308,309). A study by Tango and Takahashi found that the circular spatial scan statistic also identified larger clusters than the "true cluster" due to the inclusion of geographic areas that do not contain elevated risk (308). Statistical applications which included adaptations of this tool to detect non-circular clusters were not readily available at the time of the current study.

Local Moran's I (LISA) is commonly used in epidemiological research for identification of local disease clusters (34,303). It is also used extensively in geographic (310-312) and medical geography research (309,313). It has two weak points that are commonly cited in its use for analysis of rare events. These are:

- its inability to adjust spatial units and the number of events occurring within them to ensure that there are sufficient events for analysis of rare events such as cancer;
- it does not adjust for heterogeneous background populations (34).

The local Moran's I statistic for local cluster analysis and identification is based on two important assumptions:

1. **Normality:** This means that all observations follow identical and independent normal (Gaussian) distributions (34,314). Normality is a concern if there is heterogeneity in background and at-risk populations for spatial units. Large populations may occur near each other, resulting in significantly high values of local Moran's I due to correlations between unit population sizes rather than to any spatial patterns of adverse outcomes (e.g. disease events). Use of proportions in place of counts and a conditional Monte Carlo application (see discussion below) are commonly used corrections for possible violations of this assumption, although how well they correct has been questioned (34, 299).
2. **Randomization:** This assumes that the values observed were randomly assigned to the fixed locations. Variances of incidence proportions and correlation between area populations suggest that the randomization assumption is not well met (34,302).

   A conditional Monte Carlo application has been commonly used to correct for the possible lack of normality and randomization (34,315,316) and to validate the *p*-value of local Moran's I statistic values (317). The conditional randomization strategy treats the observations as if they were spatially uncorrelated and results in more conservative identification and presentation of local spatial clustering (302).

   A Simes statistic has been found to correct for lack of independence in the local Moran's I statistic. The Simes adjustment (318) is recognized as superior to the more conservative Bonferroni correction when large numbers of multiple comparisons are carried out (314,317-319). Use of the Simes statistic in the current study will also address Waller and Gotway's concern that the Bonferroni adjustment is too

conservative as a correction for multiple hypothesis testing (34) under conditions where a correlation may exist between neighbouring DA incidence proportions (as is the case in much of GIS analysis) (314,317-319).

The local Moran's I tool has been found to be conservative in identifying hotspots (309). In a comparative study, the local Moran's I and Kulldorf's spatial scan statistic were contrasted for identifying clusters of breast, lung and colorectal cancer in Long Island, New York (320). Significant spatial patterns for all three diseases were found by both tools, which confirmed clustering of breast cancer mortality previously found by Kulldorf and colleagues (321). However, the two methods identified slightly different cluster locations. Similar findings were made in research by Hanson and Wieczorek (322) and Nødtvedt and colleagues (323). The two methods identified different characteristics of the clusters: local Moran's I tended to identify smaller, localized clusters suggesting the core of the cluster, while the scan statistic indentified larger clusters that likely reflected the cluster's full extent (293).

While the local Moran's I statistic has been found to have relatively low power when used with rare diseases (309,324), it is important to note that adverse birth outcomes are not rare events (defined as a rate equal to or less than 1 in 1,500) (325).

The local Moran's I (I_i) tool (LISA[7]) was selected for cluster analysis in this research. This decision was based principally on:

- the tool's relatively conservative identification of hotspots and lower likelihood of false positives (309);
- its characteristic of identifying smaller, localized hotspots as well as hotspot cores (322,323), which suggests a better fit with our geographic area. The heterogeneity

[7] Local indicator of spatial association (302,314).

of DA geographic sizes (rural ones tend to be large) suggests that a spatially conservative identification method would better suit;

- the ability it grants the researcher to specify the rule by which "neighbours" are defined in the identification of clusters (as different from the specified radius from a centroid), which appears better suited for the expanse of Ontario and the heterogeneity of DA geographic sizes; and
- its common use in the fields of both epidemiology and geography, which allow for comparison to previous research findings in a variety of disciplines.

2.7. Analysis of Interactions Between Contextual and Individual Level Factors

Substantial research has shown there to be three categories of predictors of adverse birth outcomes: individual, ecologic and interaction effects between the two (6,17,128,130,146,162,213,228,278). Ecologic variables including SES, pollution and race/ethnic make-up of the population have been shown to have effects independent of the individual risk indicators as well as significant interaction effects with individual factors (182,252,281,326,327). Thus a mutually reinforcing and reciprocal relationship between people and place (328) needs to be understood and explored in any modeling effort.

2.7.1. Hierarchical Regression Analysis

Multilevel, hierarchical regression analysis has greatly facilitated and expanded research into the interaction effects between individual and ecologic level variables. One of the first epidemiological applications of this approach (to adverse birth outcomes) led O'Campo and colleagues to conclude both that there was substantial interaction between macro and individual level risk factors for low birthweight and that multilevel models should be used

in future analysis of birth outcomes (162). Her findings that ecologic indicators such as poor housing, crime and unemployment rates modified the relationship between individual level risk factors and birthweight have been consistently supported by others researching different adverse birth outcomes: preterm (46,48,329), SGA (236,330,331), low birthweight (7,86,332) and still births (21,333,334).

Additional hierarchical research has consistently supported the links presented in Schempf's model:

- Neighbourhood social characteristics such as poverty (86,335) education (46,94), crime (6,128,237), segregation (47,109), immigration (42,185,280,336,337), racial and ethnic makeup (280,338), contextual levels of smoking (93) and social support (112,253,290,339) have been found to modify individual level psychosocial factors such as stress (80,81,84-87,89-92) and individual level health behaviour factors such as smoking, diet and prenatal check-ups (80,93) which, in turn, are linked to higher levels of adverse birth outcomes.

  Geronimus (275,276) introduced and Holzman (163) later expanded on the "weathering" hypothesis which suggests that women living in high-deprivation neighbourhood environments develop "accelerated aging" that would increase risk of preterm delivery. Accelerated aging was potentially explained, in part, by delays in health care, adverse effects of unemployment, higher rates of crime, exposure to pollution, stress and other "causes" endemic to high deprivation neighbourhoods. Links between psychosocial factors, principally stress, health behaviours and biological factors were discussed at length in Section 2.5.

- Neighbourhood built-environmental characteristics such as quality of housing, roads, sidewalks, playgrounds (48,327,340) and environment damaging pollution (341-344) have also suggested a direct association with biologic pathways and adverse birth outcomes.

This body of the research suggests that each of the adverse birth outcomes generally results from a complex set of interactions between individual and ecologic factors (2,8,16,110,261,328,345). Yet these and other studies have also shown that these interactions are not consistent; individual and ecologic level characteristics exert different amounts of influence under different individual and neighbourhood conditions (48,162,163,290). Therefore, the fundamental question is whether these inconsistencies are due to different studies using different methods or to actual differences in predictors of adverse outcomes in different places; there are no universal models. The current study will test the origin of these inconsistencies.

My research focuses on better understanding the range of models that may explain adverse outcomes in different places. No research was found for this review which specifically used hierarchical regression analysis to concurrently explore different adverse birth outcomes in diverse local areas. The majority of studies reviewed focused on explaining a single birth outcome such as preterm or low-weight births. Shempf and colleagues, for example, focused on only low birthweight; they did not differentiate between outcomes when presenting their model. Although noteworthy exceptions were found (208,278,331,346), concurrent analysis of different adverse birth outcomes from diverse areas and the methodical comparison of their explanatory models remain relatively uncharted. My research has attempted to address these gaps.

Hierarchical logistic regression analysis will be used in the current study to identify significant interaction effects. Its ability to allow for both neighbourhood and individual level characteristics to be included in the modeling of adverse outcomes makes it an ideal tool for our purposes. There are a number of statistical tools, such as PROC MIXED, GENMOD, NLMIXED and GLIMMIX, which allow for hierarchical logistic regression analysis. These all complete the same basic functions although outputs and ease of use differ (,347,390). Compared with these other statistical tools, GLIMMIX allows for:

- statistical models to be fit to data with non-constant variability and with non-normally distributed responses. These models assume normally distributed random effects, but conditional on these random effects data are free to have any distribution in the exponential family, including binomial and chi-square (347).
- models where there are random as well as no random effects. In the case of quasi-likelihood estimation the first two moments are assumed to be known (347);
- models fitted to multivariate data where observations may not have the same distributions, which is applicable to the current study (348);
- more versatility in meeting the conditions of this analysis as well as more capability of handling the current study's large data sets; and
- fewer errors by an inexperienced user (349).

Each of these allowances makes GLIMMIX better suited for this analysis.

2.8. Summary

This chapter summarized the extensive past research aimed at explaining adverse birth outcomes. Researchers have become more aware that each of the different adverse birth outcomes, such as SGA, preterm and stillbirth, represents a distinctly different event with

different explanatory models. Furthermore, each outcome may represent a complex cluster of problems with a set of overlapping factors of influence (8). Predictors that explain one of the adverse outcomes do not necessarily explain the others and predictors that explain one of the problems within the cluster (e.g., late premature births) may not explain another (e.g., very premature births). While ecologic factors and their interactions with individual level variables have been shown to be important in explaining adverse outcomes, those explanations have not affectively differentiated between outcomes. More specific models are needed.

Little prior research has compared the different adverse birth outcomes. Explanatory models for each have generally been developed in separate studies. The relative importance of different explanatory factors, especially ecologic ones, for different adverse outcomes is not well understood. In addition, the relative importance of place in explaining the different outcomes has not been effectively explored. Past research has largely comprised studies modeling single outcomes in a given place. Those places are not usually comparable across studies.

The current study attempts to address these gaps. The BORN Ontario Niday data set, linked with Statistics Canada census boundary files and census data, allowed me to accurately represent the four adverse outcomes as well as nine key ecologic and individual level factors for births in Ontario across a five-year period. Data with this degree of accuracy and quality at both the provincial and local levels will produce important results not previously available.

This chapter also summarized published materials regarding analytical methods and tools necessary to meet the current study's research questions. Geographic cluster analysis represents a powerful analytic method, yet one that is faced with several challenges,

primarily in meeting assumptions when analyzing rare occurrences. Different cluster identification tools for are better able to meet these assumptions, but consideration of the characteristics of the areal units under analysis is also required in deciding which tool is best suited for the purpose. Tools for hierarchical regression analysis were also briefly reviewed. Careful consideration of the character of both the dependent and independent variables is necessary to make an effective choice for which statistical tool to use.

There are biases inherent to the data as well as the statistical tools selected. The small numbers issue, multi-gestational births, missing data, and others pose concerns that we have corrected for in part, for example through the use of proportions at DA levels, the use of statistical tools that adjust for missing data and by grouping hotspots to represent larger geographic areas. A corrective factor that should not be ignored is the size of the database, approximately 625,000 births linked to 15,808 DAs. The power offered in a database of this size will help to overcome sampling bias as well as the small numbers issue that cannot otherwise be dealt with. However we recognize that some bias is inherent in this research and that this bias needs both recognition and further research.

Chapter 3. Research Methods

3.1. Overview

This research followed a stepwise process; the execution of each step depended on the outcome of the previous one(s). Figure 3.1 presents a high-level map of the steps taken and shows the sections in which they are discussed. The research can be divided into two phases. The first phase addressed the identification of spatial clusters of significantly higher levels of adverse outcome events. It involved grooming and linking birth outcome data to DAs, the creation of a proportion for each adverse outcome (i.e. count of adverse birth outcome/total births) per DA as well as for the full province and then the identification of hotspots for each outcome. This phase is subdivided into steps one through four, shown in Figure 3.1. The second phase fitted regression models for each of the four adverse outcomes to the full province and then to local groups of hotspots (except for stillbirths, for which no local area analysis was able to be completed). This phase is captured in steps 5 through 8. Comparisons were made of local area and full-province models for each outcome as well as across the different outcomes. This work is reflected in step 9a–c.

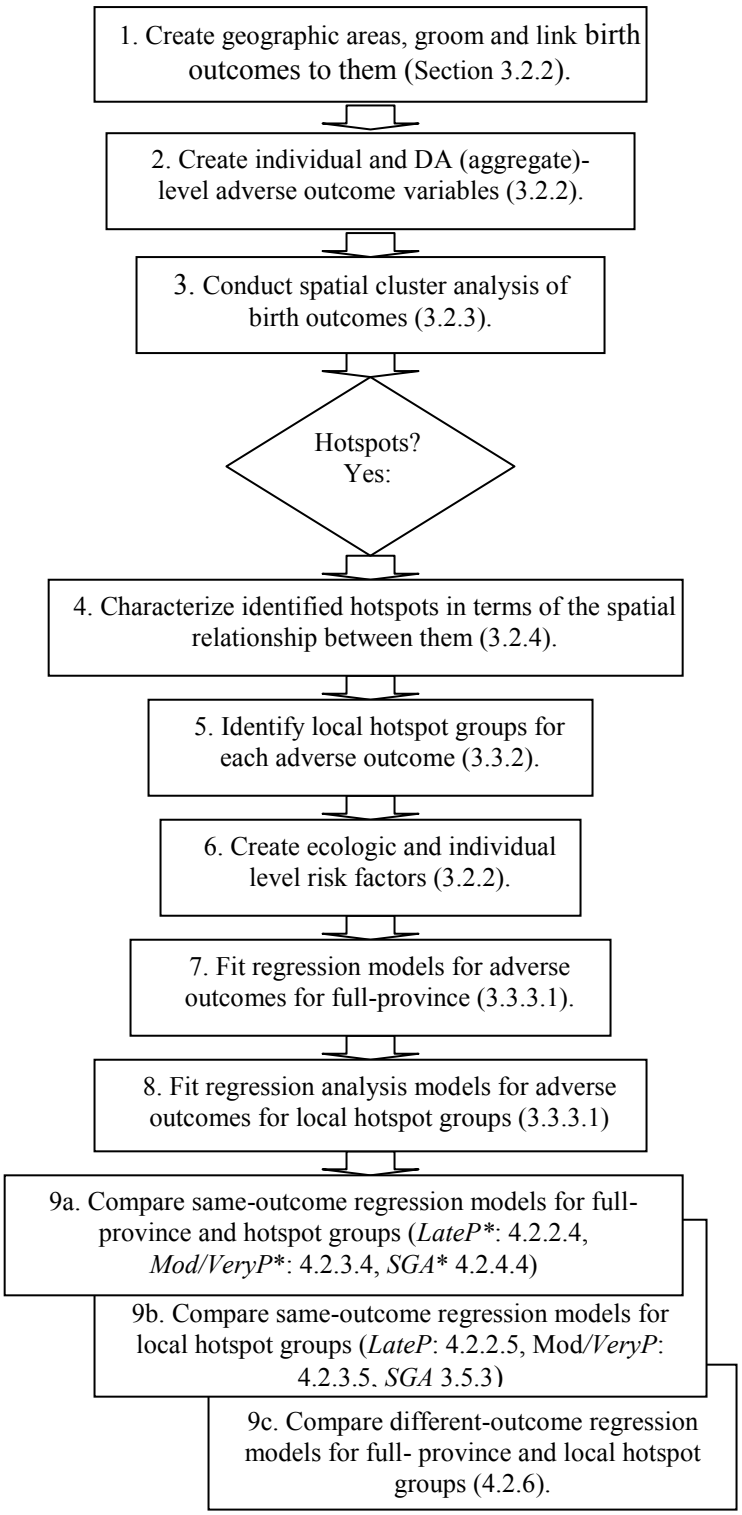


Figure 3.1 Overview of Research Steps

* See pp. xv-xvi for explanations of these abbreviations; see also Figure 3.2.

Ten different regression models were created as represented in Figure 3.2.

Outcome/ Full Prov. (Section #)	**Late Premature Births (*LateP*)**	**Moderate to very premature births (*ModVeryP*)**	**Small for gestational births (*SGA*)**	**Stillbirth *(Stillbirth)***
	Full-province model (4.2.2.1)	Full-province model (4.2.3.1)	Full-province model (4.2.4.1)	Full-province model (4.2.5.1)
Local hotspot groups (section #)	Three models (4.2.2.2)	Four models (4.2.3.2)	Three models (4.2.4.2)	Hotspot group analysis was not carried out for *Stillbirth* due to confidentiality concerns

Figure 3.2 Overview of Hierarchical Regression Models Created for this Research

The same dependent and independent variables were considered for each model fitted for the full-province as well as local hotspot groups. Local hotspot groups represent non-random samples of hotspots identified in the full province. See Section 3.3.2 for an extensive discussion on the selection of these hotspot groups. The last step involved comparing and contrasting the different models that were fitted; the results are presented as Step 9.

3.2. Geographic Cluster (Hotspot) Analysis

The goal of this first phase of the current study is to determine if there are hotspots of adverse birth outcomes and then to describe their spatial relationships to one another. Local Moran's I (LISA) was the principal GIS tool used in this phase of analysis for reasons described in Section 2.6.3.

Further investigation and hypothesis generation in this first phase involved:

- evaluating the spatial relationships of the hotspots for the different outcomes; for example, whether hotspots occur in the same geographic places;
- comparing geographic size and birth densities.

The investigation led into the second phase, which explored risk factors for the different adverse outcomes at different geographic scales and places.

3.2.1. Study Population and Data Sources

Observations for this research were taken from the BORN Ontario Niday Database. This province-wide, internet-based surveillance system collects information on maternal health characteristics and behaviours as well as maternal and birth outcomes at the time of birth (10). It was founded in 1995 by the Perinatal Partnership of Eastern Ontario as a regional database. In 2009 it was granted prescribed registry status by the Ontario Ministry of Health and Long-Term Care and since 2009 has represented close to 100% of hospital and midwife-assisted birth events. The Niday database is one of several managed and maintained by BORN Ontario (350).

This research used all 636,005 births registered in the database between 1 January 2005 and 31 December 2009. These represented about 90% of all births (live or still) in Ontario for that time frame. The proportion increased across the five years, from 82.5% in 2005 to 97.5% in 2009[8] (351).

The BORN Ontario Niday database was chosen over the alternatives of vital statistics and hospital discharge abstracts. Ontario vital statistics data appear to experience selective under-reporting of around 4% of those at higher risk for adverse birth outcomes (18,98,196). Birth information derived from hospital discharge abstracts also has several limitations. For example, outcome indicators must be derived from ICD-10-CA and ICC

[8] Proportions were estimated based on a comparison with adjusted vital statistics databases.

codes which do not directly specify the most common adverse outcomes; these must be derived (9). Maternal health behaviours such as smoking are not captured in hospital discharge statistics (9) and health characteristics such as pre-existing morbidities are inconsistently captured. Midwife-assisted births, approximately 1.8% of Ontario births in 2006, are also not captured in discharge abstracts (9). By contrast, the BORN Ontario Niday database captures birth outcomes as well as maternal health behaviours and pre-existing health problems at the time of birth. BORN Ontario uses rigorous quality control and assurance review steps to assure that the data presented was complete and accurate. Quality control steps involve automatic system edit checks during data entry to identify potential errors and duplicate records. Quality assurance mechanisms involve training, on-going data entry support, as well as on-going quality audits. Quality audits use re-abstraction to verify concordance between data in the perinatal database and mother and infant chart information in order to determine validity of the data (167). See Appendix 12 for a more complete description of quality assurance audit methods used.

The Canadian six-digit postal code for mother's place of residence, available on the BORN Ontario Niday database, was used by BORN Ontario analysts to link births to census dissemination areas (DAs). A DA is a relatively small (in population terms), stable geographic unit with a median overall population size of 540 (inter-quartile range [IQR] of 450–711). It is the smallest standard geographic area for which all Canadian census data are disseminated (352). Although DAs have relatively similar overall population sizes, their geographic size varies substantially from urban to rural places; DAs have a median size of 0.15 km^2 (IQR: 0.09–0.37) but a range of 0.002 to 70,696 km^2. While the term "neighbourhood" has been used synonymously with DA in previous research (95,130,277) this can be misleading. Neighbourhood suggests a close grouping or nearness of people

which is not necessarily the case in a substantial number of geographically large, rural DAs across the province. "Neighbourhood" will be used to refer to a local area, but caution must be used: the term does not apply equally to all DAs or groups of DAs.

3.2.2. DA Refinement and Outcome Variable Creation

My database included 636,005 births for the five-year span 2005–9. For multi-gestational births each foetus was considered an individual birth. 10,360 births were discarded from analysis because of missing, incomplete or non-Ontario postal codes. This reduced the birth count to 625,645. An additional 3,895 births were removed due to incomplete DA identification numbers or because the DAs to which they were linked had no census data. This left 621,750 births (that is individual foetuses) linked to 16,599 DAs (of the provincial total 18,922). This resulted in a median of 24 births per DA (IQR: 15-39). DAs with no births linked to them, approximately 2,320, were eliminated. DAs that had fewer than five births, 1,333, were identified. For confidentiality reasons (based on an agreement with BORN Ontario) no DA with fewer than five births would be individually analyzed (see Section 3.3.2 for a full discussion of BORN Ontario confidentiality requirements). These DAs had to be agglomerated with one or more adjacent DAs. For discussion purposes, DAs with fewer than five births are referred to as "target DAs".

All births that met the grooming standards (see Section 3.2.2) and for which there was a BORN Ontario record was treated as a birth with its own outcome(s) and predictors, including those that were multi-gestational, were included in the database. Dropping multi-gestational births completely from the research database, as has been done in a large proportion of previous research (for example (5,7,14,14-18)), would have meant the loss of

important observations (multi-gestational births represent approximately 2.1% of all births in our database). Multi-gestational was not included as an adverse outcome in this research as there was no precedent for it (for example (3-8)). It was not included as a risk factor; this is consistent with research reviewed (12,13) (although previous research has shown that different adverse outcomes, such as preterm and still births, are highly associated (8-11)). Berkowitz, in her extensive review of preterm birth studies concluded that, while strongly associated with preterm birth, multi-gestation "may not properly belong in the same category" as other risk factors (11). In this thesis the terms 'birth', 'birth event', 'delivery', and 'outcome' will all refer to the foetus or foetuses that result from a pregnancy. 'Birth outcomes', i.e. preterm, SGA, and stillbirth, refer to the gestational age, birth weight, and viability of each foetus at birth.

The steps taken to agglomerate the 1,333 target DAs were:

1. Criteria for agglomeration matching were defined. Candidate DA(s) had to be adjacent and have like urban/rural and household median income characteristics to the target DA (40). PCCF+ urban/rural categories and income quintiles were linked to each target DA (353,354). PCCF+ income quintiles (QAIPPE) were created by Statistics Canada based on a regionally adjusted measure of 2006 household income, summarized at the DA level. The urban/rural variable (CSIZMIZ) was a derived variable created by Statistics Canada; a DA was designated as rural if it was not in a town or municipality or within the commuting zone of one or more larger urban centres with populations of 10,000 or more (354).

2. Geographically adjacent DAs were identified. Statistics Canada provided a file containing the first-level, adjacent (queen's-neighbour[9]) DAs for every Ontario DA (355). All adjacent DAs relevant to target DAs were identified. All adjacent DAs were checked for birth counts as well as urban/rural and income quintile variables. Those with no birth events or where the matching criteria could not be verified were eliminated.
3. Adjacent DAs that met matching criteria were identified in two stages. First a "descending" search (based on birth count) of adjacent DAs was completed for each target DA. If there were multiple adjacent DAs that met the matching criteria, the one with the highest birth count was chosen. The descending option was chosen in order to minimize multiple DA aggregation. SAS[10] code was created in order complete this step.

    Next, target DAs that were not satisfactorily matched with an adjacent DA(s) were dealt with. There remained approximately 270 target DAs that could not be aggregated based on the criteria or for which aggregation did not achieve greater than four births. These were resolved individually. In about 250 cases, failure to aggregate (or to exceed four births) was due to lack of an adjacent DA which shared a like income quintile. For those cases a +/- 10 percentage points criterion was established where target DAs were aggregated with adjacent DA(s) that had a median

[9] Adjacency was defined as first-level (i.e., in direct contact with the "core" DA and Queen-neighbours). "Queen-neighbour" defines adjacent as a neighbouring DA that shares any boundary contact with the core DA, including even a point-length, such as a diagonal DA meeting at a corner (317).
[10] SAS Institute, Cary, North Carolina, USA.

household income within +/- 10 percentage points[11] of the target DA. Where the adjacency criterion could not be met due to an "island" effect (i.e., there were no contiguously adjacent DAs due to data or no births), target DAs were aggregated to the geographically closest DA that met the matching criteria.

A total of 582 agglomerated DAs were created. This resulted in a final count of 15,808 DAs with 621,750 births linked to them.

4. Every DA came with a unique identification code, a DAUID number. A new DAUID code was created for the DAs created through aggregation, providing a unique identifier for each of the 582 aggregated DAs. Non-aggregated DAs retained their original DAUID codes. For the remainder of this discussion, the term "final" will refer to the set of DAs which include those that were agglomerated and those that were not; the term "original" will refer to the set of DAs prior to agglomeration. In the final GIS database, for aggregated DAs the spatial boundaries between the original DAs were "dissolved". Aggregated DAs were treated as single entities.

Thus a new dataset was created which contained four variables:

1. final DAUID codes;
2. final DA birth counts;
3. original DAUID codes (for the aggregated DAs subsumed in the final DAUIDs); and
4. original DA birth counts.

[11] The +/- 10% alternative to the income quintile criteria was developed based on a survey of quintile values where matches had been made. +/- 10% approximated these matches but was somewhat more exacting. We determined that a more exact option was preferable to less.

This file was returned to BORN Ontario. Birth counts for final DAUID codes allowed BORN Ontario to verify that no final DA had fewer than five birth events. They then linked information for all births: birth weight, gestational age, stillbirth, as well as maternal characteristics and health behaviour variables to the original DAUID codes. These original DAUID codes were then stripped from the database, leaving the final DAUID codes (with the birth and maternal information linked to them). This latter step ensured that individual birth data could not be linked to any DA with fewer than five births. BORN Ontario returned a file with birth outcome and maternal characteristics/ behaviour data linked to the final 15,808 DAs.

The following variables were delivered by BORN Ontario for each birth event:

- gestational age (in weeks);
- weight (in grams);
- live-born or stillborn; and
- small for gestational age.

From these variables, four adverse birth outcome indicators were created:

1. Late premature births (*LateP*), where the gestational age was 35 or 36 weeks. Babies born before 37 weeks of gestation are generally considered preterm (8,9). Subdivisions of the preterm period into very, moderately and late premature births are encouraged to distinguish those births that have a significantly greater impact on perinatal health (4,273) as well as healthcare costs (229). Sub-division cut-off points and the labels applied to these periods are not consistent (2,9,109).

Thirty five weeks' gestational age was established as a cut-off point between late and moderate/very premature for two reasons. First, recent research strongly suggests that 35 weeks' gestational age is an important milestone in developmental health (114-118). Babies born at 35 to 36 weeks' gestational age are more likely to experience different short- and long-term health and developmental issues than those born at 34 weeks or younger (118). Second, in order to ensure that sufficient observations were allowed for both levels of this adverse outcome.

2. Moderate to very premature births (*ModVeryP*) were those births with a gestational age of less than 35 weeks.
3. Small for gestational age (*SGA*)[12] were those births with greater than 22 weeks' gestational age and where the newborn was smaller than 90% of babies born in Canada with the same gestational age and sex (9). Creation of a sex-adjusted SGA indicator required a sex-of-child variable; but for confidentiality purposes this information could not be released. The SGA variable for each birth was created by BORN Ontario staff.
4. Stillbirths (*Stillbirth*) were those births occurring at greater than 20 weeks' gestational age or where the foetus weighed greater than 500 grams without signs of life at delivery (23,356). Bivariate dependent variables were created in order to maintain comparability to previous research.

Variables for each adverse outcome were created that represented the proportion of each adverse outcome for all births in the full-province and in each DA. Because adverse birth outcomes are not exclusive of one another, with the exception of *LateP* and *ModVeryP*, a single birth may have been coded with two or more adverse outcomes. Table

[12]

3.1 displays the counts and percentages of multiple adverse outcome births. Each outcome was treated as a separate birth. Given the very small percentages of multiple outcome codes it was not expected that overlaps would distort the analyses.

Table 3.1 Count of Births with Multiple Outcome Codes, Ontario Births, 2005–9 (N = 621,750 births)

Adverse outcome(s) (total provincial count)	**Count of multiple coded adverse births (% total provincial births)**	
	SGA	*Stillbirth*
LateP (30,875)	2,544 (0.41%)	291 (0.05%)
ModVeryP (22,833)	2,085 (0.34%)	2,411 (0.39%)
SGA (54,446)	-	941 (0.15%)
Stillbirth (3,615)	-	-
**LateP+SGA+*	-	83 (0.01%)
**ModVeryP+SGA+*	-	616 (0.1%)
* = 3 outcomes coded for a birth (consider row and column) - = empty cell		

3.2.3. Geographic Cluster Analysis

The local Moran's I for each DA gives an indication of significant spatial clustering of similar values such as a high level of an adverse outcome for a DA and those DAs that surround it (302,314). A hotspot is defined as two or more contiguous DAs which have outcome values significantly higher than surrounding DAs (357). The I_i statistic, which ranges from -1 to +1, can be interpreted as an indicator of local spatial clustering as well as an indicator of the influence of individual DAs on the magnitude of a provincial (global) statistic. It also identifies cold spots and clusters of DAs which have outcome values significantly lower than those surrounding. It also identifies 'outliers,' which are individual DAs with either significantly higher or lower outcome proportions surrounded by low- or high-proportion DAs respectively (302,358). The mathematical expression of the local Moran's I statistic I_i as used in the current study's analysis takes the following form:

The local Moran's I statistic of spatial association is given as:

$$I_i = \frac{x_i - \bar{X}}{s} \sum_{j=1, j \neq i}^{N} w_{i,j} \frac{(x_j - \bar{X})}{s}$$

Key elements in the statistic are:

1. A standardized z-score for an observed attribute x is created by $\frac{x_i - \bar{Y}}{s}$,

   where:

   x_i is an observed attribute (outcome proportion) for DA*i*, $\bar{X}$ represents the mean of attribute x_i for all DAs:

   $$\bar{X} = \sum_{i=1}^{N} \frac{x_i}{N}$$

   and s is the standard deviation of x_i for all DAs:

   $$s = \sqrt{\frac{\sum_{i=1}^{N} (x_i - \bar{X})^2}{N}}$$

   where N equals the total number of DAs.

2. Spatial weight, w_{ij} = 1/#*neighbors*. First-order queen's neighbours were used in these equations; first-order indicates that only immediately adjacent DAs (i.e., those that touched any point on the boundary of the target DA) were considered.

3. I_i then equals the summation ($\sum_{j=1, j \neq i}^{N}$) of z-scores for a given attribute multiplied by spatial weight w_{ij} (denoting the strength of connection between DAs i and j for the given attribute x) across each row j of the spatial weights matrix where j does not equal i. (302,357,359)

A positive value for I_i indicates that an attribute for DA i has adjacent neighbour DAs with similarly high (or low) variable values. The I_i value is tested against the null hypothesis

Ho: $I_i = 0$. If the *p*-value is small enough (<0.05), the cluster is considered significant. A negative value for I_i indicates a DA has neighbouring DAs with dissimilar values; this DA would be considered an outlier (357).

Missing data, that is DAs with no observation value(s), were dealt with in two ways. First, DAs with missing values were identified and removed from the dataset in the initial steps (see Section 3.2.2). Second, the SpaceStats application used for the current study corrected for missing values; spatial weight sets created by adjacency evaluations were independent of missing values; and calculations of local Moran's I statistic was based only on those neighbouring DAs with data (317).

Monte Carlo conditional randomizations (N=1000) were used to correct for the lack of independence between observations (as shown by measures of spatial autocorrelation) and to validate the *p*-value of local Moran's I statistic values. Under conditional randomization, the *p*-value was fixed for each individual DA while the values for all other DAs are randomly assigned to different locations. (This process was repeated 1000 times in the current study as each DA was evaluated in turn.) A distribution is created from these simulations; the observed value is then compared to the upper and lower tails of the null distribution in order to get an estimated significance (317).

A Simes adjustment statistic was used to correct for multiple hypothesis testing and lack of independence, which arose because the z-scores for certain areas were used in the calculation of the statistic for neighbouring areas. The Simes adjustment (318) is

recognized as superior to the more conservative Bonferroni correction when large numbers of multiple comparisons are carried out, as is the case in much of the GIS analysis (314,317-319). SpaceStats[13] version 2.2 was used for all spatial statistical analysis. ArcGIS 9.2 was used for GIS database building and grooming.[14]

3.2.4. Describing and Characterizing Hotspots

The current study's first research question had two parts: 1) Did hotspots exist for the adverse outcomes? and 2) If so, where were they and how were they spatially related? The most important aspect of describing the hotspots was to explore the spatial relationships between them for different adverse outcomes. The goal here was to discover the degree to which hotspots for different outcomes represented the same geographic places.

The first analysis tool was a simple count of DAs included in hotspots for two different adverse outcomes. Based on the results of the first step, I continued with three more tools which were used to validate and explore that outcome. The second analysis tool was Cohen's Kappa coefficient, to measure the extent of agreement between I_i scores for hotspots of different adverse outcomes. DAs that were in hotspots for a given outcome, hotDAs, were given a score of 1; DAs not in hotspots were given a score of 0. If those scores were viewed as two independent ratings of the DAs, the Kappa coefficient equalled +1 when there was complete agreement between ratings and equalled -1 when there was complete disagreement. When the observed agreement or disagreement exceeds what would be expected by chance, kappa is respectively positive or negative, with its magnitude reflecting the strength of agreement or disagreement beyond what would be expected by chance alone (360,361). In the current study, if hotspot DAs for two different outcomes

[13] Biomedware, Ann Arbor, MI.
[14] ESRI, Redlands, CA.

were identical the Kappa score would have been +1; if they were completely different the Kappa score would have been -1.

The bivariate Moran's I was used to further explore the spatial relationship between hotspots. This tool measures spatial independence between two different adverse outcomes (in contrast to the univariate Moran's I tool, which measures the degree of spatial association between a single given variable). Paraphrasing Getis, the bivariate Moran's I statistic was defined as follows:

> Given a set ***S*** containing ***n*** geographical units, (i.e., DAs), bivariate spatial autocorrelation refers to the relationship between a target variable, ***t***, observed in each of the ***n*** localities and a secondary variable, ***s***, also observed in each of ***n*** localities. It is a measure of geographical proximity between *t* and *s*, defined for all ***n***(***n***-1) pairs chosen from ***n*** (362).

In short, the bivariate Moran's I assessed the extent to which the level of a given adverse outcome in one DA was spatially associated with the weighted average of another adverse outcome in neighbouring DAs (314). It gives an idea of the degree to which two variables, ***s*** and ***t,*** tend to be clustered together or evenly dispersed over the study area surface (362).

A standard Spearman's rank order correlation was used to further corroborate the findings of the bivariate analysis. The proportion of one adverse outcome was correlated with the proportion of another within the same DA for all DAs in the province. This tool measured the degree of statistical linear association between two variables, here the degree of association between the levels of two different adverse outcomes within the same DA. A score of +1 indicated that the two variables were in complete positive association (i.e., when one increases the other increases); a score of −1 would have occurred when the

variables were in complete negative association. If the two scores were in agreement, the same DAs would be expected to be in hotspots for both adverse outcomes. The degree of association between all pairs of adverse outcomes within each of the 15,808 DAs was measured.

A final way of characterizing hotspots was to compare demographic and geographic characteristics. Size (km^2), overall population and births per km^2 were compared.

3.3. Hierarchical Regression Analyses Methods

The general goal of the second phase of the current study is to build at least a partial regression model of the adverse birth outcomes within identified hotspots and how those models differ across different geographic scales, different local geographic areas and different adverse outcomes. The primary tool used in this phase was hierarchical regression analysis. This subsection reviews the steps taken to prepare for and execute that analysis.

This use of regression analysis to identify important independent predictors of an outcome was one of three uses of regression specified by Vittinghoff (133). It is important to note that the other two uses were not goals:

- prediction of future outcomes, thus a final indicator of the predictive strength of the models ( ) was not included in my results.
- isolating the effect of a single, primary, independent predictor, was also not of interest in the current study.

The two main preparatory steps were to create the independent variables that would be used as risk factors in the analysis and to identify the geographically diverse hotspots to which regression models would be fitted. The independent variables are summarized in table 3.2. The four outcome variables to be modeled are summarized in table 3.3.

Geographically diverse hotspots are summarized for three of the four adverse outcomes in tables 4.9, 4.12 and 4.15. Owing to small numbers, diverse hotspots could not be evaluated for stillbirths.

Table 3.2 Risk Factors for Regression Modeling						
Variable	**Abbreviation**	**Type**	**Frequency**	**Percent**		
Individual birth variables						
Maternal Health Problem	*HlthProb*	Binomial				
0			426,700	87.86		
1			58,966	12.14		
missing			136,084			
Teenage (<20 years)	*Teenage*	Binomial				
0			600,097	96.53		
1			21,591	3.47		
missing			62			
Older age (≥35 years)	*Olderage*	Binomial				
0			490,457	78.89		
1			131,231	21.11		
missing			62			
Smoked (at any time during pregnancy	*Smoked*	Binomial				
0			484,756	88.38		
1			63,724	11.62		
missing			73,270			
Ecologic (DA level) variables						
DA is in an urban setting	*Urban*	Binomial				
0			54,221	8.72		
1			567,529	91.28		
missing						
				Mean	**Std. Deviation**	**Median (Q1, Q3)**
Women ≥ 20 in DA with no high school diploma, %	*%NoDip*	Continuous	619,622	18	13	17 (9, 25)
Asian immigrants in DA population, %	*%Asian*	Continuous	619,347	5.8	9.77	1.86 (0, 7.068)
Median DA household income (in $1,000s)	*MedInc*	Continuous	621,750	65.95	27.14	64.28 (45.84, 83.65)
Women ≥ 20 in DA with greater than bachelor's degree	*%HigherEd*	Continuous	619,622	8	7	7 (3, 12)

3.3.1. Regression Analysis Risk Factors

Table 3.2. presents the nine risk factors used in hierarchical modeling for both provincial and hotspot analysis[15]. The four birth outcome variables are summarized in Table 3.3. The nine independent risk factors included five ecologic and four individual level variables. "Ecologic level" refers to risk factors which inform us of the character of the full dissemination area (DA), such as median household income (*MedInc*) or percentage of Asian immigrants (*%Asian*). Individual level risk factors inform us of the character or behaviour of the individual mother, such as having a pre-existing health problem (*HlthProb*). As discussed in the literature review (Section 2), these nine variables (available from BORN Ontario Niday and the 2006 Census databases) were important factors in understanding adverse birth outcomes.

Table 3.3 Outcome Variables Used in Hierarchical Analysis of Adverse Outcomes

Variable	Abbreviation	Type	Frequency	Percent
Late premature	*LateP*	Binomial		
0			588,155	95.01
1			30,875	4.99
missing			2,720	
Moderately and very premature	*ModVeryP*	Binomial		
0			596,197	96.31
1			22,833	3.69
missing			2,720	
Small for gestational age	*SGA*	Binomial		
0			541,344	90.86
1			54,446	9.14
missing			25,960	
Stillbirth	*Stillbirth*	Binomial		
0			618,135	99.42
1			3,615	0.58
missing			73,270	

[15] With the noted exception of stillbirth mortalities, for which no hotspot group analysis was carried out. See discussion in Section 3.2.2.

The four individual level risk factors from the BORN Ontario Niday database were:

1. Older maternal age (*Olderage*). This individual level risk factor indicated whether the mother was >35 years of age at time of the birth. In 2006–7, older women were shown to be at greater risk of multiple (4.2%), preterm (9.5%), and SGA births (7.9%) (18,363).
2. Teen maternal age (*Teenage*). Whether the mother was <20 years of age at time of the birth. In 2006–7 teenage mothers were found to be significantly more likely to have a higher percentage of SGA (10.7%), and preterm (8.3%) births (18,363).
3. Smoking (*Smoked*). Whether the woman said she smoked at any time during the pregnancy. Smoking during pregnancy has been shown to be a principal cause of preterm, SGA and still births (135,364).
4. Maternal health problems (*HlthProb*). This individual level risk factor indicated whether the woman had a pre-existing health problem(s) at time of the birth. Appendix 1 provides a more extensive definition and listing of the different morbidities and conditions considered in the dataset. Babies born to mothers with pre-existing morbidities are significantly more likely to be born prematurely, SGA or to be stillborn; the risk for each varies with type of health problem (32,365-371).

The five ecologic level variables from the 2006 Census were:

1. Median household income for each dissemination area (*MedInc*). This ecologic level variable indicated the median household income (including income from all sources in the household) for all households in the DA, based on census data. Neighbourhood socioeconomic status, such as median household income, has been found to be consistently associated with SGA, preterm and still birth outcomes in Ontario and across Canada (9,95,128,130,231,277,279).

2. *Urban*. The urban/rural variable was a derived variable created by Statistics Canada; a DA was designated as rural if it was not in a town or municipality or within the commuting zone of one or more larger urban centres with populations of 10,000 or more (354,372). Urban areas in Canada produced significantly higher proportions of SGA births than rural ones, 8.7% versus 7.0% respectively, in 2008. The difference in Ontario, 9.2% versus 6.6% (9), was greater.
3. Lower maternal education (*%NoDip*): This ecologic level variable indicated the percentage of women in each DA, ≥20 years of age, who did not have a high school diploma (or equivalent). Maternal education has been consistently found significant in predicting preterm, SGA, and still birth outcomes (7,18,79,130,228,231).
4. Higher maternal education (*%HigherEd*): This ecologic level variable indicated the percentage of women in each DA, ≥20 years of age, who were educated beyond a bachelor's degree. While more education has been widely recognized as important to reducing risk of adverse birth outcomes, graduate-level education has been found to be associated with delayed childbearing and hence to be a predictor of adverse birth outcomes (9,373).
5. Asian immigrant population (*%Asian*): This ecologic level variable indicated the percentage of the population in each DA that volunteered (in the 2006 Census) as being an immigrant from either East or South Asia. Women from those areas have been found to bear babies consistently below the 10% SGA cut-off (using Canadian standardized tables) while being healthy and fully formed by all other indicators (196,374).

3.3.2. Local Hotspot Group Selection

In order to analyze birth outcomes for geographically diverse hotspots, first those hotspots had to be identified. Identifying hotspots for further analysis necessitated consideration of two different sets of requirements: confidentiality established by the data custodian and the requirements of the hierarchical regression analysis. The confidentiality requirements established by BORN Ontario were that single dissemination areas were not to be analysed or results published, only clusters[16] (i.e., groups). In the data sharing agreement with BORN Ontario it was stipulated that:

- a group was defined as 13 or more contiguous geographic areas (i.e., DAs).
- an event threshold of 5 births in each DA would guarantee that analyzed groups (hotspots made up of 13 or more DAs) would have birth event counts well above 65.[17]

The assumptions of hierarchical regression analysis generally stipulate that the sample of birth events should contain five or more adverse events per predictor variable (375,376). Nine predictor variables were used in this analysis, which required that the samples of birth events (i.e., local hotspots) have approximately 45 or more adverse events. Across the adverse outcomes, hotspots had a mean of between six and seven hotDAs with a mean adverse event count between 0.8 and 2.5 per hotDA (tables 4.2–4.6). The mean number of DAs, 7, times the highest mean number of adverse events, 2.5, shows that a high mean DA adverse event count per single hotspot would be about 17; therefore, only a minority of single hotspots had the 45 adverse birth events sufficient to meet the confidentiality or analysis requirements.

[16] The term "cluster" was used in the BORN agreement; to avoid confusion with GIS analysis results I use the term "group" herein.
[17] BORN Ontario Data Sharing Agreement, 9 February 2010.

In order to meet these requirements I decided to identify and analyze local groups of hotspots. A group was defined as a set of hotspots that:

- had close geographic proximity: the closer events were, the more likely they were to be related (e.g., to share the same known or unknown ecologic variables). Groups were defined based on the need to capture as many hotspots within as small a geographic area as possible.
- had sufficient adverse birth events to allow for hierarchical regression analysis techniques to be applied and confidentiality commitments to be met.

For discussion purposes these local groups of hotspots are also be referred to as local areas.

Three geographically diverse groups of hotspots were identified for comparison purposes for each outcome. An extra, geographically large group was added to the moderately to very premature groups to allow for the inclusion of hotspots with a mix of urban and rural DAs. For stillbirths, with only 27 hotspots widely dispersed across the province, no groups met these criteria. Local hotspot group analysis was therefore not conducted for stillbirths.

It was recognized that the geographic boundaries of these groups were arbitrarily established (within defined criteria) and that modifying them could modify the regression outcomes. Steps were taken to address these concerns. For example, once group areas were tentatively identified, a "minimum" group was established that met the minimum analysis and confidentiality criteria within as small a geographic space as possible. Regression analysis was completed and *F* and *P* value results were noted. The next spatially closest hotspot(s) were added and with each addition regression analysis results were reassessed. The final groups did not differ from the initial minimum group in terms of the predictors

that were found to have statistically significant effects. A *P* value < 0.10 was considered statistically significant.

3. 3.3. The Regression Analysis Tool

The SAS 9.3 GLIMMIX procedure[18] was selected for use for all regression analyses. To develop a hierarchical regression model using this tool, at separate (i.e., individual patient) levels, one "classic regression" model was developed for each of the *J* level 2 units (i.e., DAs) using individual level predictors. The general form of these level 1 models was: $Y_{ij} = \beta_{0j} + \beta_{1j}(X_{ij} - \overline{X}_{..}) + \varepsilon_{ij}$,

where:

Y_{ij} represented a given birth outcome (e.g., gestational age) for a given individual birth, *i,* nested within a given DA, *j*. Y_{ij} was estimated by more than one individual level predictor variable;

β_{0j} represented the intercept for the *j*th level 2 unit (DA);

β_{1j} represented the regression coefficient associated with a level 1 predictor variable, *X* (e.g., maternal age), for the *j*th level 2 unit (DA);

X_{ij} represented a level 1 (individual) predictor or covariate (e.g., maternal age);

$\overline{X}_{..}$ represented the grand mean of all X_{ij} (e.g., the mean of all maternal ages); and

e_{ij} represented the error term (i.e., the amount of variation in Y_{ij} left unexplained by the model) (61).

The "hierarchical" part of the model involved both accounting for and differentiating between individual level and ecologic level variation within and across DAs

[18] SAS Institute Inc., Cary, North Carolina.

(57,61). In both provincial and hotspot regression models, the individual birth and the DA were always the two levels analyzed. Accounting for the two levels was accomplished by considering the regression coefficients, β_{0j} and β_{1j} (from the model above), as dependent variables and modelling each with appropriate DA-level predictor variables; this took the form:

$\beta_j = \lambda_0 + \lambda_1 U_j + \varepsilon_j$ and $\beta_j = \lambda + \lambda U_j + \varepsilon_j$.

Substituting these equations into the classic regression equation for Y_{ij} yielded the combined model: $Y_{ij} = \gamma_{00} + \gamma_{01} U_j + \gamma_{10}(X_{ij} - \bar{X}) + \gamma_{11} U_j (X_{ij} - \bar{X}) + \varepsilon_j + \varepsilon_j (X_{ij} - \bar{X}) + \varepsilon_{ij}$

This hierarchical model appropriately combined one individual and one DA-level covariate (X_{ij} and U_j, respectively). This form of hierarchical modeling allowed for analysis of all predictor variables together, for assessment of confounding, as well as for testing of all statistical assumptions and goodness of fit. Use of hierarchical methods also minimized the potential ecologic bias that might have resulted from working with different levels of data (377-381).

3.3.3.1. Regression Analysis Steps

A stepwise approach was used to build the regression models for each of the adverse outcomes for the full-province as well as the hotspot groups. The term "risk factor" is used to represent each of the nine independent variables in the regression analysis. The term "predictor" is used to represent an individual risk factor or the interaction effect between risk factors that was found to be statistically significant in the regression analysis.

The analysis followed a sequence of steps:

1. Fitting each model began with a full main effects analysis using all nine risk factor variables. The four variables found to be most significant (i.e., those with the highest *F*

value) were identified and rank ordered. In order to manage the potentially large number of interactions that could occur but still adequately assess important effects, a modified forward-selection approach was developed using these main effect, rank-ordered variables. This approach, described more fully in the following paragraphs, allowed the creation of a parsimonious model and reduction of the risk of over fitting the model.

2. The rank-ordered variables from the main effects models were used to develop models with two-way interactions. The first risk factor from the rank-ordered list was added to the model and one by one the remaining eight (with the exception of *Teenage* and *Olderage*, since these two individual level variables were mutually exclusive and could not form an interaction) were added both individually and as an interaction effect with the first-ranked risk factor.
3. Each time a new risk factor was analyzed, predictors (i.e., individual risk factors and/or interaction effects) with a $P>0.1$ were removed; those with $P<0.1$ remained.
4. After all eight risk factors were assessed, the second-ranked risk factor was added to the model; the remaining seven risk factors were added and the above steps were repeated. These steps were repeated for all of the top-ranked risk factors. This sequence allowed for all two-way interactions to be considered in order of ranking.
5. Three-way interactions were next considered. If interaction effects found in the final model met the rule $A \cap B$, $B \cap C$, $C \cap A$ then a three-way interaction of A*B*C was tested. No three-way interaction was found to be significant.
6. After all risk factors had been analyzed, the resulting forward-selected model was then assessed and refined using a modified backward-selection approach. For this step the standard level of $P<0.05$ was used. Beginning with the predictor with the highest P

value, the model was reduced one predictor at a time. Interaction effects were removed before their component parts. Regression analysis was rerun after each predictor was removed; the decision on which to remove next was based on the revised *P* value findings.

7. The final full-province model retained predictors with a $P < 0.07$. In hotspot group model building a *P* value of <0.1 was used due to the relatively small n.
8. When an interaction effect was present, additional steps using contrasts were taken to understand the nature of the relationship (i.e., the level of the predictor at which the interaction effect was significant). See Appendix 2 for an annotated example of GLIMMIX code used to create the reported odds ratios. The use of contrasts is described below.

    The use of contrasts refers to evaluating continuous risk factors bound to be a part of a significant interaction at different levels in order to better understand the nature of the interaction effect. For continuous*continuous and continuous*binary variable interactions, the models were recreated at high-, mid- and low-range settings for each continuous variable. The range settings for each variable were based on data distribution parameters. Low range was generally set at or below the upper boundary of the first quartile, mid range near the median and high range near or above the upper boundary of the third quartile. Odds ratios and confidence intervals were taken from outcomes for each level and used to create forest plots which demonstrate the interaction effects (see Appendices 4–7 for full outcome findings). Odds ratios for all significant predictors were then reported for these final models. A review of forest plots with continuous variables as risk factors will help to illustrate this approach (such as figure 4.6).

3.3.3.2. Logistic Regression Assumptions

There are conflicting opinions as to the degree of importance of the different assumptions of logistic regression. While most general texts on regression analysis strongly emphasise the assumptions of normality and linearity (382,383), those that address logistic regression (where the outcome variable(s) are binomial) reflect the challenges that exponential distributions place on these assumptions and put more emphasis on validity of the variables in the model and the measurement of independent variables (384-386). The following assumptions are specific to logistic regression analysis and were identified and assessed from different sources (384,386,387).

1. Validity. The outcome measure(s) should accurately reflect the phenomenon of interest. This assumption was met (see Section 3.2.2).
2. Sufficient sample size. The large sample sizes for both birth events and DAs assured that variable parameters were estimated accurately and were sufficient to fit the effects for the full province. Sample sizes for hotspot groups were based on counts of outcome events and were sufficient for regression analysis (375,376).
3. Goodness-of-fit. Model fit should be correct and only meaningful predictor variables should be included. All predictor variables included in the model were known risk factors for the adverse birth outcomes (see Section 3.3.1 for a discussion on predictor variables used).

    Model goodness-of-fit was verified using a pseudo-likelihood approach available in the SAS GLIMMIX application. The word "pseudo" is used to indicate that the indicator is computed from an estimator rather than a true likelihood (348). The goodness-of-fit statistic used is a function of the ratio of the generalized chi-square statistic and its degrees of freedom; a ratio closer to one implies a better fit model. A

better fit suggests that variability in the outcome(s) has been properly modeled and that there is no residual over-dispersion (388). Over-dispersion (i.e., where the ratio is greater than 1) indicates that estimates of standard error are too small or that predictor terms have been omitted from the model. Inferences made from the model will be biased, with greater likelihood of a Type 1 error (389).

The goodness-of-fit ratios for all models resulting from my analysis were consistently less than 1. Full-province model ratios were *LateP*: 0.93; *ModVeryP*: 0.87, *SGA*: 0.96, *Stillbirth*: 0.84. Hotspot group ratios ranged from 0.81 to 1.00 (for details, see Appendices 4–7).

Based on these findings we can assume that the models used in the current study are correct and that outliers are not a problem (347,389). I feel confident that these models fit well enough to support my findings.

4. Additivity and linearity. The outcome should be a linear function of the separate predictors; there should be additivity. If additivity is violated then an optimal solution is to include interaction effects (385,386). Significant interaction effects were found between risk factors and were included in the models.
5. Equal variance of errors. The goodness-of-fit test findings discussed above suggest that this assumption was met to a reasonable degree. Therefore unequal variance did not affect the form of the predictor. Equal variance of errors is considered a very important aspect of logistic regression modeling (385).
6. Normality of errors. Conditional residuals were plotted and assessed for normality and linearity (see Appendix 3). The assumption of normality was met sufficiently to allow for reasonable levels of accuracy in model outcomes. Outliers in these plots were assessed. No outlier events required removal. Outliers had been previously verified by

BORN Ontario in their validity checks on the data. Missing data were assumed to be random.

The plots for this assumption suggest that errors were close to normally distributed with some skewing; therefore, I feel that this assumption was sufficiently met. It is important to note that since the primary objective of the current study was the estimation of the regression line (rather than predicting individual data points), meeting this assumption was not critical to effective model creation.

3.4 Conclusions

The nature of our research questions, that we are more interested in comparing results of our analyses across the four different adverse birth outcomes and in the hypotheses generated than in their specific accuracy or exhaustiveness, minimizes the risk that the tools used or assumptions made will substantially bias conclusions drawn. The database chosen, BORN Ontario, over the alternatives available represents a trade-off of different limitations. The one limitation, that the database represents about 90% of births, is minimized by our use of proportions of adverse outcomes per DA in both hotspot and regression analysis. While specific hospitals not reporting births accounts for much of the 10% missing observations, use of proportions per DA allows for approximate representative proportions for those births that were reported.

Missing data for the different birth outcomes is a likely a function of hospital data entry and is assumed to be randomly distributed. The substantial number of missing stillbirth observations are attributed to live births and should not change conclusions (167). Correction factors in data grooming, local Moran's I as well as hierarchical regression analysis addressed missing variable as well as risk factor data.

Selection of local Moran's I as the geographic hotspot tool also represents a trade-off, as discussed in Section 2.6.3. Our primary goal in identifying hotspots was to compare locations of the clusters for the different outcomes. Local Moran's I was chosen because of its characteristics of identifying smaller more localized clusters while the options tended to choose larger clusters. This more conservative selection characteristic better fit our research goal. Also we can assume that any bias introduced by the analysis tool would have been equally shared across findings for the four outcomes and thus the hotspots identified would be comparable.

The Public Health Agency of Canada birth curves used to determine SGA births in our dataset are currently the standard in Canada. They have, however, been criticized for not correcting for ethnic background (104,374). This may result in a risk of bias toward more SGA babies in areas with high proportions of ethnic groups such as Southern and Eastern Asian. The inclusion of *%Asian* as a risk factor should help to inform this analysis.

Chapter 4. Results

Results are presented in this chapter in two sections. The first, 4.1, presents hotspot analysis findings; the second presents regression results. Each of the two sections is divided into subsections that cover the four adverse outcomes. Regression analysis results are further subdivided into findings for the full province and for local areas.

4.1. Hotspot Analysis Results

4.1.1. Identified Hotspots

Spatial clusters of significantly higher adverse outcomes, or hotspots, were found for all four adverse birth outcomes: 132 for *LateP*: 152 or *ModVeryP*, 252 for *SGA* and 27 for *Stillbirth* (Table 4.1). On the strength of the 1000 Monte Carlo simulations carried out to validate these findings, it is reasonably certain that these hotspots were not due to random chance.

Table 4.1 Numbers And Characteristics of Hotspots for Each Outcome

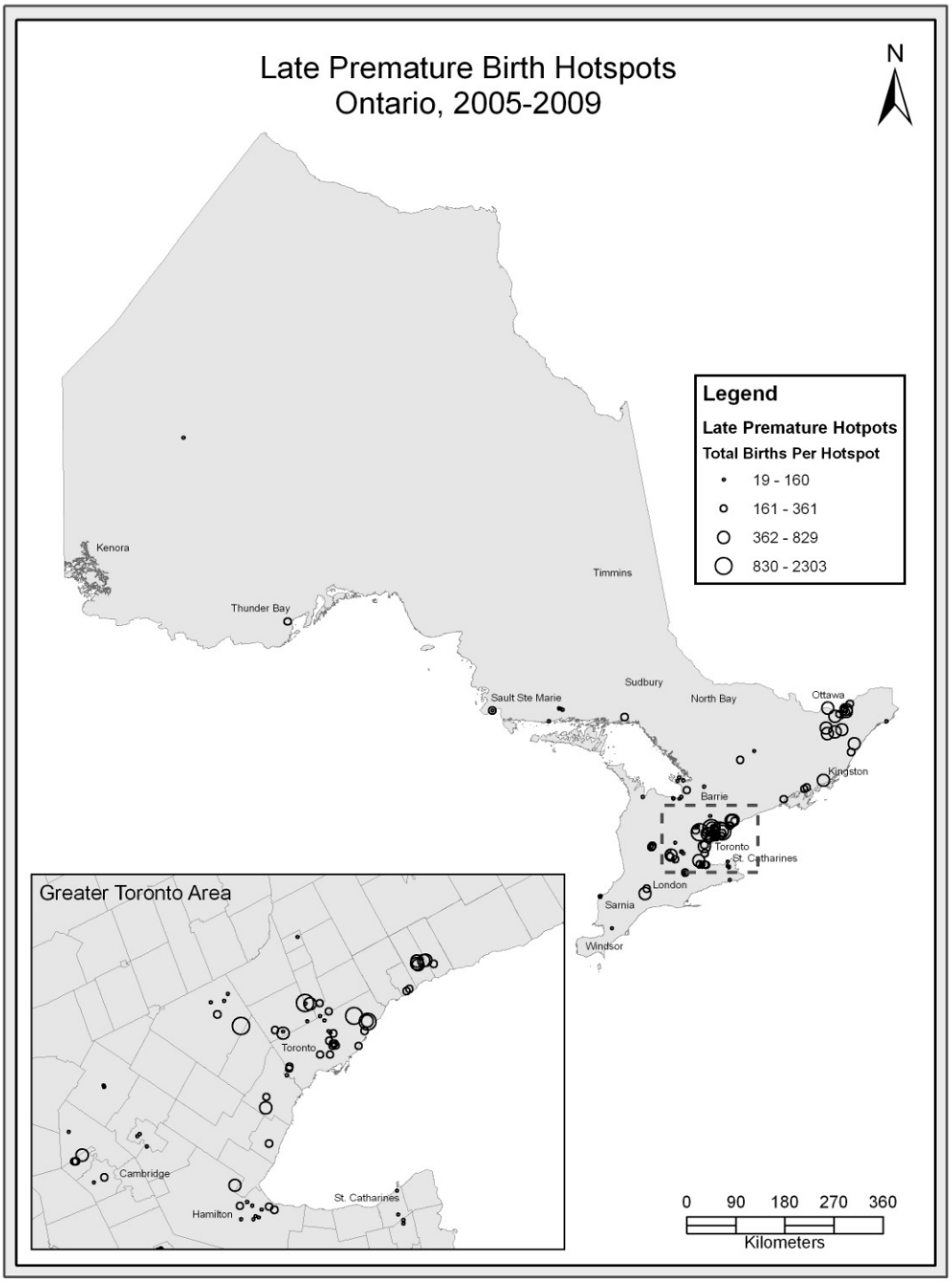
Birth outcome	Hotspot Count	Total DAs in hotspots (hotDAs) (%)*	Mean DAs per hotspot
LateP	132	789 (5%)	6
ModVeryP	152	833 (5.3%)	5
SGA	252	1,402 (9%)	6
*Stillbirth*s	27	197 (1.25%)	7

* The percentage is based on the 15,808 DAs.

The total count of DAs[19] in hotspots (hotDAs) for the different outcomes varied from 197 for *Stillbirth* to 1,402 for *SGA* (Table 4.1); mean DAs per hotspot ranged from five for *ModVeryP* to seven for *Stillbirth*. The percentage of total DAs included in hotspots ranged across adverse outcomes from 1.25% for *Stillbirth* to 9% for *SGA*. Maps showing the

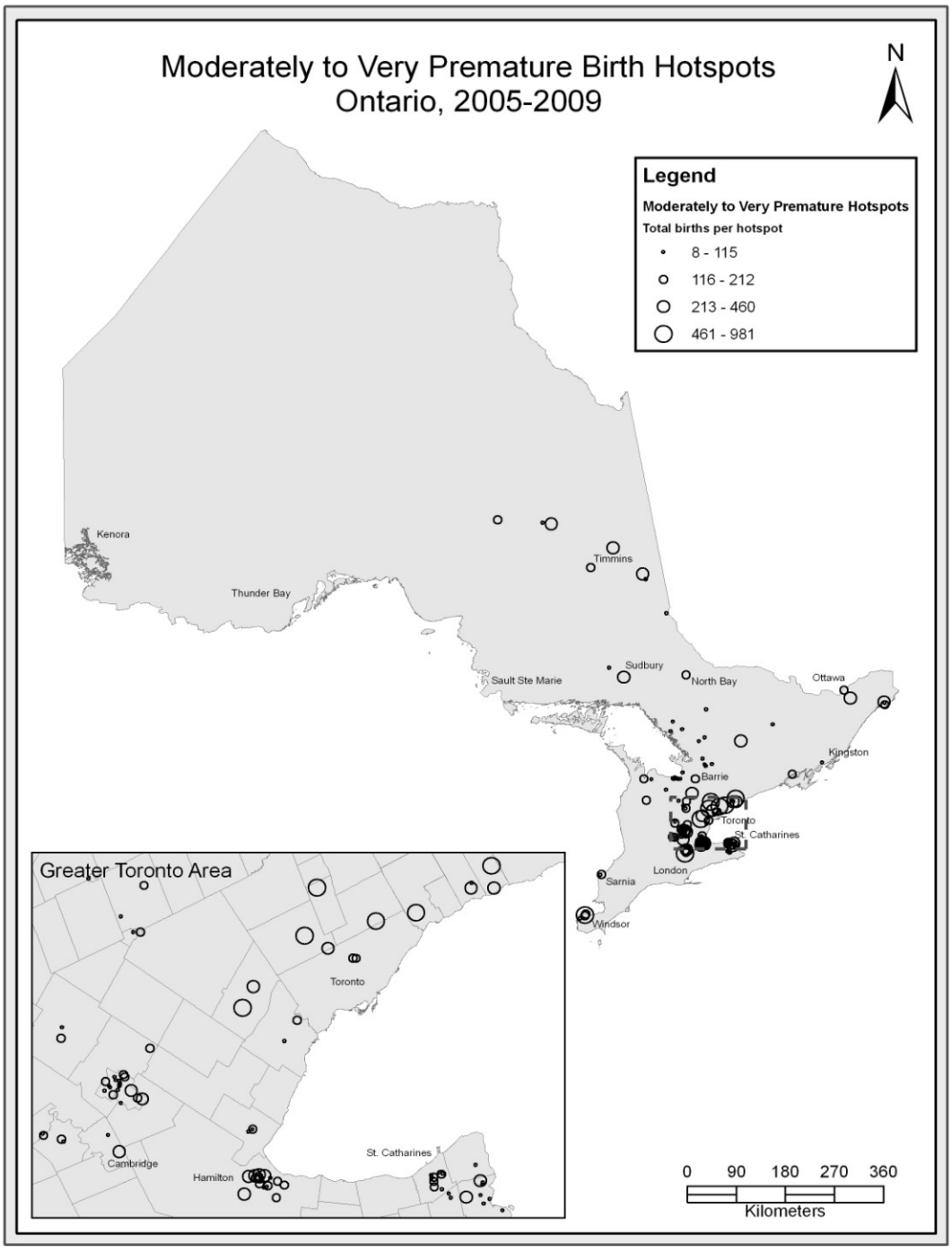
[19] Agglomerated DAs were treated as single DAs per the Methods section discussion.

geographic locations of *LateP*, *ModVeryP*, *SGA* and *Stillbirth* hotspots are presented in figures 4.1–4.4.



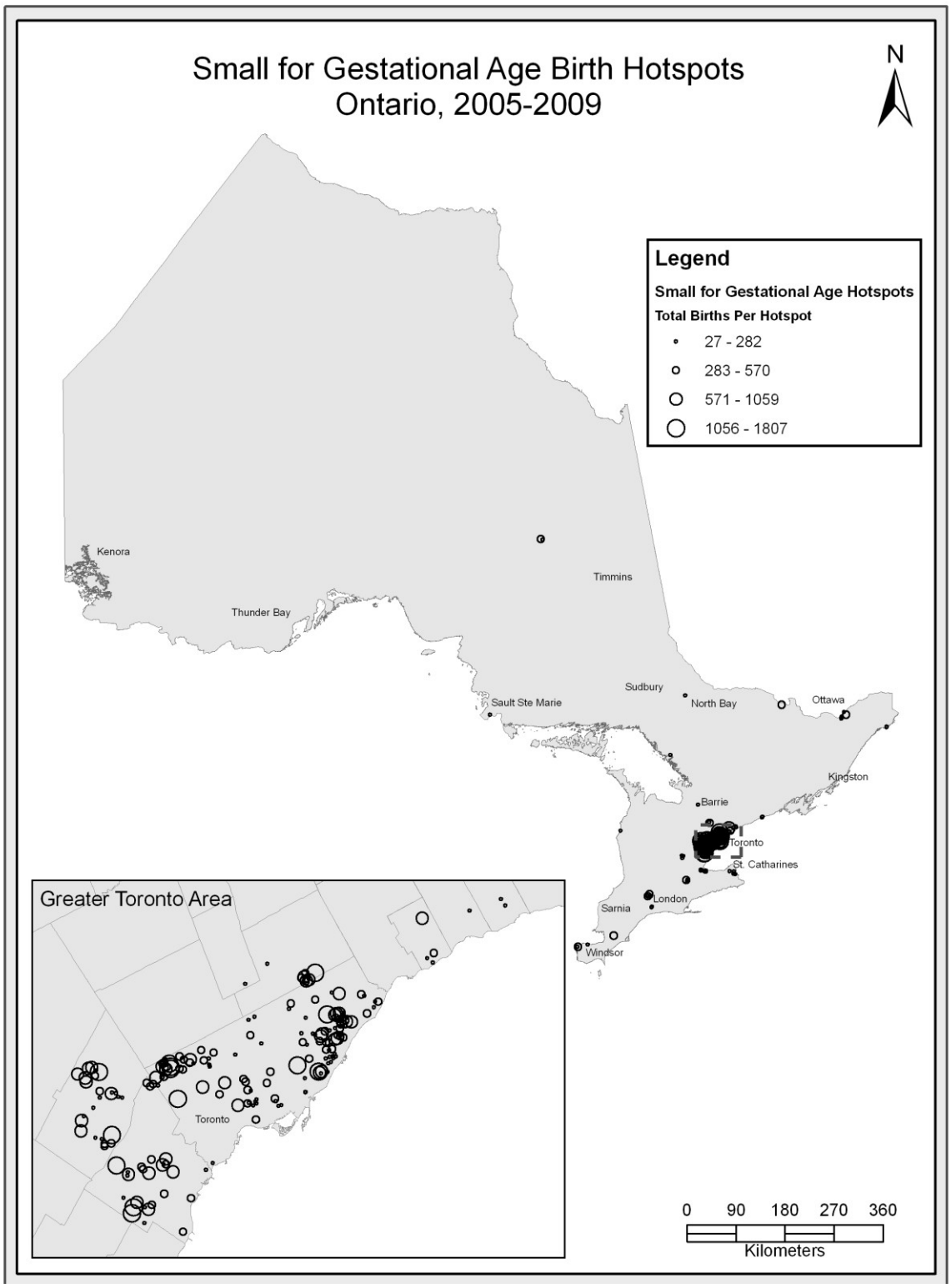
Hotspots 132
HotDAs 789
Total Hotspot births: 31,958
Hotspot LateP births (% late premature/hotspot total births): 1,981 (3.6%)

Figure 4.1 Locations of Late Premature Birth Hotspots



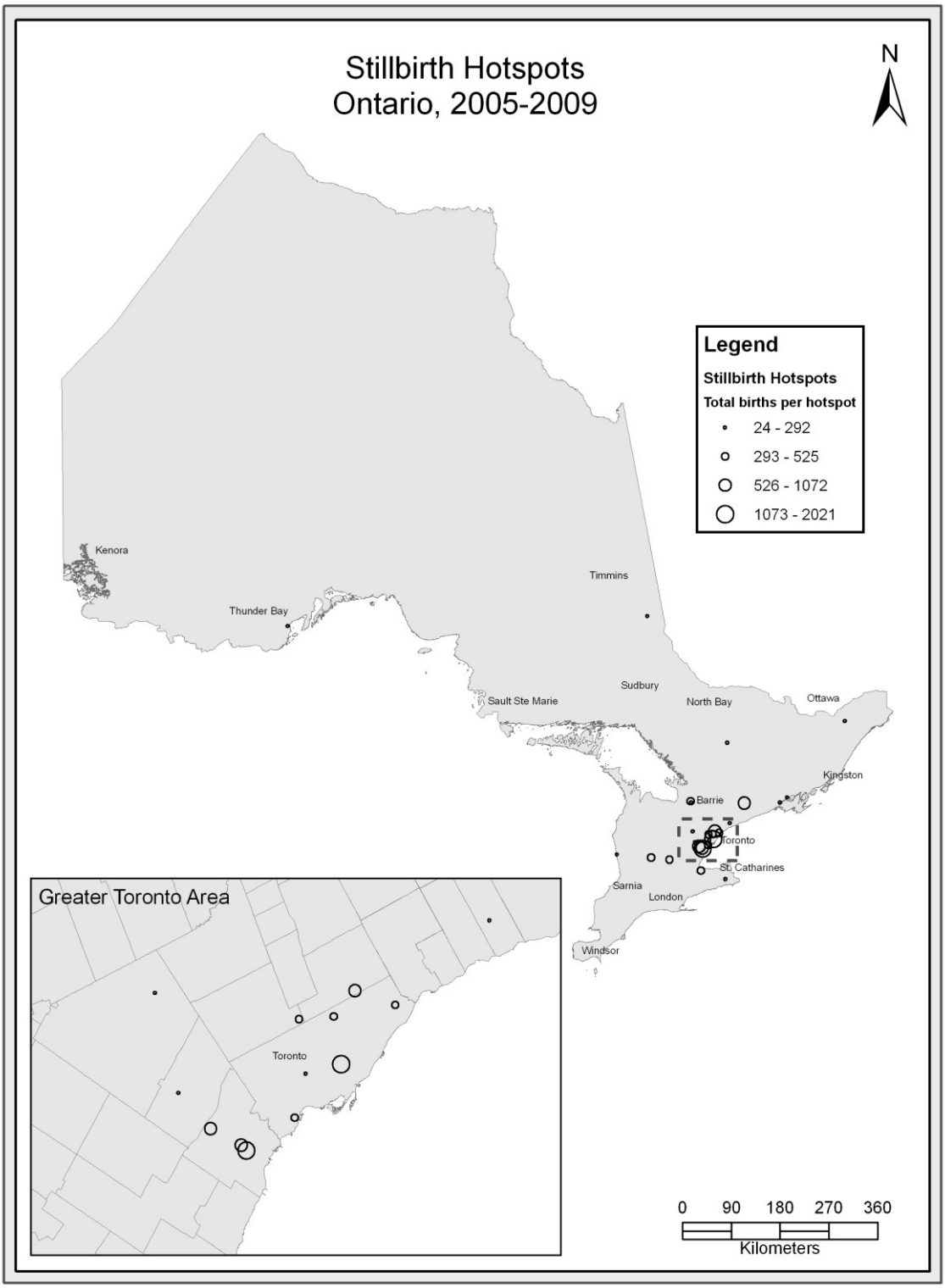
Hotspots 152
HotDAs 833
Total hotspot births: 18,670
Hotspot moderate to very premature births (% moderate to very premature / hotspot total births): 1,100 (5.8%)

Figure 4.2 Locations of Moderate to Very Premature Birth Hotspots



Hotspots 252
hotDAs 1,402
Total *hotspot* births: 85,121
Hotspot *SGA* births (% *SGA* / hotspot total births): 11,236 (13.2%)

Figure 4.3 Locations of Small for Gestational Age Birth Hotspots



Hotspots 27
hotDAs 197
Total Stillbirths: 3,615
Hotspot Stillbirths: (% stillbirths / hotspot total): 165 (0.99%)

Figure 4.4 Locations of Stillbirth Hotspots

The levels of adverse birth outcomes in the hotspots were higher than provincial levels as would be expected. However, the hotspots contained only a small portion of each adverse outcome, ranging from 3.75% to 20.1% (Table 4.2).

Table 4.2 Comparison of Hotspots: Provincial Proportions of Adverse Birth Outcomes

Birth outcome	Hotspots (hotDAs)	Hotspots adverse birth outcomes count (% of total hotspots births)	Full - province adverse birth outcomes count (% of total provincial births)	Hotspot adverse births as a percentage of total provincial adverse births
LateP	132 (789)	1,981 (6.2%)	30,875 (4.9%)	3.8%
ModVeryP	152 (833)	1,100 (5.9%)	21,450 (3.7%)	4.8%
SGA	252 (1,402)	11,236 (13.2%)	54,446 (8.8%)	20.1%
Stillbirth	27 (197)	165 (0.99%)	3,615 (0.6%)	4.6%

4.1.2. Spatial Relationships of Hotspots

Hotspots for the different adverse birth outcomes were found to be largely spatially exclusive; there was little sharing of hotDAs between the different adverse outcomes. This counterintuitive finding was observed first by a simple count of intersecting hotDAs between the different adverse outcomes, shown in Table 4.3. *LateP* and *ModVeryP* hotspots shared the greatest number, 70, about 4.5% of their combined total hotDAs. *LateP* and *Stillbirth* shared the fewest, six, about 0.6% of their combined total hotDAs.

Table 4.3 Assessment of Exclusivity of Hotspots: Shared hotDAs Across Hotspots and Kappa Coefficients

Outcome pairs	HotDAs shared (% of combined total DAs)	Kappa coefficient
LateP – ModVeryP	70 (4.5)	-0.91
LateP – SGA	55 (2.6)	-0.8
LateP – Stillbirth	6 (0.61)	-0.46
ModVeryP – SGA	81 (3.6)	-0.8
ModVeryP – Stillbirth	31 (3.1)	-0.38
SGA – Stillbirth	24 (1.5)	-0.24

Because this finding was not expected, I corroborated the disjoint nature of the hotspots with three additional tests.

1. The Kappa statistic was used to test for agreement in DA dichotomous hotspot membership scores. Moderate to strong disagreement was found between DA memberships in adverse outcome hotspots in all six of the two-way comparisons. Strong disagreement levels (between -.7 and -0.91) (390) were found in three of the six comparisons: *LateP – ModVeryP*, *ModVeryP – SGA* and *ModVeryP – SGA*. Moderate disagreement was found in the three others: *LateP*/*Stillbirth*, *SGA*/*Stillbirth*, and *ModVeryP*/*Stillbirth* (Table 4.3).

   While Kappa is not a hypothesis testing statistic, this finding suggests that the degree of sharing of hotDAs between different adverse outcomes was clearly less than would have been expected by chance alone.

2. The bivariate Moran's I found that levels of adverse outcomes in target DAs were spatially independent of levels of different outcomes in neighbouring DAs. Only weak spatial correlations between proportions of adverse outcomes (for all 15,808 DAs) were found. All *r* values were below 0.05 (in a range of -1 to 1, with 0 as complete independence) except *SGA*/*Stillbirth*, which was .06 (Table 4.4). This finding suggests that the level of an adverse outcome in a target DA has little association with, or predicts little of, the levels of any of the other adverse outcomes in neighbouring DAs.

Table 4.4 Assessment of Exclusivity of Hotspots: Bivariate Moran's I for Adverse Outcomes Across All 15,808 DAs	
Outcome pairs[20] A-B, B-A	***r* for A-B, B-A**
LateP–ModVeryP , *ModVeryP–LateP*	0.012, 0.014
LateP–SGA , *SGA–LateP*	0.019, -0.002
*LateP–Stillbirth*s, *Stillbirth*s*–LateP*	0.012, 0.001
ModVeryP–SGA,*SGA–ModVeryP*	0.039, 0.003
*ModVeryP–Stillbirth*s, *Stillbirth*s*–ModVeryP*	0.012, 0.001
*SGA–Stillbirth*s, *Stillbirth*s*–SGA*	0.047, 0.062

3. A standard statistical Spearman's *r* for all 15,808 DAs showed only weak (but significant) correlation levels between proportions of different adverse birth outcomes within each DA (*ModVeryP-Stillbirth*s was the sole exception, with a Spearman's *r* of .3; see Table 4.5). This finding suggests that the proportion of an adverse outcome in a given DA tells little about the levels of any of the other three adverse outcomes within the same DA. The significant *P* values show that the r_s values were not equal to zero.

Table 4.5 Assessment of Exclusivity of Hotspots: Spearman Correlation Coefficient for % Adverse Outcome Across All 15,808 DAs	
Outcome pairs	**(r_s , *P* value)**
LateP-ModVeryP	0.002, 0.811
LateP – SGA	0.035, <0.001
LateP – Stillbirth	0.05, <0.001
ModVeryP - SGA	0.052, <0.001
ModVeryP – Stillbirth	0.308, <0.001
SGA - Stillbirth	0.095, <0.001

The results of the four tests all supported the finding that hotspots were spatially exclusive. The first two tests, the count of shared hotDAs and the kappa coefficient,

[20] In the bivariate Moran's I test for spatial correlation, order of the variables will change the outcome. The statistic can be interpreted as the degree to which the value at one DA for one adverse outcome, A, is correlated with the weighted average of another adverse outcome, B, with the average computed over the neighbouring DAs (90). The first outcome in the order is A, the second is B.

interpreted the findings of the local Moran's I test. Although the bivariate Moran's I and Spearman's *r* were independent of the local Moran's I_i statistic, both support the finding of exclusive hotspots.

4.1.3. Demographic and Geographic Comparisons

Hotspots for the various adverse outcomes had some markedly different birth and geographic characteristics:

- *SGA* and *Stillbirth* hotspots had substantially more births on average per hotDA, a median count of 32 and 31 respectively, compared with *LateP* and *ModVeryP* (21 and 17 respectively). Median overall population sizes were not notably different, ranging between 560 and 598 (Table 4.7). This latter finding was as expected given the Statistics Canada goal of DAs representing a relatively standard population size.

Table 4.6 Hotspot Demographic Characteristics: Median Count of All Births

Birth outcome	Hotspots (hotDAs)	Median total births per hotDA	IQR* (Q1-Q3)
LateP	132 (789)	21	12-37
ModVeryP	152 (833)	17	10-27
SGA	252 (1,402)	32	20-50
Stillbirth	27 (197)	31	17-54

* IQR – interquartile range (25th to 75th percentiles, Q1 to Q3 quartiles)

- *SGA* hotspots stand out as geographically the smallest, with a median hotDA size of 0.13 km^2, 0.02 less than the provincial median of 0.15 km^2. Their size at the 75th quartile was 0.26 km^2 compared with the provincial 75th quartile size of 0.37 km^2. A corollary to this was that the median size of the hotDAs in the other three adverse outcomes were larger than the provincial median, about 0.23 km^2 with a 75th

quartile size of between about 0.8 and 0.9 km^2 (Table 4.7). This finding suggests that *SGA* hotspots were more urban in character, which supports findings from previous research (9).

Table 4.7 Hotspot Demographic Characteristics: Population and Km^2

Birth outcome	Hotspots (hotDAs)	2006 total hotDA population (% total Ontario population)[21]	population per hotDA median	IQR (Q1-Q3)	2006 total hotspot km^2 (median km^2 per hotDA)	IQR* (Q1-Q3)
LateP	132 (789)	619,237 (3.29%)	560	465-824	23,654 (0.22)	0.11-0.79
ModVeryP	152 (833)	646,014 (4.05%)	574	477-866	111,399 (0.23)	0.13-0.92
SGA	252 (1,402)	1,131,417 (15.81%)	575	460-884	71,657 (0.13)	0.08-0.26
Stillbirth	27 (197)	168,895 (1.4%)	598	483-934	7,910 (0.24)	0.11-0.87

*IQR – interquartile range (25^{th} to 75^{th} percentiles, Q1 to Q3 quartiles)

4.1.4. Discussion

Using the above methods, I observed significant geographic hotspots for all four of the adverse birth outcomes: late premature, moderate to very premature, small for gestational age and still births. This finding indicates that certain geographic areas have aetiologies or patterns of risk factors sufficient to create significantly higher levels of these adverse outcomes.

The hotspots identified by the local Moran's I statistic represent a relative minority of total adverse outcomes in the province. However, the finding that there were clusters of DAs with significantly higher levels of adverse outcomes suggests that special consideration is due to these places and to the births that they represent beyond just their relative count. Adverse birth outcomes are non-communicable; a hotspot does not occur due to a vector or carrier. While they could be explained by a chance concentration of women who shared enough individual characteristics and behaviours to produce a

[21] Per 2006 census population of 12.16 million.

significantly higher level of a given adverse birth outcome, I suggest that they are more likely explained by an aetiology that combines both individual and contextual characteristics. This hypothesis was further explored in the second phase of the current study.

Although the finding of hotspots was expected, the finding that the hotspots for the four different outcomes were largely spatially exclusive was not. Very few DAs were in hotspots for more than one adverse outcome, fewer than would have been expected by chance alone. A number of statistical tools corroborated this result. This exclusivity indicates that certain geographic areas have aetiologies or patterns of risk factors that are both sufficient to create significantly higher levels of one adverse outcome yet insufficient to create significantly higher levels of other adverse outcomes.

Adverse birth outcomes have been linked to geographic areas and geographic disparities in previous studies (23,36,76,391), yet I did not find previous research in my review that had identified spatial hotspots for multiple adverse birth outcomes using population areas as small as census dissemination areas (DAs) within such a large and varied geographic area as Ontario. In fact, previous research has shown different individual risk profiles for different adverse outcomes:

- *LateP*: maternal age 35–39 years (9,36,109,163), existing health problems (9).
- *ModVeryP*: maternal age >40 (15,36), intervention (caesarean-section or induction for cause) at <35 weeks (15), maternal morbidities (proteinuria, bleeding <20 weeks), other maternal/fetal threatening morbidities (15,36).
- *SGA*: smoking (9,36,128,261), Asian immigrant (196,374), low maternal weight gain (36), low maternal education (134).

- *Stillbirth*: maternal age >40 accompanied by major co-morbidities (17,36), and age<20 (36).

I found no research that linked these profiles to exclusive geographic areas, although past research studies have found ecologic level variables to be significantly associated with adverse birth outcomes in general and with some specific adverse outcomes such as low weight, preterm and SGA births (16). Neighbourhood economic level (43,50,94,185), education (16,79,94), ethnic and racial background (43,109,185), segregation and racism (41,392) and pollution types and levels (289,393) have all been linked to specific adverse outcomes although these results have been inconsistent.

The importance of interactions between individual and ecologic level characteristics in determining birth outcomes has also been suggested in previous research. Ecologic SES variables have been shown to interact with, and to have effects independent of, the individual risk indicators (41,79,146). A number of these interactions were found to be specific to known individual risk indicators; for example, the effects of exposure to carbon monoxide air pollution on birth weight are "considerably larger" for older mothers and smokers (289); the effect of living in racially segregated neighbourhoods is stronger for premature births among non-Hispanic Blacks than for Whites or Hispanics (47,109); and the negative association between maternal age and birth weight increases with SES disadvantage (50). Some researchers have suggested that adverse outcomes will most often result from an interaction of ecologic and individual risk factors (41,185). Yet none of these studies has gone so far as to suggest that a given set of individual and/or ecologic risk factors would result in an exclusivity of significant levels of a single adverse outcome within a given geographic area.

I surmise that individual level risk factors may interact with, or be mediated by, ecologic characteristics and behave differently depending upon the characteristics of the area of residence. A strong local ecologic risk factor or mix of factors, such as income and education, may interact with one or more individual birth-risk factors, such as smoking and poor health; the ecologic indicator(s) may be sufficient to amplify the effects of the individual risk factors over others such that those individual risk factors result in significantly higher levels of a given adverse outcome.

4.2. Regression Analysis Results

This section is broken into five major parts, one for each of the four adverse outcomes and a fifth dedicated to discussion of findings. Each of the four outcome subsections is divided again into sections for full province and local area results.

4.2.1. Introduction

Adverse birth outcomes are non-communicable, yet clusters of adjacent DAs with significantly higher levels of the four different outcomes were identified across Ontario. The second phase of the current study attempted to explain the existence of these hotspots. Hierarchical regression analysis was used to evaluate the effects of individual and of contextual characteristics in explaining the observed distributions (41,394,395). Adverse birth outcomes are inherently individual level variables, as are several of their known risk factors (e.g., smoking and maternal age). But several other important risk factors (e.g., household income and education) were only available to this research as aggregated compositional characteristics; there was one contextual characteristic (population density). Hierarchical regression allowed us to include both individual and DA level compositional and contextual variables in our models.

My strategy for explaining the observed hotspots revolved around the two remaining research questions:

1. What were the predictors of the observed hotspots? and
2. Do predictor models differ:
   a. within the same outcomes between those fitted to the full province and those fitted to local groups of hotspots, as well as between those fitted to geographically diverse hotspot groups?
   b. across the different outcomes between those fitted to the full province, as well as between those fitted to geographically diverse hotspots?

These questions are answered across the following seven sub-sections. Analysis results for each of the four different adverse outcomes are presented and discussed first. Next, regression models for the four different outcomes are compared, contrasted and discussed.

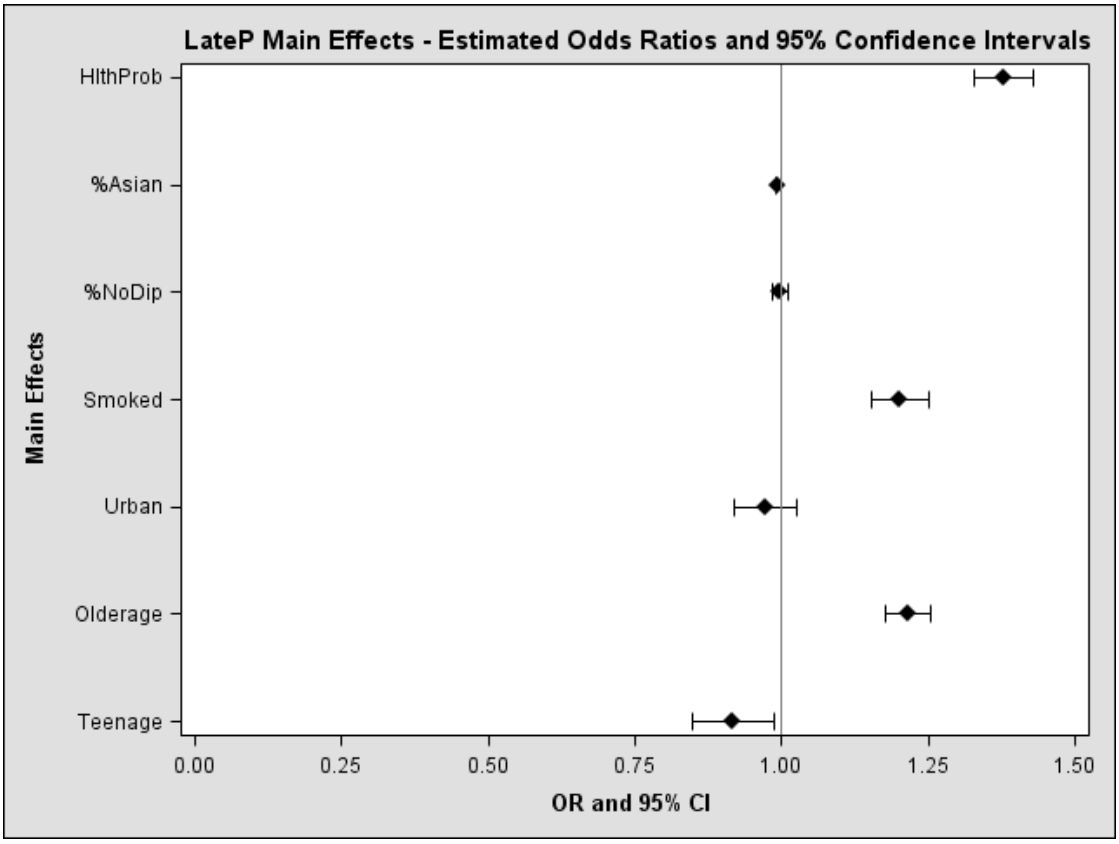
4.2.2. LateP Results

This section presents the regression analysis results and discussion for late premature (*LateP*) births (gestational age ≥ 35 weeks, <37 weeks) for the full province and hotspot groups. There were 30,875 late premature birth events in my data. From these I identified 132 hotspots comprised of 789 hotDAs. Of the 31,958 total births in these hotspots, 6.2% were late premature births, compared with 4.9% for the province as a whole.

4.2.2.1. LateP Full Province Results

Figure 4.5 presents a forest plot showing odds ratios and confidence intervals for the seven risk factors (main effects) used in the final full province model of late premature births. Main effects are given for comparison purposes only; once interaction effects are identified the association between the individual risk factors and late premature births should only be considered with recognition of the interaction and its modifying effects (144), shown in figures 4.6 and 4.7.

A forest plot was used to display the effect of each predictor (listed on the y axis on the left) on late premature birth. The effect of each predictor is represented by an estimated odds ratio (OR) and 95% upper and lower confidence intervals (CI), graphically presented as ⊢♦⊣ . The diamond represents the estimated OR and the two vertical bars at either end of the center line represent the upper and lower CI boundaries. The vertical line at 1.00 (on the horizontal axis) represents "no effect". If the confidence interval overlaps this line (as with *Urban* in Figure 4.5) the effect of the predictor on the outcome does not significantly differ from "no effect" at the 95% level of confidence. An estimated odds ratio to the right of the no-effect line represents a predictor that increases the chance of a late premature birth outcome. A predictor with an odds ratio to the left of the line represents a "protective" effect: the predictor tends to decrease the chance of the adverse birth outcome. In Figure 4.5, for example, *HlthProb* increases the risk of a late premature birth (i.e., women with an existing health problem had an estimated odds ratio of late premature birth about 1.4 times, or 40%, greater than women without a health problem). All odds ratio and



- *HlthProb*: pre-existing maternal health problem
- *%Asian*: Percentage of South and East Asian immigrants in DA
- *%NoDip*: Percentage of women >20 in DA without high school diploma
- *Smoked*: the woman *Smoked* at any time during pregnancy
- *Urban*: the DA has an *Urban* population concentration
- *Olderage*: the woman is >35
- *Teenage*: the woman is <20

Note that *%HigherEd* and *MedInc* were not included in the final *LateP* model hence are not represented in this table.

Figure 4.5 Late Premature Births Full-province Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

confidence interval estimates for the following Section 4 tables can be found in Appendix 4. Table 4.8 exhibits all the risk factors[22] and their significant two-way interaction effects included in the final regression model for late premature births. This table contains

[22] All risk factors in the final model are included in this table; some may not be individually significant but gain significance in an interaction effect with another variable. An example of this is *%NoDip* with a *P* value of 0.422; its significance comes from an interaction with *Olderage*, which had a *P* value of 0.035.

hypothesis tests for the significance of each of the risk factors and predictors specified in the final model. The full odds ratio and regression coefficient tables are presented in Appendices 4 and 11 respectively.

Table 4.8 Full-Province *LateP* Final Regression Model			
		***F* statistic**	***P* value**
1.	*HlthProb*	16.33	<0.001
2.	*Teenage*	19.14	<0.001
3.	*Olderage*	29.05	<0.001
4.	*Urban*	6.35	0.012
5.	*Smoked*	82.11	<0.001
6.	*%NoDip*	0.65	0.422
7.	*%Asian*	5.00	0.025
8.	*Teenage*Urban*	9.81	0.002
9.	*%Asian*Urban*	5.72	0.017
10.	*%NoDip*Olderage*	4.43	0.035
11.	*Teenage*HlthProb*	5.97	0.014

Note that the effects of six of the seven risk factors for late premature birth (Table 4.8) were modified by an interaction with another risk factor. Interactive relationships are shown at the bottom of the table as two risk factors linked by an asterisk (for example *Teenage*Urban*). Only *Smoked* was found to have a non-modified relationship with late premature birth. Individual risk factors included in a significant interaction effect are always shown (and needed) in the final model. Once an interaction effect is recognized, estimating the odds ratio for each variable requires the use of the interaction effect (396).

Smoked was found to have a significant, unmodified effect on the risk of a late premature birth; smoking at some time during the pregnancy increased the odds of a late premature birth by 1.2 times (CI: 1.16, 1.25), or about 20%, compared to non-smokers.

The estimated odds ratios and corresponding confidence intervals for interaction effects found in the model are displayed in figures 4.6 and 4.7. Two figures were required because binomial/continuous and binomial/binomial interactions require different

configurations to illustrate their effects. Note that the odds ratios shown for all predictor variables were adjusted for all other variables in the model.

Figure 4.6 displays the interactive effects between binomial and continuous risk factors. Odds ratios were estimated for low, mid and high levels of the continuous risk factors (which were all ecologic level). The interaction effect (a*b) and the three contrasting levels of the continuous variable are noted on the y axis, for example *Older*%NoDip* (with high, mid, and low ranges of *%NoDip*). The three levels were approximately based on divisions at the 25th, median and 75th percentiles of the continuous variables. Presenting odds ratios estimated at three different levels allowed for the modification effect of the continuous covariate on the risk factor to be better understood.

Odds ratio and confidence interval estimates presented in Table 4.6 were taken from three tables found in Appendix 4, models 4.3a – 4.3c. Model 4.3a presents odds ratio estimates for *%NoDip *Olderage* where *%NoDip* is set at a low level, 0.1 (that is 0.1, or 10%, of women 20 years or older did not have a high school diploma). The first row for the predictor *%NoDip*Olderage* can be read as: older aged women ("indep" Reference Value columns) living in a low 0.1 (10%) *%NoDip* DA have an estimated odds ratio of 1.19 (CI 1.15-1.24) greater risk of a late premature birth than younger women. The following Appendix table 4.3b shows that older women living in a mid *%NoDip* level DA, 0.2 (20%), have an estimated odds ratio of 1.22 (CI 1.18-1.26) of a late premature birth compared with younger women. Table 4.3c shows that older women living in a high *%NoDip* area, .3 (30%), have an estimated odds ratio of 1.26 (CI 1.2-1.32). Odds ratios and confidence intervals presented in figures throughout this chapter were taken from their respective Appendixes as shown in this example.

Figure 4.6 demonstrates that there was a significant interaction effect between *Olderage* and *%NoDip* (*Olderage*%NoDip*) on the risk of a late premature birth. The interaction is shown by the increase in odds ratios as the level of *%NoDip* increases. Older age women living in a low *%NoDip* area had an estimated risk of late premature birth about 1.2 times (or 20%) greater than younger women. In a high *%NoDip* area the comparable odds ratio was higher, about 1.25 (or 25%). The superimposed arrow demonstrates the risk effect of the interaction, either risk increasing as with *Olderage*%NoDip* or risk decreasing as with *Urban*%Asian*.

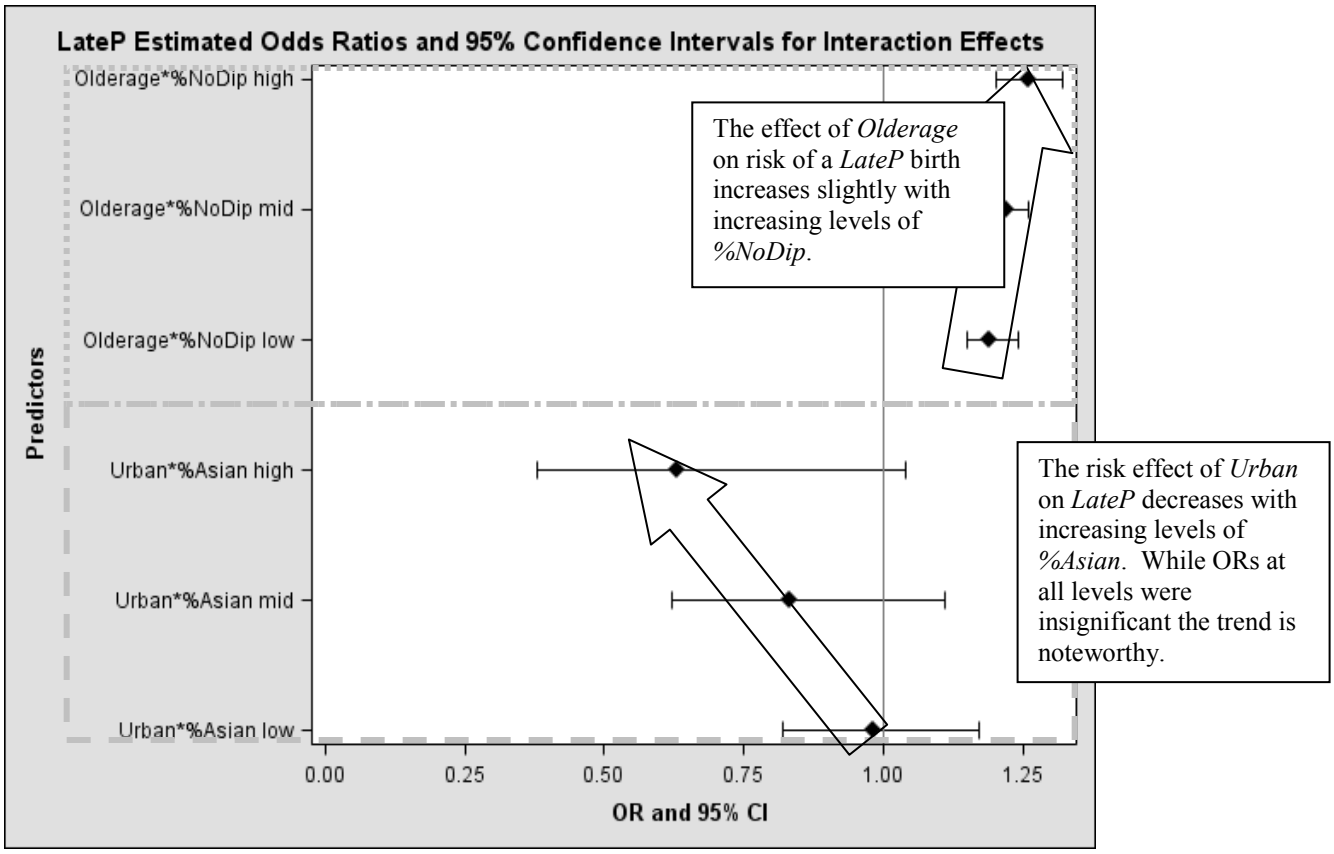


Figure 4.6 *LateP* Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

Figure 4.6 also demonstrates that the interaction between *Urban* and *%Asian*. Women living in an *Urban* (vs. rural) DA with a high percentage of Asian immigrants (*%Asian*) have a lower risk of late premature birth compared to women in an urban area with a low proportion of Asian immigrants. While all levels were insignificant, the trend is noteworthy. A significant effect not shown in Figure 4.6 was in the effect of *Urban* versus rural on *%Asian*. For women living in an *Urban* DA, a 2% increase in the percentage of Asian immigrants slightly reduces the risk, by about 0.99 (CI: 0.991–0.998), which means 1% less. For women living a rural DA, a 2% increase in the Asian immigrant population represents an increased risk of *LateP* of about 1.18 (CI: 1.03, 1.38) times (or 18%) greater (see Appendix 4).

Figure 4.7 displays two interaction effects between binomial variables: *HlthProb*Teenage* and *Urban*Teenage*. With binomial variables we can only compare levels 0 to 1, for example non-teenage to teenage and rural to urban. Each binomial interaction, *a*b*, is presented in four combinations:

a is contrasted 1 versus 0 when *b* = 1,

a is contrasted 1 versus 0 when *b* = 0,

b is contrasted 1 versus 0 where *a* = 1,

b is contrasted 1 versus 0 where *a* = 0.

The first set of interactions dealt with the effect of *HlthProb*[23] (1 vs. 0) at two different levels of *Teenage*, 1 and 0. The interaction effect *HlthProb*Teenage* (Figure 4.7) for the first two combinations reads as:

- *HlthProb 1 versus 0, Teenage = 1*: for teenagers (*Teenage* = 1) the risk of a late premature birth if they have a health problem (*HlthProb* = 1) was about 1.1 times

[23] See Appendix 1 for a full list of morbidities and other health problems.

(or 10%) greater than if they did not have a health problem (*HlthProb* = 0). This finding was shown to be insignificant as demonstrated by the tail of the plot overlapping the line of no effect. For teenagers, whether or not they had a health problem had no significant effect on the risk of a late premature birth.

- *HlthProb 1 versus 0, Teenage = 0:* for non-*Teenage* (*Teenage* = 0) the risk of a late premature birth if they have a health problem (*HlthProb* = 1) was about 1.37 times (or 37%) times greater than if they did not have a health problem (=0). This finding was significant.

The superimposed arrow highlights the direction of risk (increasing or decreasing) as the level changes from 0 to 1. In general, the effect of an existing health problem on the risk of a late premature birth was substantially greater for non-teenage women than for teenagers.

In the next two combinations of the *Teenage*HlthProb* interaction, the effect of *Teenage* (1 vs. 0) is shown at two different levels of *HlthProb*, 0 or 1. For women with a health problem (=1), *Teenage* (=1) had a lower risk of late premature birth, about 0.6 times (or 40%) less, than non-*Teenage* (=0). For women without a health problem (=0) teenagers again had a lower risk, about 0.8 times (or 20%) less, of a late premature birth than non-*Teenage* women. Both interaction effects were significant.

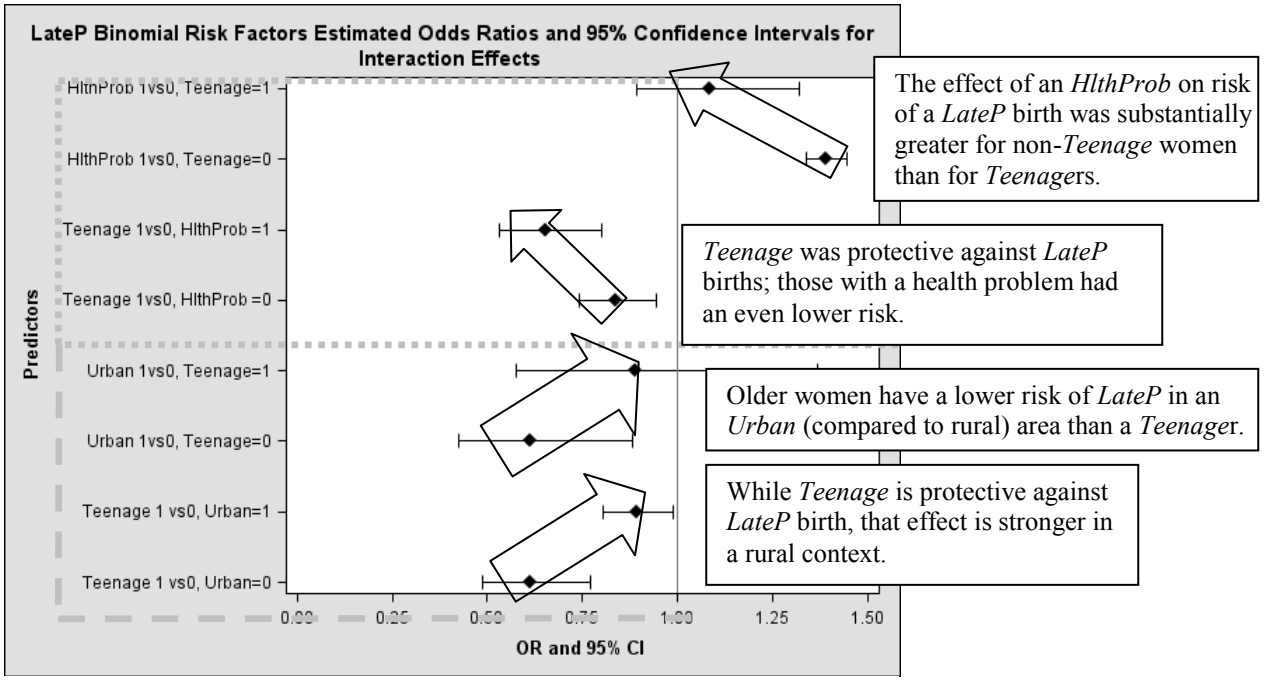


Figure 4.7 *LateP* Binomial Variables Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

The first combination in the presentation of the *Urban*Teenage* interaction, *Urban* = 1 vs. 0, *Teenage* = 1 and *Teenage* = 0, shows that non-teenage women (*Teenage* = 0) have a lower risk of late premature births in urban DAs than in rural ones while for teenagers the effect of *Urban* versus rural was insignificant (although with a higher level of risk than for non-teenagers).

The second combination, *Teenage* 1 vs. 0, *Urban* = 1 and *Urban* = 0, shows that in *Urban* DAs (*Urban*=1), teenage women have about 0.9 times (or 10%) less risk of a late premature birth than non-teenagers. In rural areas (*Urban* = 0) teenage mothers have a markedly lower risk, about 0.6 times (or 40%) less than non-teenage women. In general *Teenage* (vs. non-*Teenage*) women have a higher risk of a late premature birth in an urban area compared to a rural setting.

4.2.2.2. LateP Hotspot Group Results

Three hotspot groups were identified for late premature births: Northern Toronto, St Catharines and Southwest Ottawa. Table 4.9 presents descriptive information for each group.

Table 4.9 Late Premature Births (*LateP*) Hotspot Groups Descriptive Information

Group	Location	km^2	Hot spots	hotDAs	#births	#*LateP*	% *LateP*
N Toronto	17 kms N/NW of Toronto city centre	248	12	64	3,723	218	6
St Catharines	St Catharines city boundaries	67	4	25	316	40	13
SW Ottawa	55 km. S/SW of Ottawa city centre	161	4	14	1,173	73	6

N Toronto – North Toronto SW Ottawa – Southwest of Ottawa

Table 4.10 exhibits the final regression models for each of these three hotspot groups. This table contains hypothesis tests for the significance of each of the risk factors and predictors specified in the final model.

Table 4.10 Final Model for Three *LateP* Hotspot Groups

	***F* statistic**	***P* value**
Northern Toronto		
Olderage	0.56	0.456
%NoDip	1.32	0.256
*%NoDip*Olderage*	4.86	0.028
Southwest of Ottawa		
Olderage	15.57	0.002
%HigherEd	1.53	0.240
*%HigherEd*Olderage*	10.18	0.002
St Catharines		
HlthProb	1.43	0.248
%NoDip	0.39	0.537
*%NoDip*HlthProb*	9.45	0.002

Figure 4.8 presents odds ratios and 95% confidence limits for the risk factors (main effects) in the final model of late premature births for each hotspot group. See Appendix 4 for the findings on which these forest plots were based.

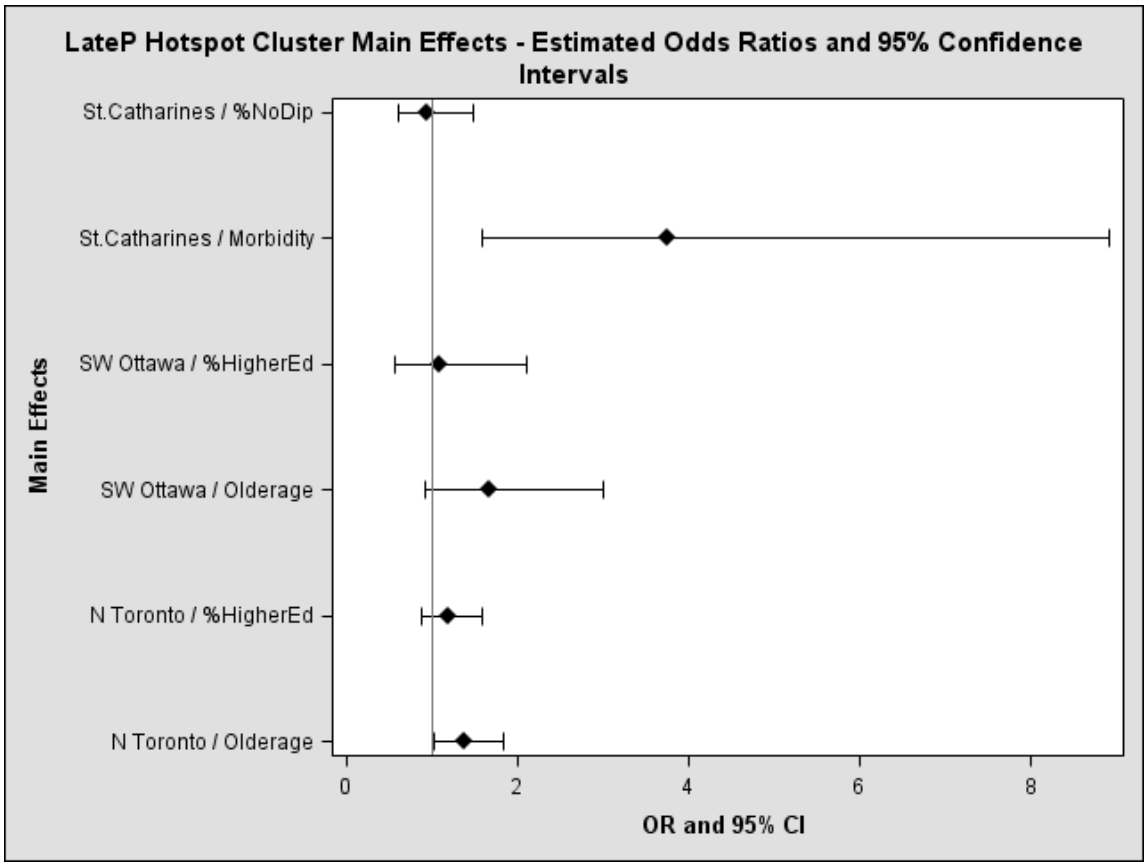


Figure 4.8 *LateP* Hotspot Group Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

St Catharines Hotspot Group

The St Catharines group was located within St Catharines city limits (See Table 4.9 and Figure 4.1). Its 67 km^2 include four hotspots made up of 25 hotDAs. There were 316 births between 2005 and 2009, 13% of which were late premature.

Those at greatest risk of a late premature birth in St Catharines were women with an existing health problem living in low education areas (i.e., areas with a high level of no diploma, *%NoDip*; see Figure 4.9). At the lowest level of *%NoDip* whether women had a health problem or not had no significant effect on their risk of a late premature birth; at mid

%NoDip levels (about 15%) the effect of an existing health problem became significant. At high *%NoDip* levels, women with a health problem had an estimated risk of late premature birth 4.2 times (or 320%) greater than that of women without a health problem who lived in a like DA. Note that the relatively small number of adverse events in St Catharines (compared, for example, to Toronto) results in wide confidence intervals.

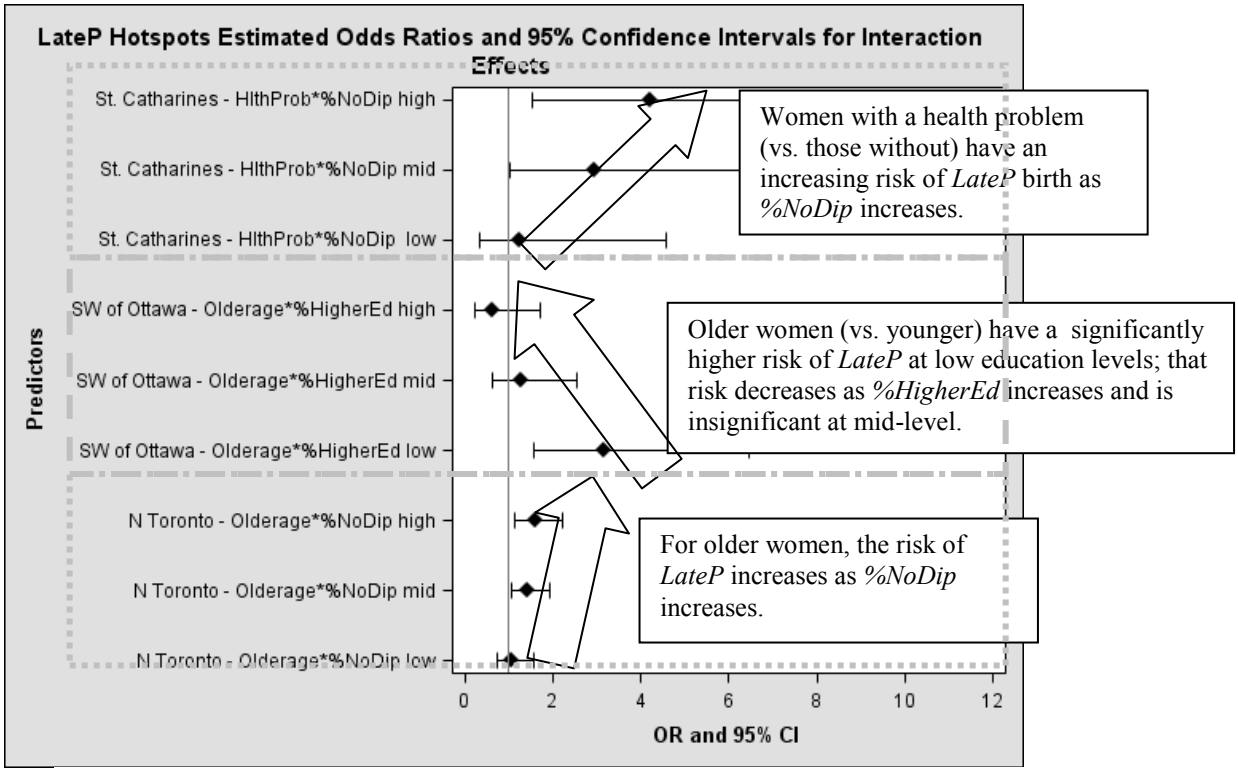


Figure 4.9 *LateP* Hotspot Groups Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

Southwest of Ottawa Hotspot Group

The Southwest of Ottawa group of late premature birth hotspots was located 55 km South/Southwest of Ottawa city centre (See Table 4.9 and Figure 4.1). Its 161 km^2 included four hotspots made up of 14 hotDAs. There were 1,173 births between 2005 and 2009, of which 6% were late premature. In these hotspots, those at highest risk of late premature

birth were older women living in areas with lower percentages of higher education *(%HigherEd*). Those women had an estimated risk of late premature birth 3.18 times (or 218%) greater than younger women living in like areas. The effect of *Olderage* on late premature birth decreased with increasing levels of *%HigherEd* and became insignificant at mid level. Findings displayed in Appendix 4 show that at 16% *HigherEd*, older age women have an estimated risk of late premature birth 0.64 (CI: 0.25, 0.83) times (or 36%) less than at 11% *HigherEd*.

Northern Toronto Hotspot Group

The subpopulation at highest risk of late premature birth in these hotspots included older women living in areas with lower levels of education (Figure 4.9). In areas of higher education, *Olderage* did not have a significant effect on the risk of late premature birth; but at mid *%NoDip* levels it became significant. Older age women living in a 10% *NoDip* area had an estimated risk of late premature birth 1.43 times (or 43%) greater than younger women; at high levels of *%NoDip* (12%) a like comparison had an odds ratio of about 1.6 (or 60%).

4.2.2.3. *LateP* Regression Results Discussion

The findings from both the full-province and hotspot group analyses demonstrate that ecologic level variables have a substantial effect on the risk of a late premature birth. They act as risk modifiers in three of the four predictors in the full province model and in all of the predictors in the hotspot group models. Of the individual level variables, only the relationship of *Smoked* with late premature birth was not modified. Within hotspot groups, every individual level risk factor was modified by an ecologic one. *HlthProb* and *Olderage*

associations with late premature birth were modified by education variables *%NoDip* and *%HigherEd* (Figure 4.9).

The full-province results shown in Figure 3.7 demonstrate that *Teenage* has a strong risk reduction effect in its interactions with other risk factors. The level of effect varied depending on the ecologic characteristics of where they lived; their risk was lower in rural areas than in urban. The overall protective relationship of *Teenage* to late premature births suggests that younger bodies are better equipped to deliver full-term babies, especially when individual or ecologic risk factors are introduced. While previous research has shown that teenagers have a higher risk of all adverse birth outcomes (9,36), other research has suggested that the "bulk" (180) of those higher risks are due more to contextual characteristics than to maternal age (9,36) and that older teenage women are capable of bearing healthy babies (180). The large majority of teenage mothers in our database, 99.3%, were between 15 and 19; other reports on births in Ontario (397) suggest that about 88% of teenage mothers in Ontario in 2005 were between 17 and 19, inclusive. I surmise that the large majority of teenage mothers represented in the database for the current study were older teenagers and at lower risk than older women when faced with the same contextual or individual health factors. See the discussion below regarding older age women and the weathering hypothesis.

The interaction between *Teenage* and *Urban* is perplexing; that is, risk of a late premature birth was significantly lower for teenagers versus non-teenagers living in a rural DA than in an urban one. A tentative exploration of the database found that:

- A disproportionate percentage of teenage births, about 15%, were in rural DAs;

- Forty-seven percent of rural teenage mothers smoked compared with 37% of urban teenage mothers; and
- Percentages with morbidities were about equal, at approximately 14%.

Rural areas may represent a generally higher-risk environment than urban areas for a substantial portion of women giving birth. Hypothetically, of those women interacting with high-risk individual and ecologic factors, teenagers had less risk of delivering a late premature birth than women >19 years of age. This disparity forms an extension of Holzman's weathering hypothesis (163), discussed below.

Although *Olderage* was found to be an important risk factor for late premature births, it was consistently and substantially modified by the level of education for the DA in which the women lived. This effect modification was shown in both the full-province and hotspot group analyses and for both ecologic indicators of education, *%NoDip* and *%HigherEd* (i.e., the greater the level of education, the lower the risk of *LateP* for older women). While a substantial amount of research has shown that level of education (7,18,79,130,228,231) and older age (9,15,36,145,163) are both highly associated with preterm birth, relatively few studies have examined the interaction between them. Astolifi found a strong interaction between older maternal age and education for populations in Italy (169). Holzman (163) and O'Campo (41), among others, found an interaction between age and neighbourhood economic status.

In her discussion of the weathering hypothesis (275,276), Holzman (163) suggested that women living in high-deprivation neighbourhoods may develop "accelerated aging" that would increase their risk of preterm delivery. This accelerated aging was potentially explained, in part, by delays in health care, adverse effects of unemployment, higher rates

of crime, exposure to pollution, stress and other "causes" endemic to high-deprivation neighbourhoods. My findings support this hypothesis to the point of suggesting that DAs with low ecologic levels of education are indicative of high-deprivation neighbourhoods and that, as Holzman suggested, living in those areas accelerates aging and, in turn, increases risk of preterm birth for older women. Older women living in less deprived areas, indicated by higher levels of education, would presumably not suffer this accelerated aging and thus have lower risk.

The weathering hypothesis may also explain the perplexing finding (discussed above) of the risk-decreasing effect of *Teenage* in its interaction with *HlthProb*. The basic premise of the Weathering hypothesis is that women living in high-deprivation areas and/or practicing high-risk health behaviours will experience the increased risk of preterm delivery normally associated with older women due to accelerated aging (163). I hypothesize that for women living in the same high-deprivation DAs as well as those with health problems or those who smoke, older teenagers will have a lower risk of preterm birth compared with older women. In other words, accelerated aging will not create the same risk for them as for older women. My finding that *Teenage* has a risk decreasing relationship in its interaction with *HlthProb* supports this hypothesis.

An extension of this hypothesis may also explain the risk-increasing relationship found in the interaction between *Teenage* and *Urban*. While teenagers will have lower risk of late premature births than older women in high-deprivation areas, in less-deprived areas and in interactions with protective factors older women will not face the risk of accelerated aging. In those environments, teenage women will have greater risk of a late premature birth than older women. In the main effects (Figure 4.5), *Urban* was found to have an insignificant protective relationship with late premature births. If this hypothesis is correct,

then urban dwelling should be more protective in its interactions with older women but risk-increasing for teenage women. My findings that *Urban* is more protective for non-teenage women and that it increases risk for teenagers (Figure 4.7) supports this hypothesis. In turn, the finding that *Teenage* (versus non-*Teenage*) has a strong risk-decreasing effect in rural areas suggests that rural DAs are highly associated with high-deprivation and high-risk behaviours for women.

Small population areas are more likely to represent homogenous contextual and compositional characteristics (46,340) and to more accurately reflect health disparities as well as underlying population health determinants (398). The use of small population areas in the current study allowed comparisons within more homogenous contexts (e.g., low *MedInc* or high *%NoDip*), than if larger population areas had been used (as has often been the case in previous research). Women residing in a small subpopulation area would be more likely to be coping with the same ecologic levels of deprivation. Of those women, teenagers are less likely than older women to have an adverse-outcome birth. Those small population area comparisons may account for my contrary but consistent findings of the risk reducing role of *Teenage* in late premature births. If the proposed explanation is correct, the same protective role of *Teenage* should be evident in the risk level for other adverse outcomes. In the St Catharines group of hotspots, *HlthProb* was modified by *%NoDip*. I surmise that this finding could also be explained under the weathering hypothesis, (i.e., that women living in areas of low education age early biologically and are less able to cope with morbidities and other health challenges during pregnancy).

An important observation to note is the complete absence of median household income in my models of late premature births. This absence runs counter to a large amount of prior research. Socioeconomic status as measured by neighbourhood income has

consistently been found to be associated with SGA, preterm and still birth outcomes in Ontario and across Canada (9,95,128,130,277,277,279). It is possible that education, as found by Urquia (196), Kramer (128) and others, is simply a more effective predictor of late premature births than median income; if nothing else, it does have the advantage of being more easily modified.

4.2.2.4. Contrasting *LateP* Full-Province with Hotspot Group Results

The predictors found in the hotspot group models were a subset of the full-province model. Education (measured either by *%NoDip* or *%HigherEd*) interacting with *Olderage* appears in three of the four models, with the exception of St Catharines. The striking difference is not in what was in the hotspot models, as what was not. *Smoked*, *Teenage*, *%Asian* and *Urban* were all significant predictors in the full-province model but did not appear in any of the hotspot group models.

I suggest that this difference may be due the basic concept of a hotspot as a cluster of adjacent DAs sharing a significantly higher average level of an adverse outcome and surrounded by neighbours with lower levels. The aetiology sufficient to create a hotspot (i.e., the combination of risk factors that would allow for a significantly higher level of late premature births in a cluster of DAs) is likely to be quite different from that of the full province. The full-province model was fitted to all late premature births, wherever they may have occurred; a hotspot group model was fitted to late premature births within an extreme area (i.e., an area not representative of the province or the late premature births within it). A hotspot model would reflect the hyper-conditions that were sufficient to create it. Although *%NoDip* interacting with *Olderage* and *HlthProb* were not the only predictors of late premature births (the provincial model includes several others), they were the ones

sufficient to create a *LateP* hotspot. This relationship may explain the similarities as well as the dissimilarities between the province-level and hotspot analysis as well as the strong similarities between the local hotspot group models.

4.2.2.5. Contrasting *LateP* Hotspot Group Results

Models for the different hotspot groups were strikingly similar both in terms of risk factors represented as well as in the overall character of the models. Ecologic variables of education, indicated by both *%NoDip* and *%HigherEd*, were present in all three areas and modified two of the three highest risk factors, *Olderage* and *HlthProb*. The risk of a late premature birth increased for older age women and women with morbidities in DAs with low levels of education. There are likely other risk factors not included in this research that would add to that explanation but interestingly *MedInc* and *Smoked*, which were included in our modeling, did not.

4.2.3. *ModVeryP* Results

This section presents regression analysis results and discussion for moderately to very premature (*ModVeryP*) births (<35 weeks' gestational age) for both the full province and hot spot groups. There were 21,450 moderate to very premature births; from these we identified 152 hotspots, comprised of 833 hotDAs. Of the 18,670 total births in these hotspots, 1100 or 5.9%, were *ModVeryP* compared with 3.8% for the full province.

4.2.3.1. *ModVeryP* Full-Province Results

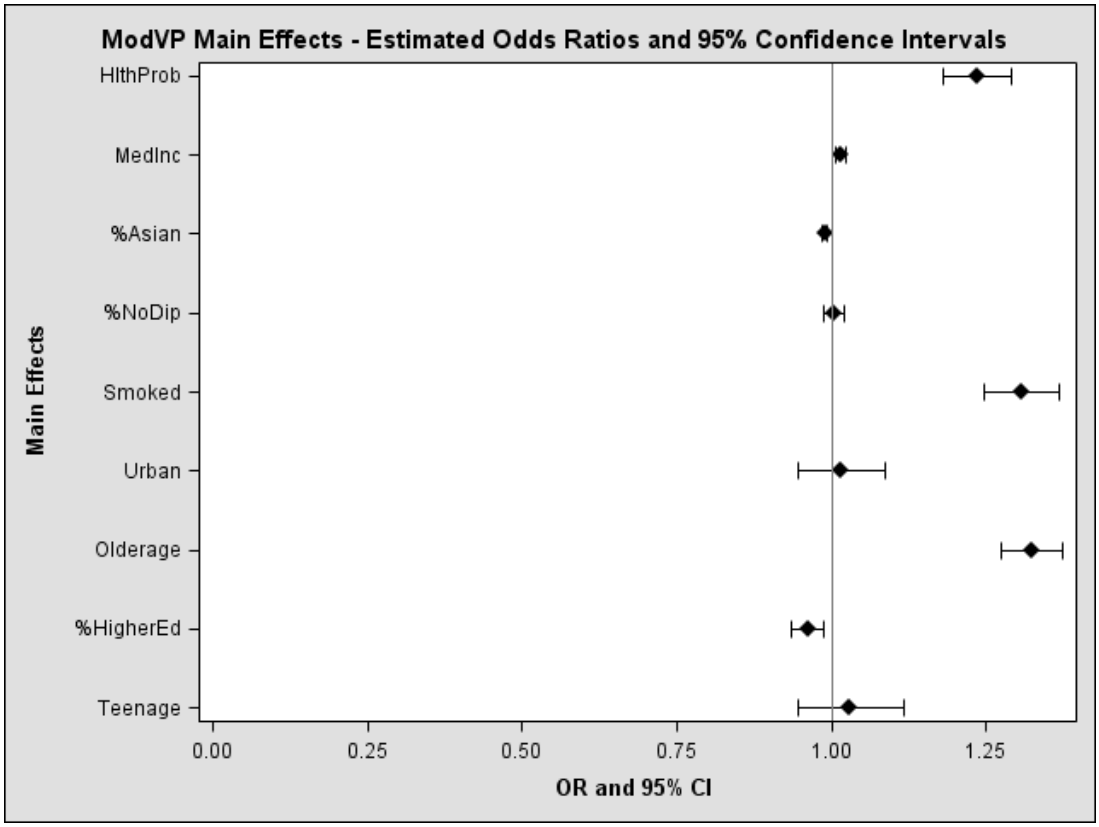
Figure 4.10 presents odd ratios and confidence intervals for the nine risk factors (main effects) found in the full-province final model for moderate to very premature births. These

main effects are given for comparison purposes only. A detailed explanation for interpretation of forest plots was given in Section 4.2.2.1.

Table 4.11 exhibits all risk factors and two-way interaction effects included in the final regression model for moderately to very premature (*ModVeryP*) births. This table contains hypothesis tests for the significance of each of the risk factors and predictors specified in the final model. The effects of eight of the nine individual risk factors were modified by an interaction with another risk factor. Only *%HigherEd* was found to have a non-modified relationship with moderately to very premature births. Women living in DAs with a high level of *%HigherEd* had a significant but only slightly lower risk 0.98 (05% CI: 0.97, 0.99), (or 2%), of a moderate to very premature birth compared to those living in lower *%HigherEd* DA. The full odds ratio and regression coefficient tables are presented in Appendices 4 and 11 respectively.

Table 4.11 Full-Province *ModVeryP* Final Model

	***F* statistic**	***P* value**
1. Olderage	45.31	<0.001
2. Smoked	8.57	0.003
3. HlthProb	0.01	0.904
4. %Asian	0.34	0.562
5. MedInc	15.35	<0.001
6. %NoDip	2.01	0.156
7. %HigherEd	6.55	0.01
8. Teenage	5.27	0.022
9. Urban	1.64	0.20
10. Teenage%Asian*	4.44	0.035
*11. HlthProb *Teenage*	8.02	0.005
*12. Smoked*Urban*	5.03	0.025
*13. Smoked*Teenage*	5.82	0.016
*14. Smoked*MedInc*	5.19	0.023
15. Smoked HlthProb*	6.58	0.01
16. Olderage%NoDip*	6.00	0.014



- *HlthProb*: pre-existing maternal health problem
- *Olderage*: the woman is >35
- *Teenage*: the woman is <20
- *Smoked:* the woman smoked at any time during pregnancy
- *Urban*: the DA has an urban population concentration
- *MedInc*: Median household income for DA
- *%NoDip*: Percent of women >20 in DA without high school diploma
- *%HigherEd*: % of women >20 in DA with graduate level education
- *%Asian*: Percent of South and East Asian immigrants in DA

Figure 4.10 Moderately to Very Premature Births Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

The estimated odds ratios and corresponding confidence intervals for the interaction effects found in the province-wide regression model are displayed in figures 4.11–4.13. Figure 4.11 displays interaction effects between continuous and binomial risk factors.

The first interaction effect in Figure 4.11, *Smoked*MedInc*, is between women who smoked at some point in their pregnancy and the median household income for the DA in which they lived. (See Appendix 5 for full data tables on which these forest plots were

based.) The odds ratios for *Smoked* (vs. did not smoke) are shown for high, mid, and low levels of DA *MedInc*. The effect of *Smoked* was modified by *MedInc*; it decreased with increasing income levels and, while *Smoked* was significant at the lowest level of *MedInc*, it became insignificant at the mid level of *MedInc*. Women who smoked and lived in lower median income DAs were at higher risk, about 1.2 (or 20%), of a moderate to very premature birth than women who did not smoke. At mid *MedInc*, whether women smoked (or not) was insignificant to the risk of a moderate to very premature birth.

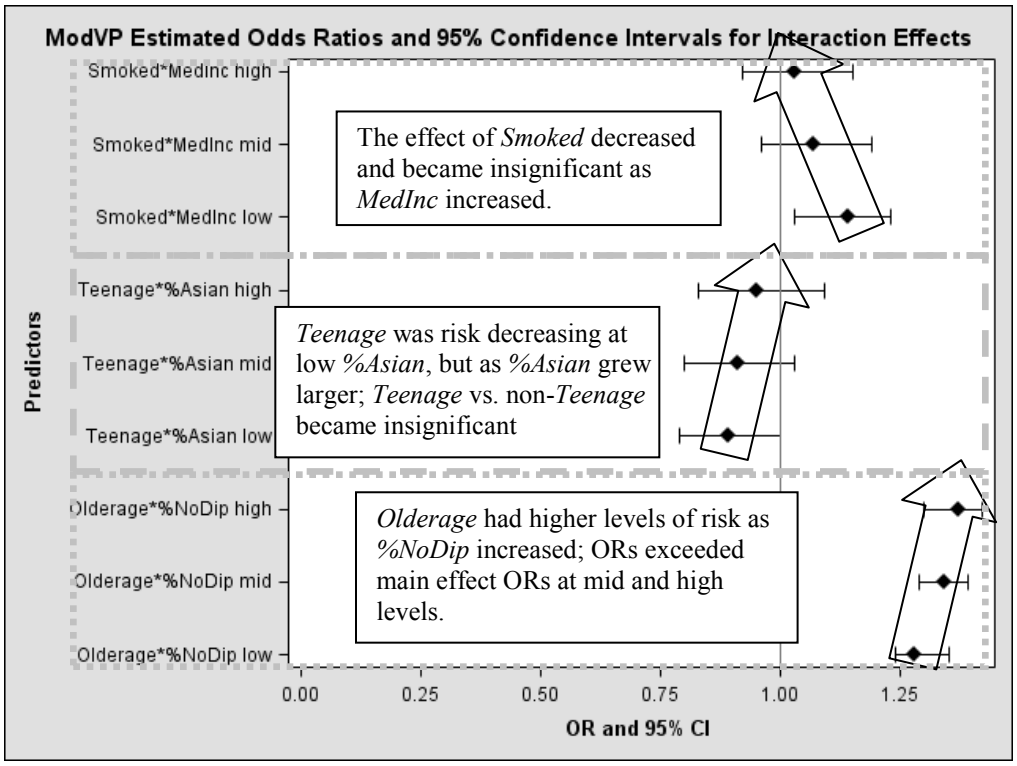


Figure 4.11 Moderately to Very Premature Births Estimated Odds Ratio and 95% Confidence Intervals for Interaction Effects

The next interaction, *Teenage*%Asian*, can be interpreted much the same way. The odds ratios for *Teenage* (vs. not) are shown at three different DA levels of *%Asian*. *Teenage* women living in a low *%Asian* DA had an estimated risk of a moderate to very premature

birth about 0.9 times (or 10%) less than non-*Teenage* women living in a like *%Asian* DA. The interaction effects are insignificant at all levels; yet the trend shown by the superimposed arrow suggests that increasing levels of *%Asian* increased the risk of a moderate to very premature birth for teenage mothers.

The third interaction, *Olderage*%NoDip*, demonstrates that the risk of a moderate to very premature birth for older age (vs. non-older age) women increased as DA levels of *%NoDip* increased. At low levels of *%NoDip,* older age women have about 1.3 times (or 30%) greater risk of a moderate to very premature birth than younger women; in high *%NoDip* DAs older age women have about 1.4 times (or 40%) greater risk of a moderate to very premature birth.

Figures 4.12 and 4.13 present interaction effects between binomial variables from the full- province model. Four interactions are presented: *Urban*Smoked*, *HlthProb*Smoked*, *Smoked*Teenage and HlthProb*Teenage*. Note that with binomial variable interactions there are only two levels, 0 and 1, not the three levels of low, mid and high, as there were for continuous variables (Figure 4.11) and four comparisons are made for each interaction rather than three. For example, in Figure 4.12 the first interaction is *Smoked *Urban*. Combinations of comparisons are shown in the left margin; the first two interaction combinations present the *Urban*, 1 vs. 0, under two conditions of *Smoked*, 1 and 0.

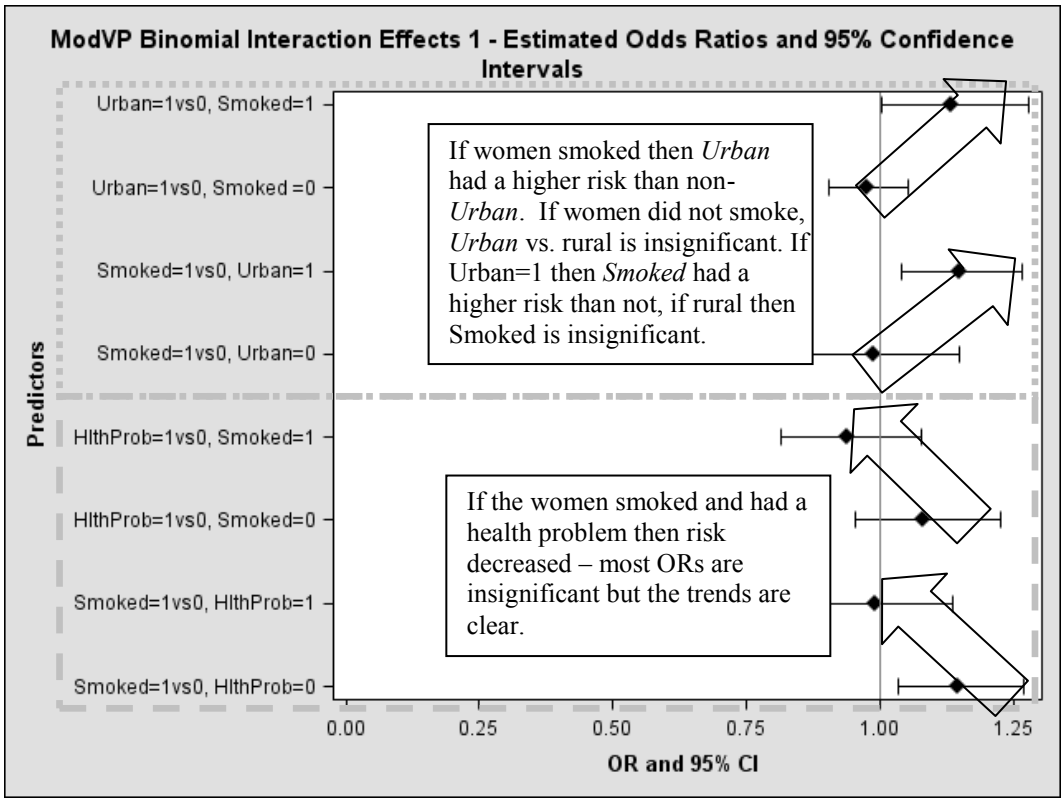


Figure 4.12 Moderately to Very Premature Binomial Interaction Effects: Estimated Odds Ratios and 95% Confidence Intervals

- *Urban* = 1 versus 0, *Smoked* = 1: for all women who smoked (*Smoked* = 1), those who lived in an urban area (*Urban* = 1) had a risk of a moderate to very premature birth about 1.1 times (or 10%) greater than those who lived in a rural area (= 0).
- *Urban* = 1 versus 0, *Smoked* = 0: for all women who did not smoke (=0), those who lived in an *Urban* area (=1) had an insignificant risk (note that the right confidence interval arm crosses the line of no effect) of a moderate to very premature birth about 0.9 times (or 10%) less than (vs.) those who lived in a rural area (*urban* = 0).

In summary, living in an *Urban* versus rural DA only affected the risk of a moderate to very premature birth for smokers; for non-smokers, urban versus rural did not matter.

The next two combinations of *Smoked***Urban* consider the risk of *Smoked* versus did not smoke, *Smoked* = 1 versus 0, and *Urban* = 1 versus 0 (i.e., rural). Note the difference: this comparison indicates that for all women who lived in urban DAs (*Urban*=1), those who smoked had odds of a moderate to very premature birth about 1.15 times (or 15%) greater than non-*Smoked* (=0). These odds are significant.

Smoked = 1 versus 0, *Urban* = 0: for all women who lived in rural DAs (U*rban* = 0), those who smoked (=1) had odds of a moderate to very premature birth about 0.99 (or 1%) less than those who did not smoke. Note that the odds are insignificant; for women who lived in a rural area, whether they smoked or not was insignificant to the risk of their having a moderate to very premature birth. Overall these interactions suggest that the combination of *Urban* (= 1) and *Smoked* (= 1) increases risk of a moderate to very premature birth, whereas living in a rural area and smoking does not significantly increase risk.

The interaction of *Smoked* and an existing health problem (*HlthProb*) can be interpreted in much the same way. Note that all interactions are insignificant except for *Smoked* = 1 versus 0, *HlthProb* = 0; women who did not have a health problem but smoked had about 1.14 times (or 14%) greater chance of a moderate to very premature birth than those who did not smoke. While all other interaction effects are insignificant two trends (shown by the superimposed arrows) are worth noting:

- Women who smoked (=1) and had a health problem (=1) seemed to be at less risk than those who did not smoke (=0) and had a health problem; and
- Women who had a health problem (=1) and smoked (=1) appeared at less risk than those without a health problem (=0) who also smoked.

Two more binomial interactions are presented in Figure 4.13: *Teenage*Smoked* and *Teenage*HlthProb*. For *Teenage* (=1), whether they smoked or not (1 vs. 0) was insignificant to the risk of a moderate to very premature birth. For non-teenagers, if the women smoked they had about a 1.2 times (20%) greater chance of a moderate to very premature birth than if they did not smoke (=0). For women who smoked (=1), if they were teenage they had about 0.85 (or 15%) less risk of a moderate to very premature birth than (vs.) older women. For women who did not smoke (=0), whether they were teenage or older was insignificant.

The interactions and trends (shown by the superimposed arrows) suggest that *Teenage* has a risk-decreasing, or protective, role in the *Teenage*Smoked* interaction; non-teenage women who smoke are clearly at greater risk than teenagers who smoke. This protective effect for *Teenage* was also demonstrated in the *Teenage** *HlthProb* interaction:

- For teenage women (=1), the existence of a health problem versus no health problem was insignificant to their risk of a moderate to very premature birth, while for non-teenage women the existence of a health problem increased their risk of a moderate to very premature birth by about 1.2 times (or 20%).
- For women with a Health Problem (=1), *teenage* had a risk decreasing effect; teenagers with a health problem had about 0.8 times (or 20%) less chance of a moderate to very premature birth than older women. For women without a health problem (=0), teenagers had about 1.11 times (or 11%) greater risk of a moderate to very premature birth than older women.

These specific odds ratios and general trends both underscore the risk-decreasing effect that *Teenage* has in its interaction with *HlthProb*. Yet without a health problem, teenagers have a higher risk than non-teenagers of a moderate to very premature birth.

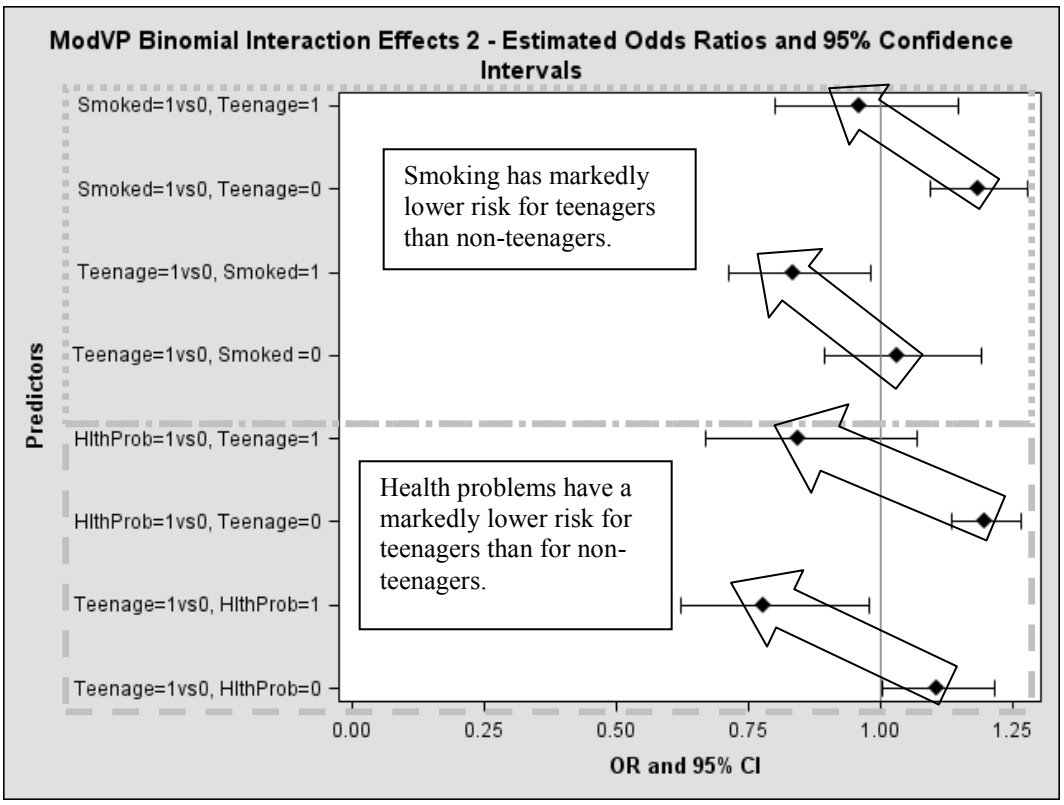


Figure 4.13 Moderately to Very Premature Binomial Interaction Effects: Estimated Odds Ratios and 95% Confidence Intervals

4.2.3.2. *ModVeryP* Hotspot Group Results

Four hotspot groups were identified for moderate to very premature birth outcomes: Hamilton, Cambridge, North Ottawa Valley and South Georgian Bay (see Section 3.3.2 for discussion on the identification method). The latter two represent larger geographic areas than the first two; these larger groups were selected because of an interest in

- expanding analysis beyond southern Ontario urban areas, and
- including a stronger representation of rural and urban DAs in the regression models.

In addition, the hotspots represented in the North Georgian Bay and the North Ottawa Valley were too spread out for a smaller area to capture a sufficient number of hotspots and hotDAs to meet confidentiality and analytical requirements. Table 4.12 presents descriptive information for each of the local hotspot groups. Square kilometre information demonstrates the size differences discussed above.

Table 4.12 *ModVeryP* Hotspot Groups Descriptive Information

***ModVeryP* Groups**	**Location**	**km^2**	**Hot spots**	**hotDAs**	**# births**	**# adverse**	**% ModP**
Hamilton	Hamilton city proper, borders lakeshore	145	17	117	2,451	192	7.8
Cambridge	Cambridge city proper and environs	1,248	21	87	1,617	131	8.1
S Georgian Bay	Area within 50 km. of Georgian Bay shore, beginning at Parry Sound to the east to Bruce Peninsula to the west	23,909	27	80	1,428	135	9.5
NOttVly	440 km. NW of Ottawa city centre	156,395	9	29	894	60	6.7

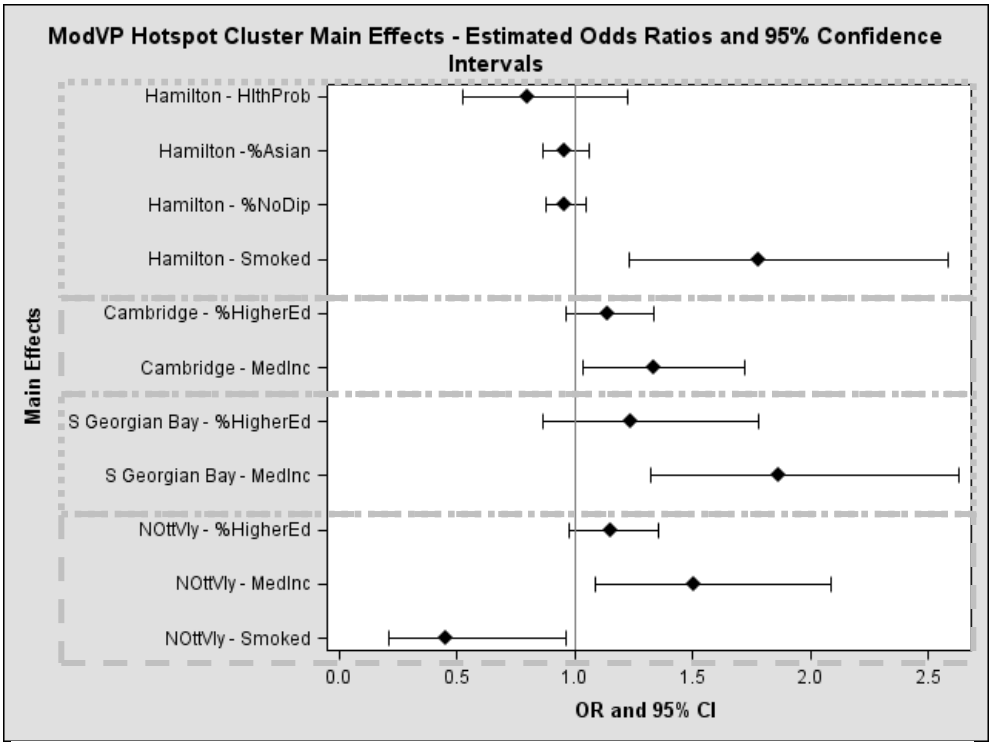
S Georgian Bay – South Georgian Bay NOttVly – North Ottawa Valley

Table 4.13 presents the final regression models for the four hotspot groups as well as the *F* statistics and *P* values for testing the null hypothesis that predictors have no association with the risk of a moderate to very premature birth. Note that a *P* value of about 0.10 was used as a cut-off point for hotspot regression model building. This allowance was made because of the relatively small number of adverse events and additional power required for interaction testing for the hotspot groups. The trends and significant subgroup comparisons provide very useful and insightful results. Full odds ratio and coefficient tables are presented in Appendices 5 and 11 respectively.

Table 4.13 Final Models for Four *ModVeryP* Hotspots Groups		
	***F* statistic**	***P* value**
Cambridge		
MedInc	6.54	0.01
%HigherEd	0.95	0.33
MedInc %HigherEd*	2.68	0.105
Hamilton		
Smoked	14.41	<0.001
%NoDip	4.09	0.04
%Asian	3.04	0.08
HlthProb	2.77	0.10
*%NoDip*HlthProb*	4.88	0.03
*%Asian*Smoked*	4.11	0.04
South Georgian Bay		
MedInc	0.82	0.37
%HigherEd	4.44	0.04
MedInc%HigherEd*	3.47	0.07
North Ottawa Valley		
MedInc	7.33	0.01
Smoked	0.15	0.70
%HigherEd	0.58	0.45
*%HigherEd *Smoked*	2.93	0.09

Figure 4.14 displays main effects for the four different groups. Main effects were generated as a first step in regression modeling. The odds ratios are presented for comparison purposes only. The effect of each factor on the risk of a moderate to very premature birth should only be considered with recognition of any known interaction and its modifying effect.

Odds ratios for interaction effects for the Cambridge and Hamilton *ModVeryP* hotspot group models are presented in Figure 4.15. Note that the different interactions presented involve different variable types, continuous and binomial, which require different configurations to adequately demonstrate the interaction effects. The findings on which the forest plots are based are presented in Appendix 5.



S Georgian Bay = Southern Georgian Bay Hamilton = City of Hamilton
Cambridge = City of Cambridge NOttVly = North Ottawa River Valley

Figure 4.14 Moderately to Very Premature Hotspot Group Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

Hamilton

The Hamilton hotspot group is located within the City of Hamilton; hotspots reside within a 145- km^2 area bordering the lake shore. The Hamilton group encompassed 17 hotspots comprising 117 hotDAs. See Table 4.12 for additional descriptive data about the Hamilton hotspot group.

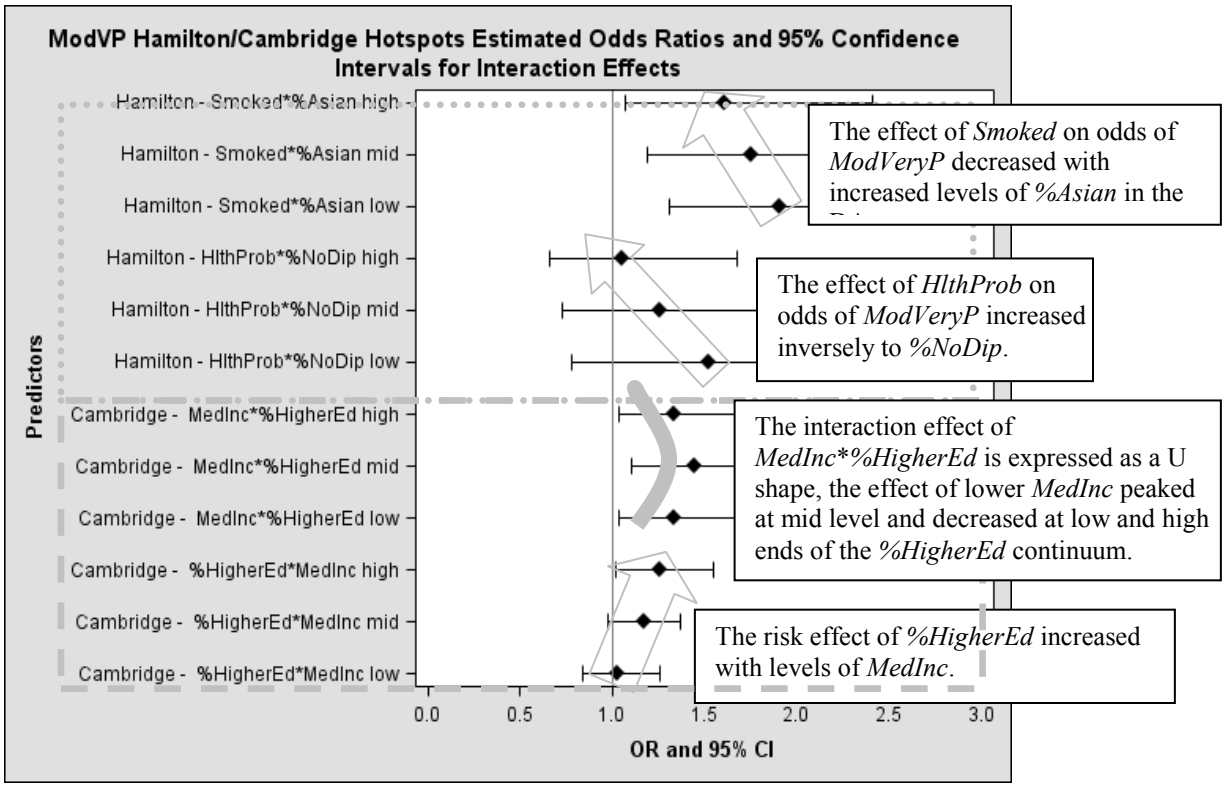


Figure 4.15 Moderate to Very Premature Hamilton and Cambridge Hotspot Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

The women at greatest risk of a moderate to very premature birth in the Hamilton group were those who *Smoked* and lived in a low *%Asian* DA. *%Asian* had a risk decreasing effect in its interaction effect with *Smoked*; as *%Asian* increased the level of risk for women who smoked decreased. Women who smoked and lived in a low (1%) Asian neighbourhood had an estimated risk of *ModVeryP* 1.9 times greater than a non-smoker living in a like *%Asian* neighbourhood; in a high (2%) *%Asian* neighbourhood a comparable risk was about 1.6.

For women with a health problem, those who lived in a relatively better educated area had a higher risk of *ModVeryP* than those living in more poorly educated areas. While

all odds ratio estimates were insignificant at all levels, a trend was clear: for women with a health problem, risk of a moderate to very premature birth decreased as *%NoDip* increased. This trend is supported by additional regression findings for the Hamilton hotspot (Appendix 5). These findings show that for women with a health problem, those who lived in a DA with 16% *NoDip* had a risk of moderate to very premature birth 0.8 times (CI: 0.67, 0.96) (or 20%) less than those who lived in a 10% *NoDip* DA.

Cambridge

The Cambridge *ModVeryP* hotspot group covers the city of Cambridge and its environs, an area approximately 1,248 km^2 containing 21 hotspots made up of 87 hotDAs. (See Table 4.12 for additional descriptive data about this group.) The model for Cambridge comprised only one interaction effect predictor, made up of two ecologic level variables: *%HigherEd* and *MedInc*. Women at greatest risk of a moderately to very premature birth in Cambridge were those in areas with higher levels of *MedInc* and *%HigherEd*. The interaction effect between these two risk factors was complex.

The *%HigherEd*MedInc* interaction results presented in Figure 4.15 demonstrate that the effect of *%HigherEd* on the odds of *ModVeryP* increased with level of *MedInc*; this increase became significant at the highest *MedInc* level. For all women living in high *MedInc* DAs, residents of DAs with 14% *HigherEd* had about 1.26 times (or 26%) greater risk of a moderate to very premature birth than those living in DAs with 9% *HigherEd*.

The *MedInc *%HigherEd* interaction was more complex. The ∩ shape superimposed on the plot reflects a trend in the nature of this relationship; while the differences between the ORs at the different levels are not significant, the trend reflects a risk increasing effect of a low median area income ($60,000 vs. $90,000) on the odds of a

moderate to very premature birth at the two ends of the *%HigherEd* continuum while moderately higher at the mid-level. Women who lived in DAs with lower *MedInc* income versus those with higher *MedInc* had a significantly higher risk of moderate to very premature birth at all levels of *%HigherEd*, but the odds of a moderate to very premature birth for those living in DAs with 9*% HigherEd* were 1.44 compared with 1.34 for those living in DAs with 3% and 9% *HigherEd*. While these differences were not significant, the trend is interesting to note.

Southern Georgian Bay

Odds ratios for interaction effects for the South Georgian Bay and North Ottawa Valley *ModVeryP* hotspot group models are presented in Figure 4.16. The Southern Georgian Bay hotspot group covers the southern half of Georgian Bay. Hotspots are within 50 km of the lakeshore beginning at Perry Sound to the east and ending at Bruce Peninsula on western shore. The group covers an area of 23,909 km ^{2} and encompasses 27 hotspots comprising 80 hotDAs. See Table 4.12 for additional descriptive information.

The interaction between of the two risk factors *MedInc* and *%HigherEd* was complex. Figure 4.16 demonstrates the interaction as two markedly different plot lines: the first represents the association between *%HigherEd* and *ModVeryP* modified at three different levels of *MedInc*; whereas the second represents the association between *MedInc* and *ModVeryP* modified at three different levels of *%HigherEd*.

The differences between the two different sets of points are distinct. In the first, the risk effect of *%HigherEd* on risk of a moderate to very premature birth was modified across increasing levels of *MedInc*. Significant at the low *MedInc* level, the effect became insignificant at mid-level. At the mid level of median household income *%HigherEd* had

no significant effect on whether the woman has a moderately to very premature baby. For women living in DAs at the lowest *MedInc* level, those residing in DAs with 9% *HigherEd* had a risk of *ModVeryP* about 1.7 times (70%) greater than those with 4% *HigherEd*.

The second set of points represents the effect of *%HigherEd* on the association between *MedInc* and *ModVeryP* as a ∩ shape. Again the differences between the different levels are not significant, but like the findings for Cambridge the ∩ shaped trend is interesting to note. While low *MedInc* ($35,000 versus $55,000) represents a significant

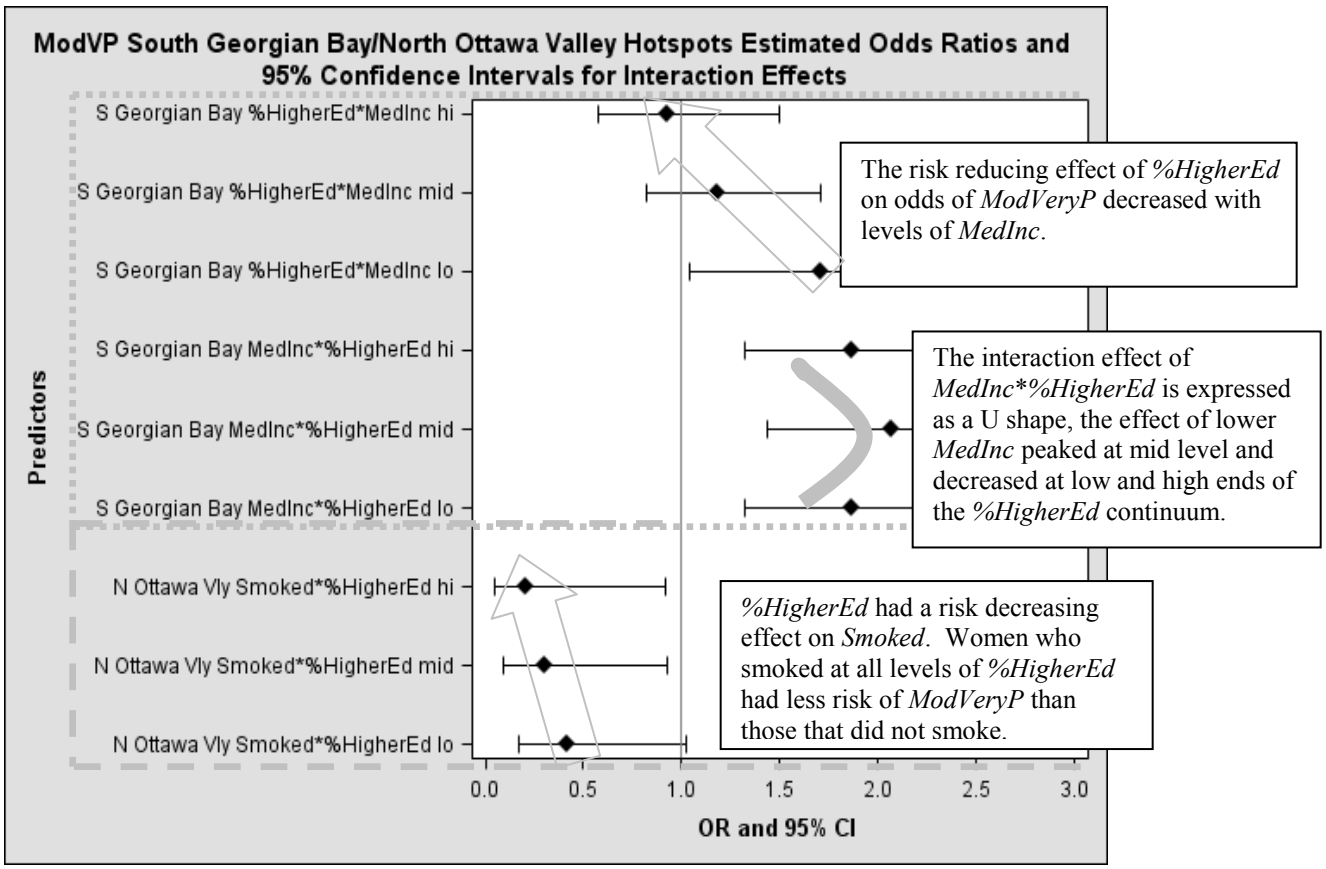


Figure 4.16 Moderately to Very Premature South Georgian Bay and North Ottawa River Valley Hotspots Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

risk factor for at all levels of *%HigherEd*; the risk peaks at the mid-level and was less at the low and high levels. Women living in a mid *%HigherEd* and $35,000 *MedInc* area have an

estimated risk of *ModVeryP* 2.01 times greater than those living in a like DA with $55,000 *MedInc*. Comparable odds for areas with low and high levels of *%HigherEd* were equal, at 1.86.

North Ottawa Valley

The North Ottawa Valley hotspot group was located about 440 km northwest of Ottawa City Centre. It was geographically the largest hotspot group of those identified; it includes nine hotspots, composed of 29 DAs (hotDAs), in an area of about 156,395 km^2. The 29 hotDAs range in size between about 0.2 to 70,696 km^2, with a median of 3.5 (IQR: 0.2, 9693). It is important to remember that the population size for the different DAs is about the same. (See Table 4.12 for additional descriptive information.) Women at greatest risk of *ModVeryP* in this group were those who:

- lived in lower *MedInc* areas; and
- *Smoked* and lived in lower *%HigherEd* DAs.

MedInc was found to be significant as a risk factor for moderate to very premature births with no modifying factors. A woman living in a $30,000 *MedInc* area had an estimated risk of a moderate to very premature birth about 1.9 times (95% CI: 1.17, 3.12) (or 90%) greater than one living in a $45,000 DA (Table 4.14).

Smoked and *%HigherEd* were significant in an interaction effect as a predictor of *ModVeryP*. *%HigherEd* modified the association between *Smoked* and *ModVeryP,* the effect of smoking decreased as *%HigherEd* increased; this modifying effect became significant at the mid-level of *%HigherEd*. For all women who lived in mid *%HigherEd* DAs, those who smoked had a risk of moderate to very premature birth about 0.3 times (or 70%) less than those who did not smoke. Comparable odds in high *%HigherEd* DAs were

0.21 times (or 79%) less. The finding of *Smoked* in a risk reducing role is inconsistent with other findings in this research.

4.2.3.3. ModVeryP Regression Results Discussion

The full-province analysis results suggest that the effects of individual level risk factors on risk of a moderate to very premature birth can differ substantially, depending on interactions with ecologic level variables. Comparisons between full-province and hotspot group models as well as between the group models underscore this finding and demonstrate the geographical differences. The effects of most individual level risk factors, *Olderage*, *Smoked*, *Teenage*, on the risk of a moderately to very premature birth were substantially modified by ecologic level variables. While the finding of the importance of ecologic level risk factors was consistent with a large body of previous research (8,9,41,399) the character of the interaction effects found in the current study contradict an equally large number of earlier findings.

For example, smoking has been widely recognized as among the most prevalent causes of moderate to very preterm births (9,142) and our main effects findings were comparable: the effect of smoking at some time during the pregnancy had one of the strongest risk-increasing effects on moderate to very premature births. Yet in an interaction effect, *Smoked* was modified by DA household median income to the extent that its effect on risk of moderate to very premature births was insignificant at mid-income levels. This finding suggests that ecologic levels of median household income may exert influence by patterning individual health behaviours in ways that adjust for the adverse effects of smoking. Diet and exercise are cited as two of these behaviours (8) but so was the actual behaviour of smoking during pregnancy. Smoking during the first 15 weeks of pregnancy

has been shown to not have a significant effect on the developing foetus, whereas smoking after 15 weeks does (142). I surmise that the decreased risk effect of smoking may be due in part to more women in higher-income DAs stopping smoking at earlier stages of pregnancy as well as practicing other risk-decreasing health behaviours.

Two other examples are the risk increasing interaction between *Olderage* and *%NoDip* (Figure 4.11) and *Urban* and *Smoked* (Figure 4.12). Both of these interactions demonstrated the strong effect-modifier role that ecologic level variables can exercise. I would cite the weathering hypothesis (163) discussed in Section 4.2.2.3 as a possible explanation for these effects. Women living in deprived areas and/or those who practice poor health behaviours such as smoking and consumption of alcohol and other drugs may develop "accelerated aging" (163) that increases risk of preterm birth.

I suggest that the findings of the consistently strong risk-decreasing effect of *Teenage* in a number of interactions (Figure 4.12) may also be explained by the weathering hypothesis (see Section 4.2.2.3 for a more extensive discussion). These findings run counter to a substantial body of research (9,36,180). Yet, the current study's findings of the importance of the role of ecologic level variables corroborate research conclusions from the seminal review of preterm research edited by Behrman and Butler (8) as well as research by O'Campo, Diez Roux and others that suggest adverse birth outcomes are the result of consistent, complex associations between individual and ecological-level predictor variables (8,9,18,128,277,400,401).

There are limits to the weathering hypothesis, which fails to explain a number of my findings. As shown in section 4.2.2.3 it worked well with late premature births where *Olderage* was very influential in explaining the risk of late premature births, and it may work well with later, more moderately premature births within the *ModVeryP* subgroup. In

this case, other predictors identified in my model are left to explain the very and extremely premature births. If this assumption is followed, then *Smoked* and *HlthProb* interacting with each other as well as with other ecologic and individual variables may possibly explain the earlier stages of prematurity. This premise would be supported by findings from previous research (9,36,109) that suggested biological factors such as health problems and smoking play a stronger role in preterm births than in SGA outcomes. The CIHI research (9) also included aging as a biological factor but since those studies did not subdivide preterm it is difficult extend those findings to this discussion.

The counterintuitive findings in the *Smoked*HlthProb* interaction (i.e., that women who smoked and had a health problem had lower risk of moderate to very premature birth than women without a health problem), may have been due to additional medical attention possibly received by women with a health problem. Women with a health problem may also have quit smoking early in the pregnancy, which would have greatly reduced their risk of an adverse outcome (8,161).

4.2.3.4. Contrasting *ModVeryP* Full-Province and Hot Spot Groups Results

Although the risk factors which comprise hotspot group models are a subset of the nine in the provincial model, every one of the interaction effects was unique. Education and median income had substantially greater presence in the hotspot models than in the full-province model. Represented by either *%HigherEd* or *%NoDip*, education was a part of each of the four hotspot group models. The two education indicators appeared only once in the provincial model; *%HigherEd* was unmodified and *%NoDip* was part of an interaction effect with *Olderage*. *MedInc* was a part of two hotspot models, Cambridge and South Georgian Bay, but appeared only once in the provincial model. *Smoked* was present in four

interactions in the full-province model and was found in two of the four hotspot group models.

One of the striking contrasts between the full-province and local models lay in the risk factors that were not present. *Teenage* was included in three provincial level interactions but had no significant influence in the local hotspot models. *Urban* and *Olderage* were also present in provincial models but did not have a presence in hotspot models.

The hotspot group models are simpler and more parsimonious than the provincial model; two are made up of one predictor, the others two. This characteristic is likely due in part to the smaller subpopulation sizes available for hotspot groups, but it may also be due in part to differences in diversity of the areas modeled. The provincial model represents a substantially larger, more multifaceted population, whereas the hotspot groups represent smaller, more homogenous subpopulations.

The differences between the two levels of models may also be due in part to the character of the populations being modeled. The full-province model was fitted to all moderate to very premature births in the province but the hotspot models were fitted to an extreme subpopulation (i.e. moderate to very premature births within hotspot DAs). The models that were fitted to hotspot births describe an aetiology sufficient to create a group of DAs with significantly higher levels of moderate to very premature births than the surrounding, neighbouring DAs. This group represents a different set of births than were modeled at the provincial level. This concept is more fully discussed in Section 4.2.2.4.

4.2.3.5. Contrasting *ModVeryP* Hotspot Group Results

A comparison of the models fitted to the hotspot groups demonstrates strong common threads as well as striking differences. Education was found to be a consistently influential factor in hotspot models; two, Cambridge and South Georgian Bay, share the predictor *MedInc*%HigherEd*. But the effects of these predictors were quite different when contrasted between groups. The two identical set of predictors in the models in Cambridge and South Georgian Bay were opposite in effect: in Cambridge the predictor had a risk-increasing effect whereas in South Georgian Bay it had a risk decreasing effect.

A possible explanation for this difference may be that pursuit of a career following graduate studies did not play as substantial a birth-delaying role in South Georgian Bay as it may have in Cambridge. A tentative analysis of the two subpopulations showed marked differences in median household incomes and prevalence of higher education between the two areas. The South Georgian Bay hotspot group has an overall median household income of about $51,000 (Q1, Q3: $43,000, $67,000) and median *%HigherEd* of about 4.5% (Q1, Q3: 2.8, 6.4); for the Cambridge group median household income was about $75,000 (Q1, Q3: $57,000, $89,000) and *%HigherEd* about 7.4% (Q1, Q3: 2.2, 15.7) (Appendix 9). The substantially lower median income and *%HigherEd* factors of South Georgian Bay compared with Cambridge's suggest that in South Georgian Bay, higher education levels may not have indicated career building and associated delayed childbearing (9) that may be more prevalent in Cambridge as indicated by its higher *MedInc* and *%HigherEd* characteristics. A definitive explanation falls outside the scope of the current study, but this tentative analysis suggests the importance of characteristics of a place, either as modifiers or confounders, that can markedly change the effects of a given predictor.

Yet while *%HigherEd* at different levels of *MedInc* had opposite effects in the two different hotspot groups, *MedInc* at different levels of *%HigherEd* had an identical effect in the two areas, a ⋂-shaped trend curve. While differences between the different levels of *%HigherEd* were not significant, the trend is interesting; a lower *MedInc* (vs. higher) had a significant risk-increasing effect at all levels of *%HigherEd*, women in the mid *%HigherEd* DAs had a markedly higher risk those at the higher and lower ends of the continuum.

A possible explanation for this ⋂-shaped interaction trend may be that *%HigherEd* acts as an ecologic indicator of an area norm that favours and reinforces older age childbearing. In DAs with a low level of *%HigherEd* the culture may be weak and there may have been less delayed childbearing. In the DAs with high levels of *%HigherEd* the education level may have been high enough that it had a risk reducing effect; in the *LateP* analysis the risk effect of *Olderage* on late premature birth decreased at the highest level of *%HigherEd*. At the mid-level I surmise that the culture of delayed childbearing was strong enough to result in an increased risk but the ecologic education level may not have been strong enough to offset the risk introduced by the lower to higher *MedInc* contrast.

An exploratory analysis comparing percentage of older women at the different *%HigherEd* levels across the two hotspot groups provided inconclusive evidence. The highest percentages of births to older women were in the low and high *%HigherEd* DAs in both hotspot groups; the lowest percentages were in mid *%HigherEd*. This evidence seemingly contradicts my finding of higher *ModVeryP* events in the mid *%HigherEd* DAs. Cell sample sizes were too small to be fully confident in these results; additional research with larger sample sizes will be needed to be more conclusive.

It is interesting to note that the ∩ shape has the same effect in two hotspot groups with such differences in *MedInc* and *%HigherEd*. This suggests that the ∩-shape trend may result more from the relative than absolute differences in each place. It is important to note that the tails of the odds ratios overlapped at the different levels of *%HigherEd* which suggests that the differences are not significant, but the ∩-shape trend appears consistent.

The perplexing interaction between *Smoked* and *%HigherEd* in North Ottawa Valley presented an effect where women who smoked had a lower risk of moderate to very premature birth than women who did not smoke, an effect that became more protective as the level of higher education increased. Two possible explanations for this relationship present themselves. One is that in DAs with higher education levels, women who admitted that they smoked at some point may have quit earlier in the pregnancy as well as had better health behaviours, such as diet or exercise, and minimized the risk of a moderate to very premature birth. Simultaneously, some women who did not admit to smoking may have continued to smoke throughout. A second is that women in higher education DAs who smoked were more likely to seek out early education and medical care, in contrast to women who did not smoke. Neither of these suggested explanations is satisfactory, but a full explanation is beyond the scope of this analysis.

Another perplexing interaction effect was found in Hamilton between *HlthProb* and *%NoDip*; results showed risk of a moderate to very premature birth for women with a health problem decreased as the DA level of *%NoDip* increased. One possible explanation is that Hamilton's Healthy Babies, Healthy Children program is having a substantial effect. This program has included extensive prenatal health and education services as well as public health nurse home visits for expectant mothers. These intervention programs may

have had positive results among women with an existing health problem(s) and those who lived in high-risk environments (e.g., low-education areas).

While province level outcomes were relatively consistent with past research, the hotspot outcomes are remarkable for their strikingly different, perplexing and counterintuitive characteristics. In partial explanation it is important to recognize that:

- There were substantial differences between the hotspot groups themselves. They encompassed DAs of markedly different sizes and *Urban* versus rural characteristics as well as diverse geographic locations and populations. Because one of the goals of the current study is to explore existing known predictors, I did not assume that these were the only risk factors that might effectively explain adverse outcomes. The finding of such perplexing results strongly suggests the likelihood of unknown explanatory variables, confounders or modifiers.
- The moderate to very premature outcome spans a range of gestational ages that are sometimes broken down into two or three additional subgroups (2,8,94). We cannot assume that the different hotspots represented an equal mix of the different gestational age levels within moderate to very premature births. If they did not—if for example Cambridge represented more moderately premature and Hamilton more extremely premature births—then it would be reasonable to expect that the models would be different.

It is interesting to note that the models fitted to such markedly different hotspot groups did not differ more. The Cambridge and South Georgian Bay models were made up of identical predictors; North Ottawa Valley and Hamilton shared *Smoked* and two different indicators of education. Education, especially *%HigherEd*, was highly influential in all four

models. If my suggestion that the markedly different effects of these similar predictors were due to variables, modifiers or confounders not included in this research is correct, then it would follow that the relationships between these predictors and moderate to very premature births are more complex than much of the research to date has suggested.

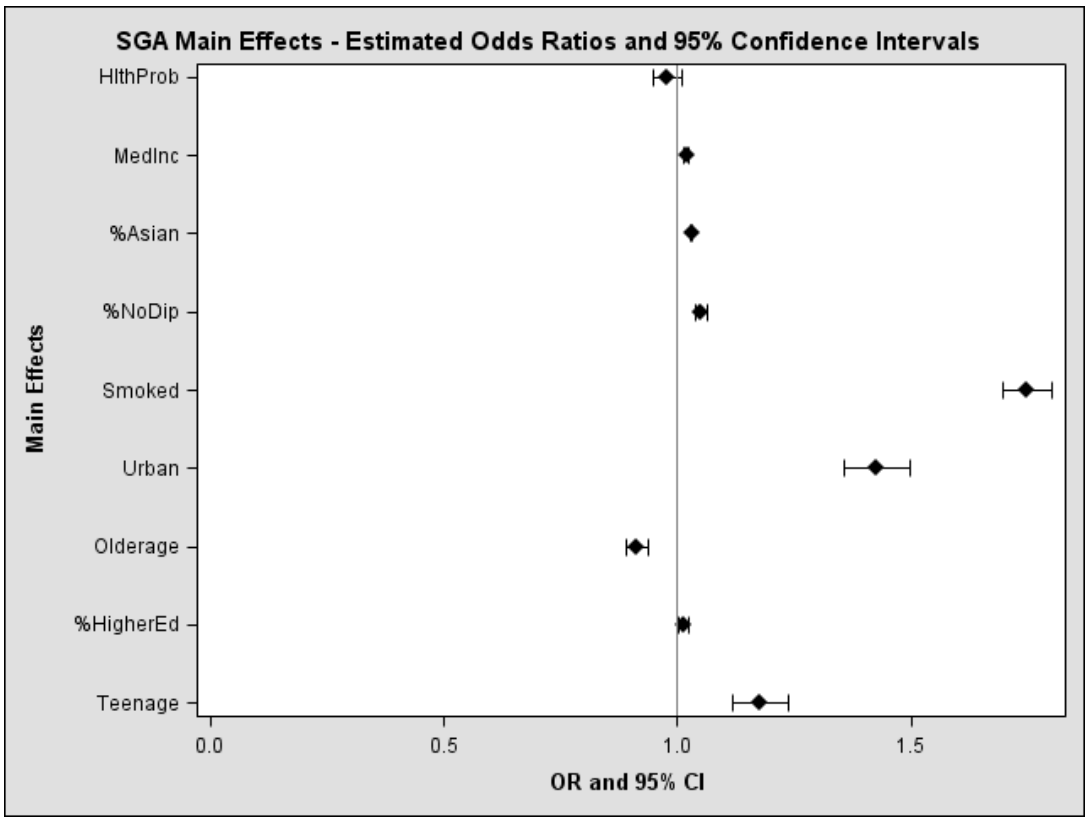
4.2.4. SGA Results

Small for gestational age (SGA) births are the most common adverse birth outcome in the province, with 54,446 SGA events (8.8%) of births in the database for the current study (Table 4.1). There were a total of 252 *SGA* hotspots comprised of 1,402 hotDAs, representing a total of 85,379 births and 11,236 SGA births, the largest count of the four adverse outcomes. SGA hotspots had a 13.2% SGA rate compared with a full province rate of 8.8% (Table 4.2).

4.2.4.1. SGA Full-Province Results

Figure 4.17 exhibits the nine predictor variables (main effects) found in the final hierarchical regression model of *SGA* for the full province. Main effects are given for comparison purposes only; Figures 4.18–4.22 present the final interaction effects for the fitted model.

Table 4.14 exhibits the final model for *SGA* for the full province. This table contains hypothesis tests for the significance of each of the risk factors and predictors specified in the final model. Thirteen interactions are presented; all individual risk factors are modified. The full odds ratio and regression coefficient tables are presented in Appendices 6 and 11 respectively.



- *HlthProb*: pre-existing maternal health problem
- *Smoked*: the woman smoked at some time during pregnancy
- *Olderage*: the woman is >35
- *Teenage*: the woman is <20
- *MedInc*: median household income for DA
- *%Asian*: percentage of South and East Asian immigrants in DA
- *%NoDip*: percentage of women >20 in DA without high school diploma
- *Urban*: the DA has an urban population concentration
- *%HigherEd*: percentage of women >20 in DA with graduate level education

Figure 4.17 Small for Gestational Age Births Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

Table 4.14 *SGA* Births Final Model		
	***F* statistic**	***P* value**
1. *Teenage*	0.57	0.449
2. *Olderage*	1.90	0.167
3. *MedInc*	10.25	0.001
4. *%NoDip*	0.66	0.416
5. *%HigherEd*	3.84	0.05
6. *Urban*	123.25	<0.001
7. *Smoked*	220.64	<0.001
8. *HlthProb*	11.01	0.009
9. *%Asian*	22.96	<0.001
10. *%NoDip*Smoked*	14.34	0.001
11. *MedInc*Smoked*	5.17	0.023
12. *Urban*Smoked*	54.08	<0.001
13. *%Asian*Smoked*	24.62	<0.001
14. *%Asian *Olderage*	30.52	<0.001
15. *MedInc*%NoDip*	15.35	<0.001
16. *MedInc*%HigherEd*	7.89	0.005
17. *MedInc*Teenage*	6.40	0.011
18. *%HigherEd*Olderage*	18.20	<0.001
19. *Teenage*HlthProb*	6.05	0.014
20. *Smoked*HlthProb*	6.25	0.012
21. *Olderage*Smoked*	31.46	<0.001
22. *%NoDip*Urban*	26.55	<0.001

Two figures, 4.18 and 4.19, present odds ratios for the six binomial by continuous interactions. Odds ratios are presented at three different levels of the continuous variable in order to demonstrate the change in interaction effect across levels. (See Appendix 6 for the analysis results on which these tables are based.)

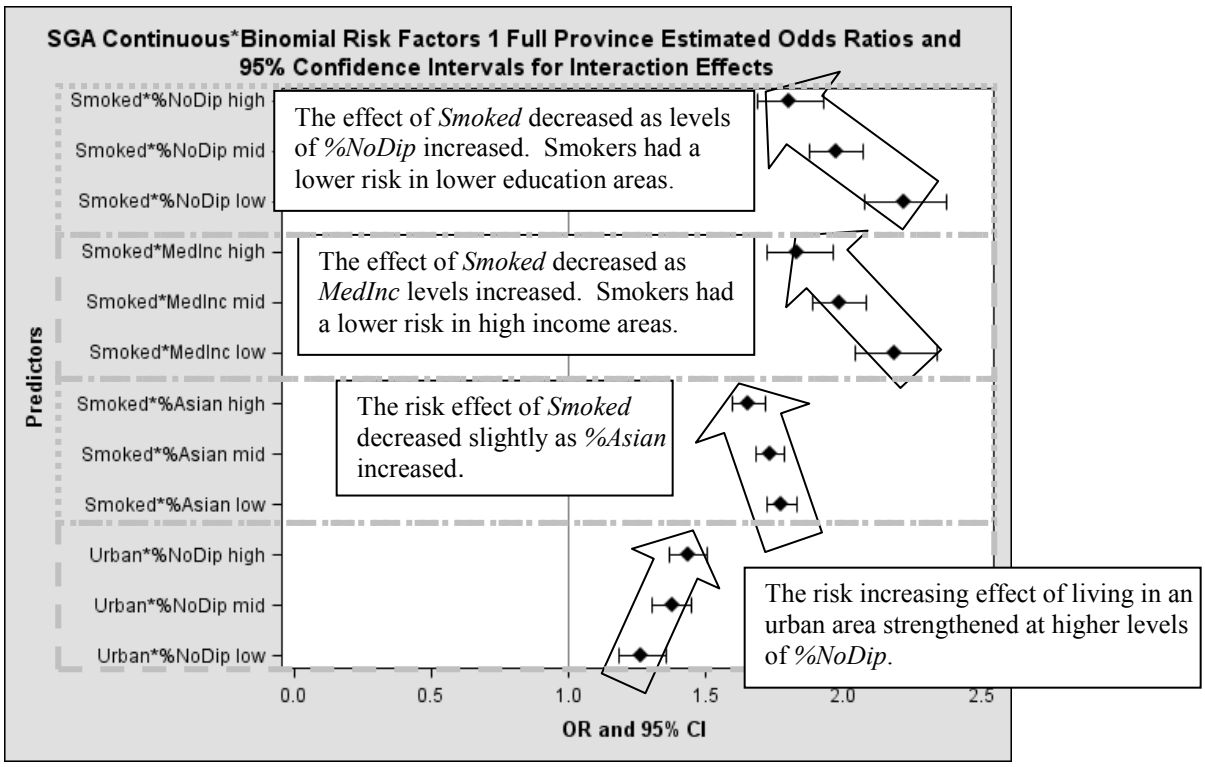


Figure 4.18 SGA Continuous*Binomial Risk Factors Part 1: Full-Province Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

The first three interactions presented in Figure 4.18 all represent *Smoked* and demonstrate two consistent themes within these findings:

- *Smoked* consistently increased risk of *SGA*; and
- Ecologic variables modified and reduced the effect of even this most consistent risk factor.

%NoDip had a risk reducing effect on the relationship between *Smoked* and *SGA*; women living in DAs with lower levels of education, those who smoked (versus those who did not) had a lower risk of an SGA birth than women in areas with higher levels of education. While smokers at all levels of *%NoDip* had a substantially greater risk than non-smokers, the odds ratio in those DAs with a low *%NoDip* were more than 2.2 times (or 120%) greater, where in DAs with high levels of *%NoDip* they were about 1.7.

MedInc had a risk reducing effect on the association between *Smoked* and *SGA*. Women who smoked and lived in a low *MedInc* area were found to be at a higher risk of an SGA birth; yet even in the highest *MedInc* DAs, women who smoked had a risk of SGA birth about 1.7 times (or 70%) greater than non-smokers.

%Asian had a slight risk reducing effect on the association between *Smoked* and *SGA*. When *Smoked*%Asian* was assessed, women who smoked and lived in a low *%Asian* DA were at the highest level of risk of a SGA birth in this interaction.

An *Urban*%NoDip* interaction is also presented in Figure 4.18. The effect of *Urban* increased with increasing levels of *%NoDip*; urban dwellers who lived in high *%NoDip* areas were at greater risk of an SGA birth than rural residents.

The first interaction presented in Table 4.19, *Teenage*MedInc*, increases risk; the higher the level of DA household median income, the greater the risk of an SGA birth for teenage women versus non-teenage women. The odds decreased as *MedInc* decreased; for births in the lowest *MedInc* DAs, being a teenager had no effect on the risk of *SGA*.

The second interaction, between *Olderage*%Asian*, was a risk-decreasing one. In main effects (Figure 4.17) *%Asian* had a slight risk-increasing relationship with *SGA* but in the interaction effect with *Olderage*, the risk-decreasing effect of *Olderage* (vs. younger-aged) increased with *%Asian* and became significant at mid-level.

The risk-decreasing effect of *Olderage* was demonstrated again in its interaction with *%HigherEd*. The risk of *SGA* for older women (vs. younger women) decreased at higher levels of *%HigherEd*. This protective relationship was significant at all levels; older age women living in the highest *%HigherEd* areas had a risk of *SGA* 0.9 times (or 10%) less than younger women living in the same area. It is important to note that *%HigherEd* had slight a risk-increasing relationship with *SGA* in main effects (Figure 4.17) while

Olderage had a protective relationship. Lower levels of *%HigherEd* modified this protective relationship, decreasing it; higher levels increased it beyond the level found in main effects.

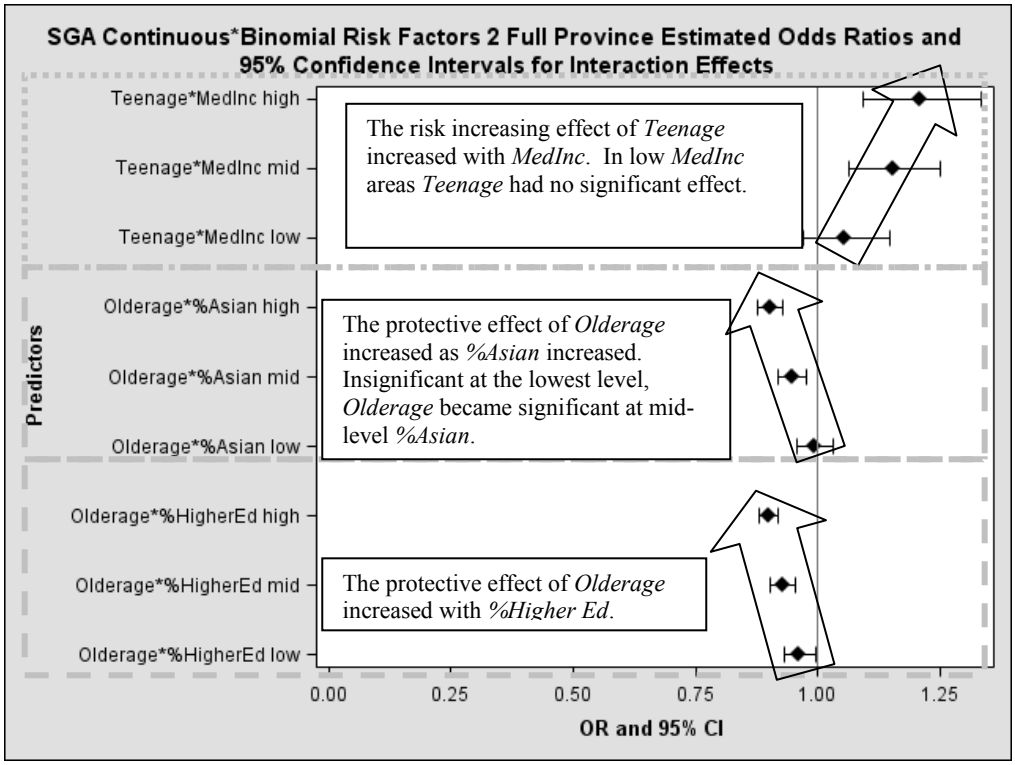


Figure 4.19 SGA Continuous*Binomial Risk Factors Part 2: Full-Province Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

Figure 4.20 presents interactions between continuous variables, *MedInc*%NoDip* and *MedInc*%HigherEd*.[24] In main effects, Figure 4.17, all three risk factors, *%NoDip*, *%HigherEd* and *MedInc*, had risk-increasing relationships with *SGA*, although *%HigherEd* and *MedInc* were slight (1.01 and 1.02 respectively).

[24] See Appendix 6 for data analysis results on which these figures are based.

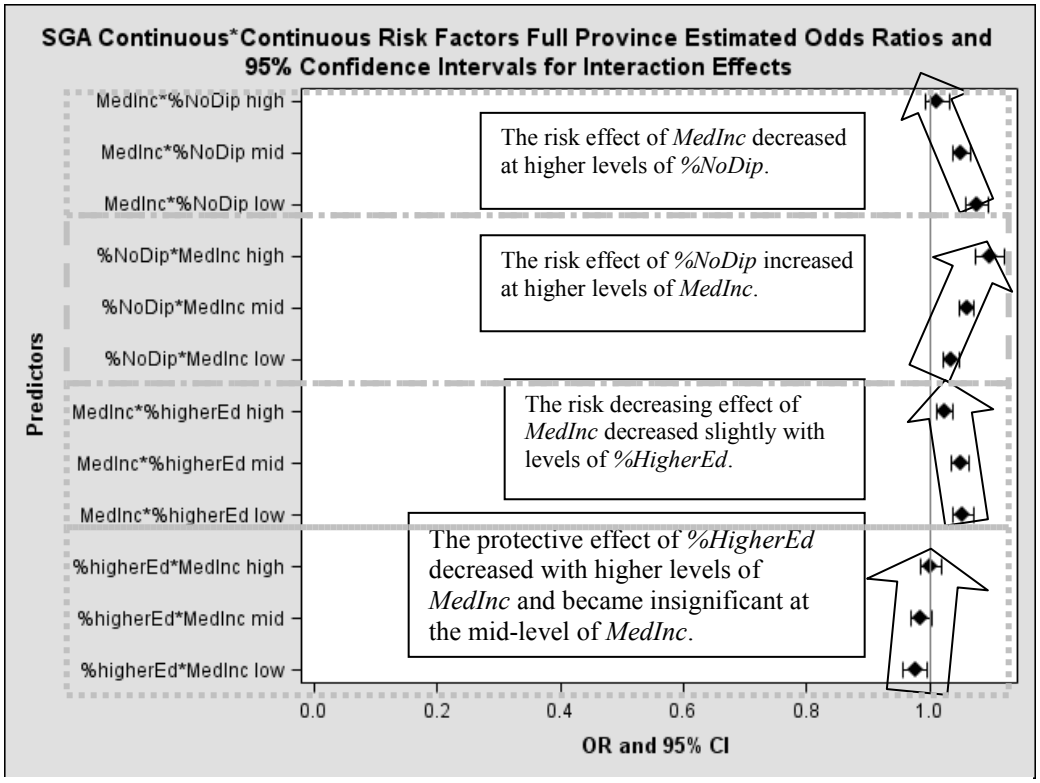


Figure 4.20 SGA Continuous*Continuous Risk Factors: Full-Province Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

The interaction effects between the ecologic variables *%NoDip* and median household income (*MedInc*) presented in Figure 4.20 suggest that education (as indicated by *%NoDip*) has greater influence over risk of an SGA birth than *MedInc* in DAs with high *%NoDip* levels. The first interaction, *MedInc*%NoDip*, demonstrates that the effect of *MedInc* ($45,000 vs. $65,000) was greater for women in more highly educated DAs (low *%NoDip*); as levels of *%NoDip* increased, that effect decreased and became insignificant at the highest level. This finding was corroborated where the effect of *%NoDip* was shown at different levels of *MedInc*. The effect of *%NoDip* increased as levels of *MedInc* increased; for all women living in high *MedInc* DAs, those who lived in DAs also with lower education

levels (14% *NoDip*) versus higher education levels (4% *NoDip*) were at greater risk of an SGA birth.

%HigherEd had a different interaction effect with *MedInc* than *%NoDip* did. Generally as the level of *%HigherEd* increased, the risk effect of *MedInc* decreased. Conversely, as the level of *MedInc* increased, the risk-decreasing effect of *%HigherEd* weakened and became insignificant; at the lowest level of *MedInc, %HigherEd* had a significant protective relationship with SGA births, at mid-*MedInc* it became insignificant.

Figures 4.21 and 4.22 present the effects of interactions between binomial risk factors.[25] Interactions represented are *Urban*Smoked*, *HlthProb*Smoked*, *Smoked*Olderage* and *HlthProb*Teenage.* The findings from the first three of these interactions continued to demonstrate the strong risk increasing effect of *Smoked* on *SGA*.

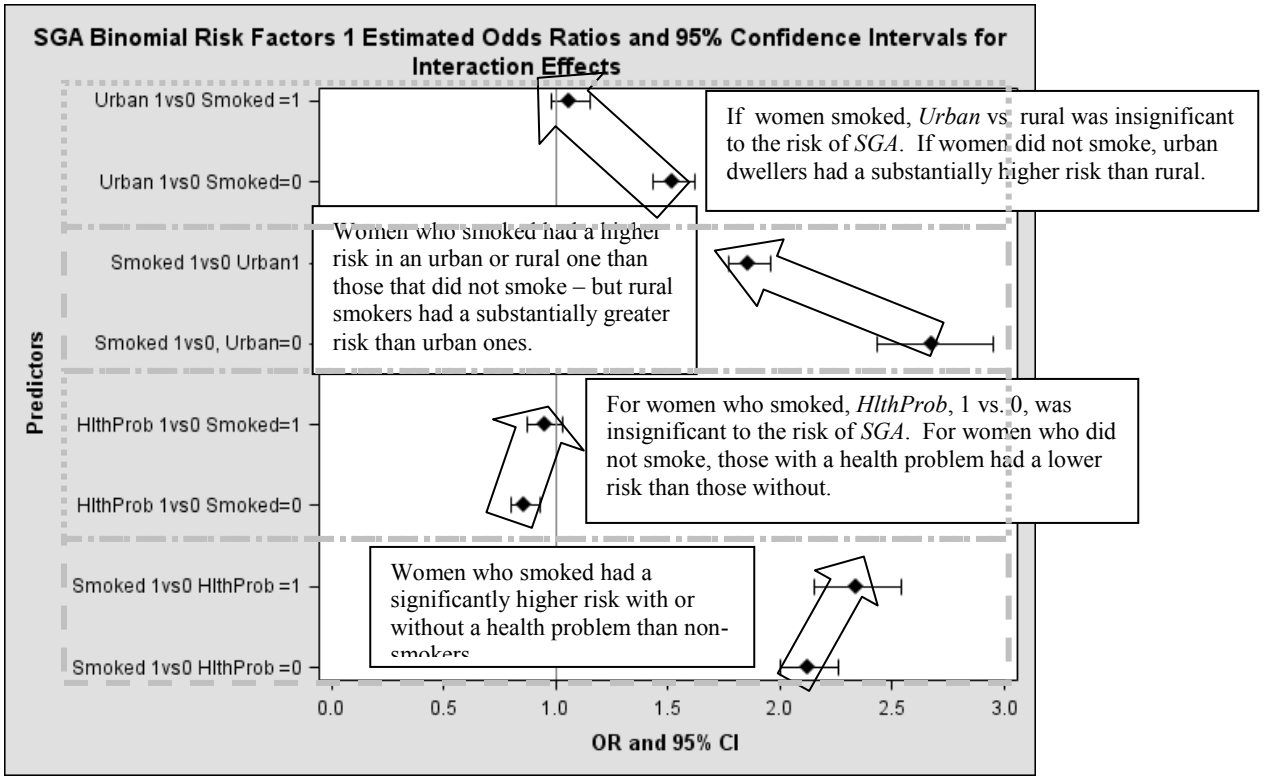


Figure 4.21 SGA Binomial Risk Factors Part 1: Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

[25] See Appendix 6 for the analysis results on which these figures are based.

In the first two combinations, the risk of living in an urban versus rural DA was contrasted between women who smoked and those who did not. The first combination of the *Urban*Smoked* interaction, *Urban* 1 versus 0*, Smoked* =1, shows that among women who smoked (*Smoked* = 1), those who lived in an *Urban* DA (=1) had an insignificantly higher risk of an SGA birth compared to rural dwellers (*Urban* = 0). The second combination, *Urban* = 1 versus 0*, Smoked = 0,* shows that for all women who did not smoke (=0), those who lived in an *Urban* DA (=1) had a risk of an SGA birth about 1.5 times (or 50%) greater than rural DA dwellers.

In the second set of combinations the risk of *Smoked* versus not was contrasted between women who lived in *Urban* DAs and those who lived in rural ones. The findings from *Smoked* 1 versus 0*, Urban* =1*,* show that for all women who lived in an *Urban* area (*urban* = 1), those who smoked had a risk of an SGA birth about 1.9 times (or 90%) greater than those did not smoke (*smoked* = 0). The findings from the second combination, *Smoked*, 1 versus 0, *Urban* = 2, show that for women who lived in rural DAs, those who smoked had a risk of SGA birth about 2.5 times (or 150%) greater than those who did not smoke.

The interaction between *Smoked* and *HlthProb* (i.e., whether the women had an existing health problem at the time of the pregnancy) was interpreted much the same way: if women smoked, then whether or not they had an existing health problem did not have a significant effect on their risk of a SGA birth. For women who did not smoke (*smoked* = 0), those who had a health problem (=1) had a lower risk of an SGA birth, about 0.85 times (or 15%) less than those without a health problem. For women who had a health problem, if they smoked then their risk of SGA was about 2.3 times (or 130%) greater than those who

did not smoke. For women without a health problem, those who smoked had about 2.12 times (or 112%) greater risk of an SGA birth than those who did not.

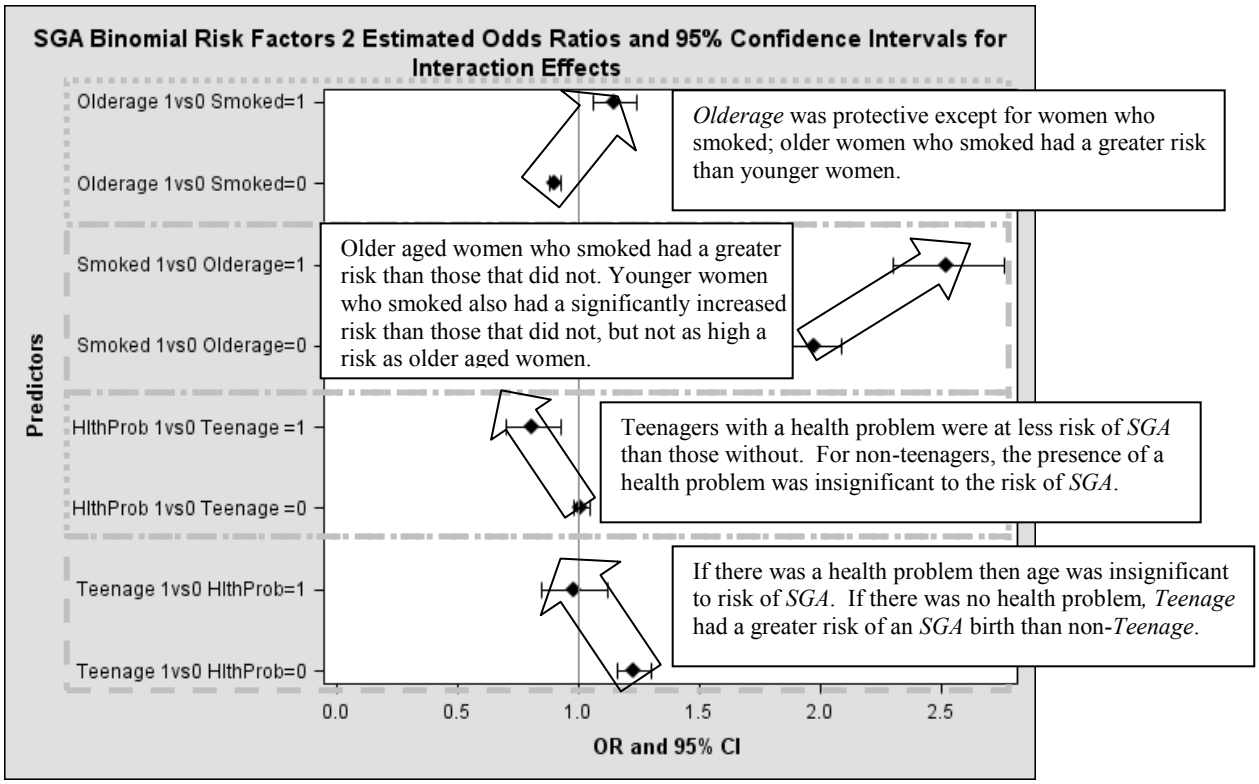


Figure 4.22 SGA Binomial Risk Factors Part 2: Estimated Odds Ratios and 95% Confidence Intervals for Interaction Effects

The interactions presented in Figure 4.22 continue to demonstrate the substantial risk relationship between *Smoked* and *Olderage*. For all women who smoked, if they were older age then their risk of an SGA birth was about 1.15 times (or 15%) greater than for younger women. Among those who did not smoke, older age women had about 0.9 (or 10%) less risk of an SGA birth than younger ones. The risk of an SGA birth was markedly higher for women of any age if they smoked; but for older age women the risk effect was substantially greater than it was for younger women.

The second interaction effect presented in Figure 4.22 is between *Teenage* and *HlthProb*. For teenage women the existence of a health problem had a risk-decreasing

effect; teenagers with a health problem had an estimated risk of an SGA birth about 0.8 times (or 20%) less than teenagers without a health problem. For non-teenage women the presence of a health problem (vs. no health problem) did not have a significant effect on their risk of a SGA birth. When women without a health problem were considered, those who were teenagers had higher risk of an SGA birth than non-teenagers.

4.2.4.2. *SGA* Hotspot Group Results

Three hotspot groups were identified for SGA birth outcomes: Eastern Toronto, London/St Thomas, and Northwest Toronto. Table 4.15 presents descriptive information for each of these hotspot groups.

Table 4.15 *SGA* Hotspot Groups Descriptive Information

Group	Location	km^2	hotspots	hotDAs	# births	# adverse	% SGA
E Toronto	14 km. E/NE of Toronto city centre	100	55	201	10,403	1639	16
London	London and St Thomas	316	8	50	1,354	156	12
NW Toronto	26 km. NW of Toronto city centre	142	24	81	4,826	713	15

E Toronto = East Toronto NW Toronto = North West Toronto

Figure 4.23 presents main effects for each of these hotspot groups. Main effects are given for comparison purposes only; Figures 4.24 and 4.25 present the final interaction effects for eight of the nine risk factors.

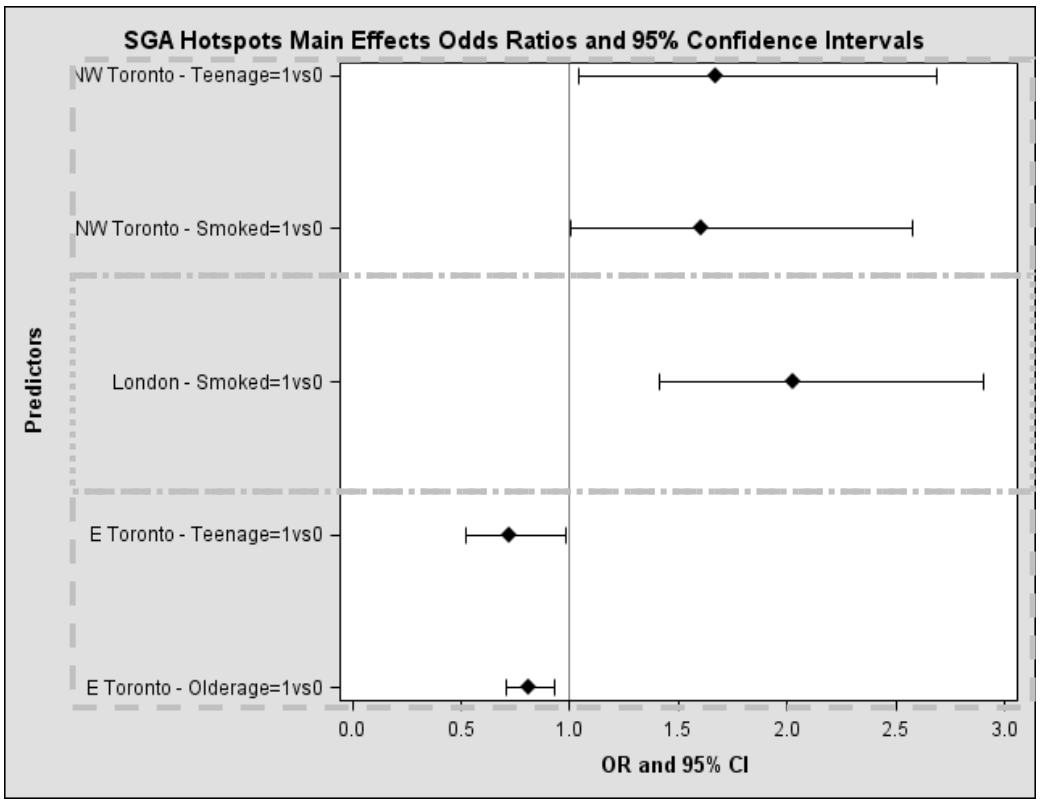


Figure 4.23 Main Effects for SGA Hotspot Groups

Table 4.16 exhibits the final regression models for the three *SGA* hotspot groups. This table contains *F* statistics and *P* values for testing the null hypothesis that the predictors in the final model have no association with risk of SGA births (347). No interaction effects were found in these three hotspot groups. Odds ratios for predictors found in the *SGA* hotspot

Table 4.16 Final Model for Three *SGA* Hotspot Groups

	***F* statistic**	***P* value**
Northwest Toronto		
Smoked	4.11	0.05
Teenage	4.78	0.03
London		
Smoked	15.46	<0.001
East Toronto		
Olderage	9.32	0.002
Teenage	4.30	0.04

group models are presented in Figure 4.24. Full odds ratio and regression coefficient tables are presented in Appendices 6 and 11 respectively.

Northwest Toronto *SGA* Hotspot Group

The Northwestern Toronto hotspot group covers about 142 km^2 and is located 26 km northwest of Toronto city centre. It contains 24 hotspots made up of 81 hot DAs. There were 4,826 births in the years 2005–9, 15% of which were *SGA* (Table 4.15). In this group, women at greatest risk of *SGA* were those who were teenage and those who smoked. Findings shown in Figure 4.24 demonstrate that teenage women were estimated to have a risk of a SGA birth about 1.67 times (or 67%) greater than non-teenage women. For women who smoked, the odds of *SGA* were about 1.6 times greater than for those who did not smoke. The two variables did not have an interaction effect.

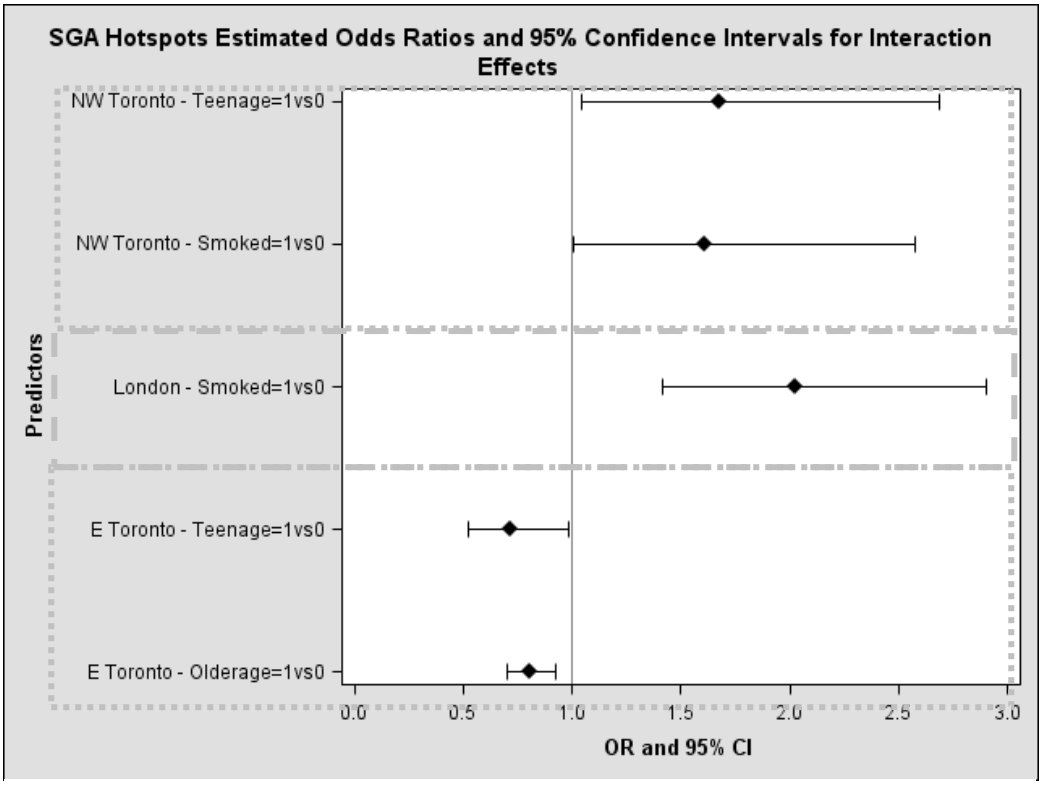


Figure 4.24 *SGA* Hotspot Groups: Estimated Odds Ratios and 95% Confidence Intervals for Significant Predictors

London / St Thomas *SGA* Hotspot Group

The hotspot group of London/St Thomas covers approximately 316 km^2 and contains eight hotspots made up of 50 hotDAs. There were 1354 births in the years 2005–9, of which 12% were *SGA* (Table 14.5). Women most at risk in this group were those who smoked. For women who smoked, the odds of an SGA birth were about two times (or 100%) greater than for those who did not smoke (Figure 4.24).

East Toronto *SGA* Hotspot Group

The Eastern Toronto *SGA* hotspot group covers an area of about 100 km^2 and is about 14 km east/northeast of Toronto city centre. It encompasses 55 hotspots made up of 201 hotDAs. Table 4.15 contains additional descriptive information. About 10,400 births were represented in this group; 16% were *SGA*. Within these hotspots, the group at greatest risk of an SGA birth was women between the ages of 20 and 35 years. Both *Teenage* and *Olderage* predictors were found to have significant risk-decreasing relationships with the odds of a SGA birth. Figure 4.24 demonstrates that for older age women, the odds of an SGA birth are about 0.8 times (or 20%) less than for non-older age women. For teenage women the estimated odds are even less, about 0.72 times (or 28%) less than for non-teenage women (333).

4.2.4.3. SGA Regression Results Discussion

Findings for the full province were complex in the sheer volume of interactions presented but also relatively simple in terms of the several strong common themes that presented themselves. This complexity corroborated findings from previous research; SGA births have a more complex aetiology than any of the other three adverse outcomes (6,8,36,125). In the full-province findings, all predictors were made up of interaction effects; there were

no single variable predictors. Every individual-level risk factor but one (existing health problem) was modified by an ecologic level one.

Of the 13 significant predictors in the full-province model, seven represented an individual*ecologic level interaction. *Smoked* was the most influential risk factor, found in six of the 13 interactions. This result concurs with findings from a substantial amount of population-based and clinical research (8,128,134,136,137,261,402). In four of those six interactions, an ecologic variable modified the *Smoked* relationship; in three, the ecologic variables *MedInc*, *%Asian* and *%NoDip* reduced the odds of an SGA birth for women who smoked (Figures 4.18 and 4.19). These risk-decreasing interaction effects sharply contrasted with the risk-increasing interactions with the individual risk factors *Olderage* and *HlthProb*.

The risk reducing effects of the *MedInc*Smoked* interaction may have been due at least in part to variation between how much or how long women smoked during pregnancy. Research has shown that stopping smoking by 15 weeks' gestational age reduces the impact on the foetus and that rates of SGA births do not differ from non-smokers (8,225). Women living in higher *MedInc* areas have been shown to be more likely to seek prenatal examinations and education (130) and may stop smoking earlier in pregnancy than others. I also surmise that women in higher *MedInc* DAs gain from a surrounding culture that is more supportive of healthier diets and lifestyles (see supporting discussion in Section 2.5.3.2).

The risk reducing interaction between *%Asian* and *Smoked* may have resulted in part from the "healthy immigrant" effect, where immigrants bring with them cultural norms of better health behaviours (196) and stronger social networks, including possibly higher levels of social capital, that are more pervasive in areas where they live (194,283). These

social norms and networks may have resulted in women stopping smoking earlier in pregnancy as well as having diets and other health behaviours that could have minimized the effect of smoking.

%Asian was initially added as a known risk factor for SGA births. Immigrant women from South and East Asia have been shown to bear babies that by Canadian standards are small for gestational age (123,374) but are otherwise healthy. In my analysis, *%Asian* was found to have a significant risk-decreasing interaction relationship with all adverse events (see sections 4.2.2, 4.2.3, and 4.2.4) except stillbirths, where it was insignificant. The risk decreasing relationship of *%Asian* may be explained at least in part by the healthy immigrant effect. Additional research is needed to better explore these hypotheses.

The perplexing interaction between *Smoked* and *%NoDip,* where the effect of *Smoked* decreased with increasing levels of *%NoDip,* was more difficult to explain, especially given the high-risk-increasing relationship between *Smoked* and SGA births. One possible scenario that might explain this counterintuitive finding is that DAs where there were both very high percentages of %*NoDip* and where women reported having smoked in pregnancy may be indicative of DAs with high proportions of Aboriginals in the population. Aboriginal women over 20 years of age statistically:

- smoke at higher rates than the Ontario population as a whole, 72% versus 18% (403,404);
- are less likely to have completed high school, 51% versus 28%, (403,404); and
- are more likely to have babies weighing greater than about 4,000 grams (macrosomia) (405), 22% versus 12.2% (64,403). One of the determinants of

macrosomia is diabetes, and Aboriginal women are more likely to be diabetic than the Ontario population in general (15% versus 4%) (403,404).

The Aboriginal population was also expanding at a faster rate than the Ontario population in general, about 26% compared to 8% (64). While only 2% of Ontario's population was Aboriginal, with a 2.6% fertility rate compared with 1.5% for Ontario as a whole (64) their birth events may have resulted in this counterintuitive effect.

Previous research has suggested that risk of a SGA birth is positively associated with poverty (16,128,130,277). But the findings of the current study did not consistently concur with those earlier findings. Education, as indicated by both *%NoDip* and *%HigherEd*, was the most influential of the ecologic level effect modifiers in my analysis and was a risk modifier in five interaction effects. Specifically:

- The risk-increasing effect of a lower median income was insignificant in areas with low levels of education.
- The risk-increasing effect of poor education was amplified in high *MedInc* DAs. If *MedInc* had a stronger influence, I would have expected the effect of poor education to have to diminish as *MedInc* increased.
- The effect of *MedInc* was deceased at higher levels of *%HigherEd;* for women living in DAs with higher levels of *%HigherEd*, the difference between a $45,000 versus $65,000 median household income had an insignificant effect on their risk of an SGA birth.

If these findings had agreed with those of previous research, stronger associations should have appeared between lower income and education levels.

A possible explanation for the above discrepancy could be my use of smaller population areas; but several of the studies noted used DA-level data (9,130,277). Another possible explanation might be my use of a continuous indicator of median household income, rather than quintile categories and the ensuing comparison of top and bottom quintiles used in several of the cited studies (9,130,277). Because categorization of continuous variables is known to bias outcomes in logistic regression analysis (406) as well as other analysis, it is not a recommended practice for continuous variables (407-410). The use of markedly smaller population areas combined with the use of the continuous income variable may account for the current study's mixed support of previous findings.

The perplexing interaction effect of *MedInc*Teenage* (i.e., that the risk of SGA birth to a teenage mother increased synonymously with higher levels of *MedInc*) may be explained by my extension of the weathering hypothesis (see Section 4.2.2.3). I hypothesized that *Teenage* would be risk-decreasing in high-deprivation areas or with risk-increasing individual factors, but risk- increasing when interacting with protective factors. My finding that teenage women have a higher risk of SGA births than non-teenage women at higher levels of *MedInc* supports this hypothesis.

My finding that low education was a predictor of SGA births was consistent with previous research outcomes, which have generally found SGA birth outcomes to be inversely associated with education levels (6,16,392). In the current study, increasing levels of *%NoDip*:

- were a more influential predictor of an SGA birth than *MedInc*;
- increased the risk effect of *Urban* on the risk of an SGA birth (9); and
- decreased the risk effect of *Smoked on* SGA births.

My finding that the effect of *MedInc* ($45,000 vs. $65,000) on the risk of a SGA birth decreased as *%NoDip* increased suggests that education was the more influential of the two risk factors. For women in DAs with high levels of poor education, income level had an insignificant effect on the risk of an SGA birth. This premise was supported by outcomes from the *MedInc***%HigherEd* interaction: the risk effect of *MedInc* decreased at higher levels of *%HigherEd*.

4.2.4.4. Contrasting Full-Province and Hotspot Group SGA Results

The predictors found in the hotspot group models were representative, to a limited degree, of the full province model. *Smoked*, *Olderage* and *Teenage*, all highly influential in the provincial model, were all present in two of the three hotspot group models. Four differences between the full-province and hotspot group models were of note:

1. In the full-province model, all predictors were from interaction effects, whereas in the hotspot groups there were no interaction effects. *Teenage*, *Smoked* and *Olderage* were all modified in the full-province model, not so in the group models.
2. Ecologic level variables were effect modifiers in 10 of the 13 full-province model interactions, but there were no ecologic level variables in the group models.
3. The full-province model had 13 predictors, the north-western and Eastern Toronto groups have two, and London had only one.
4. While the provincial and hotspot groups models share risk factors, i.e. *Smoked*, *Teenage* and *Olderage,* a larger number are not shared; *MedInc*, *HlthProb*, *%NoDip*, *%HigherEd*, *Urban* and *%Asian* are not present in the local group models; and none were close to significant in the incremental model building steps.

To explain these differences between full-province and hotspot group models a summary of an earlier discussion regarding *LateP* results (see Section 4.2.2.3) is presented here: SGA births in hotspots were not a representative sample of provincial SGA births; they were taken from DAs that were found to have significantly higher levels of *SGA* events. The aetiology sufficient to create SGA births in such concentration is likely to be quite different from that of all SGA births across the full province. While *Smoked*, *Teenage* and *Olderage* were not the only predictors of SGA births (the provincial model includes a wide variety of others), they were apparently the ones sufficient to create the *SGA* hotspots in the groups evaluated. I do not suggest that these factors fully explain the stark dissimilarities between the province-level and hotspot models, but it does appear that the differences found were real differences and not the outcomes of underpowered tests or biased data.[26]

4.2.4.5. Contrasting SGA Hotspot Group Results

The group models seem to have substantial commonalities. *Smoked* and *Teenage* are each significant in two models. *Smoked* has a relatively strong risk-increasing role with SGA births in both Northwest Toronto and London. Exploratory analysis corroborated the influence of *Smoked* in the London area. Of all women who had an SGA birth, about 43% of women in the London hotspot group smoked, compared with 17% in the full province.

The most striking difference was between the Eastern and Northwestern Toronto groups. While *Teenage* was shared as a predictor, its relationship with risk of an SGA birth was strikingly different between the two groups. *Teenage* had a risk-increasing relationship in both main effects (Table 4.23) and in Northwest Toronto (Table 4.24) but was found to

[26] There is some risk of bias due to the hotspot groups not being selected as representative of all hotspots. See Section 3.3.2 for further discussion on hotspot group identification.

have a risk-decreasing relationship in the East Toronto model. *Olderage*, which had a risk-decreasing effect in main effects, was also risk-decreasing in Eastern Toronto.

Exploratory analysis corroborated this difference between the two groups. A comparison of the two areas showed that in the Northwest group 5% of SGA births were to teenage women, whereas in the eastern group only 2.4% were to teenage women. An ad hoc variable, *Midage* (i.e., women >19 and <35) was created as an indicator of non-*Teenage*/non-*Olderage* observations. When all other factors were held constant, *Midage* women in the Eastern Toronto group were found to have a significantly greater risk of an SGA birth, about 1.26 times (or 26%) greater, than teenage or older age women. Descriptive analysis of this *Midage* group found that a significantly greater percentage of them smoked, 17% versus 15% for non-*Midage* women. I suggest that *Teenage* was found to be protective in Eastern Toronto (vs. the risk relationship of *Teenage* in the Northwest) at least in part because:

- They had a substantially lower proportion of area SGA births than teenage women in the northwest group; and
- They had proportionately fewer SGA births than *Midage* women in their own hotspot group.

This result may have been due in part to lower smoking rates among teenage and older women than among middle-aged women.

While these exploratory findings are insightful, it is important to note that the confidence intervals for the *Teenage* odds ratios in both hotspot groups (Figure 4.24) are both relatively wide and close to 1. Only about 25 teenage women had SGA births in each area. I am not as confident in these results as I would want to be to draw firm conclusions

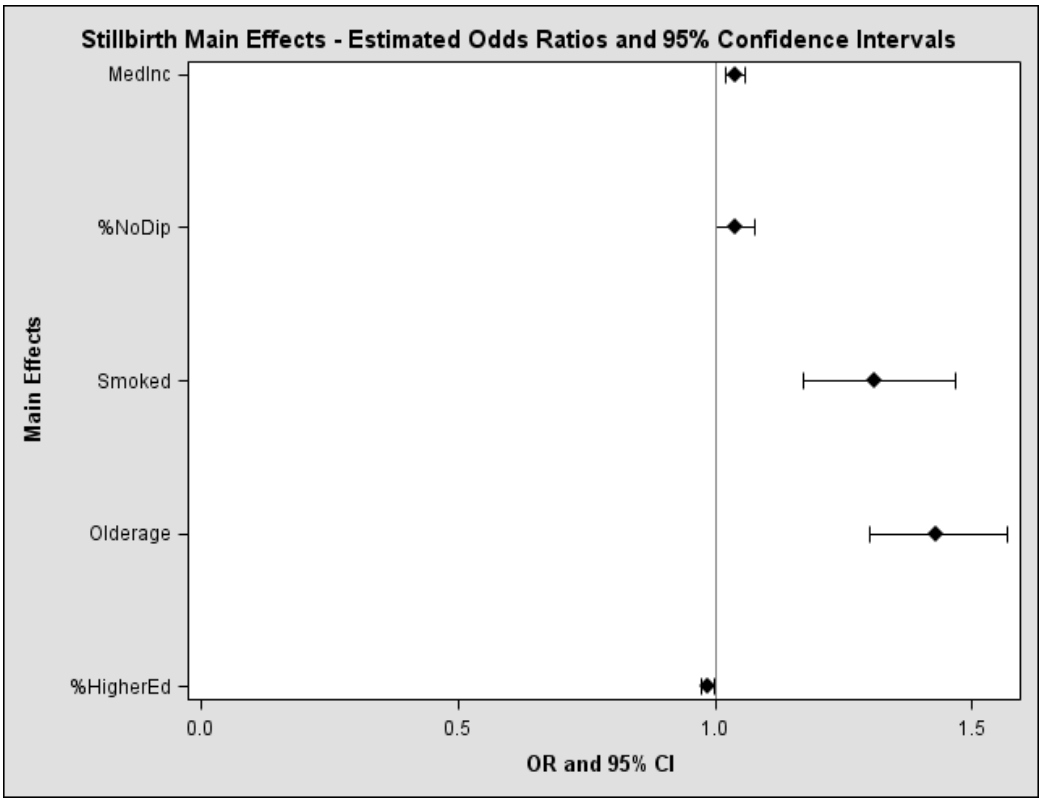
about the explanatory differences between these two areas. Additional research with larger sample sizes would better explain the almost double percentage of teenage SGA births in Northwest compared to East Toronto.

4.2.5. Stillbirth Results

Stillbirths were the least-common adverse outcome, with 3,615 events in the data set. From these events 27 hotspots were identified, made up of 197 hotDAs. Within those hotspots the *Stillbirth* rate was 0.99%, about 1 in 100 births. The rate for the full province was 0.6% (Table 4.2). Because of the relatively small event size and the lack of local groups that would meet selection criteria, *Stillbirth* hotspot groups could not be identified for analysis.

4.2.5.1. Stillbirth Full-Province Results

Figure 4.25 exhibits main effects for the five risk factors found in the final regression model for *Stillbirth*. Main effects are given for comparison purposes only; Figure 4.26 presents the final interaction effects for two of the five risk factors.



- Smoked: The woman smoked at some time during pregnancy
- Olderage: The woman is >35
- *%HigherEd*: % of women >20 in DA with graduate-level education
- *MedInc*: Median household income for DA
- *%NoDip*: Percentage of women >20 in DA without high school diploma

Figure 4.25 *Stillbirth* Main Effects: Estimated Odds Ratios and 95% Confidence Intervals

Table 4.17 exhibits the final regression model for *Stillbirth*. This table contains hypothesis tests for the significance of each of the risk factors and predictors specified in the final model. Three of the risk factors remained as individual predictors in their relationship with *Stillbirth*, *Smoked* and *%HigherEd* were found to have an interaction effect. The full odds ratio and regression coefficient tables are presented in Appendices 7 and 11 respectively.

Table 4.17 *Stillbirths* Final Model		
	***F* statistic**	***P* value**
Olderage	66.71	<0.001
MedInc	22.37	<0.001
Smoked	9.36	0.002
%HigherEd	0.09	0.763
%NoDip	4.78	0.029
%HigherEd*Smoked	4.63	0.031

Figure 4.26 presents estimated odds ratios for significant predictors of all stillbirths in the province.[27] Both individual and the one interaction effect predictors are presented in this figure. The women at greatest risk of stillbirth in the province were those who were older aged and smoked and also lived in DAs with a high level of *%HigherEd*. Women who lived in areas with high levels of *%NoDip* and in areas with lower levels of *MedInc* were also at slightly greater risk; there was no significant interaction between *MedInc* and *%NoDip*.

[27] See Appendix 7 for the analysis results on which these figures were based.

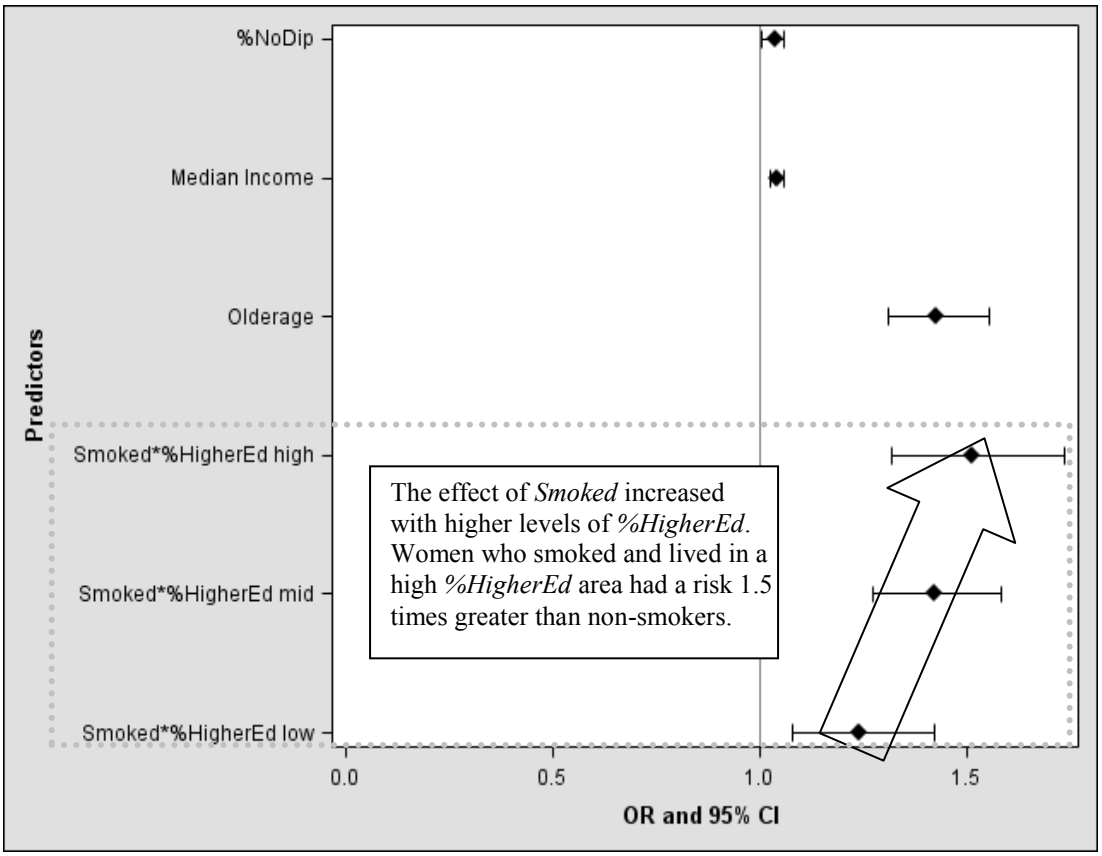


Figure 4.26 *Stillbirth*: Estimated Odds Ratios and 95% Confidence Intervals for Individual Risk Factors and Interaction Effects

The *Smoked*%HigherEd* interaction effect shown in Figure 4.26 demonstrates that the effect of *Smoked* increased with levels of *%HigherEd*. Women who smoked and lived in a high *%HigherEd* area had a risk of *Stillbirth* about 1.5 times greater than women who did not smoke. In the main effects (Figure 4.25) the odds of *Stillbirth* for women who smoked were about 1.3 times greater than for non-smokers. Note that in the *Smoked*%HigherEd* odds ratio plotted in Figure 4.26, women who smoked were compared with women who did not smoke at different levels of *%HigherEd*. When levels of *%HigherEd* were compared for women who did not smoke, *%HigherEd* had a slight protective effect (Appendix 7).

These findings differ from those of a number of previous Canadian research studies:

- Luo and Liu (130,277) both concluded that low neighbourhood income was highly predictive of stillbirths in Ontario. Both of these studies used Statistics Canada median household income estimates for DAs as we did; both also categorized this variable into quintiles. The findings of the current study allowed confirmation that *MedInc* is significantly, although weakly, associated with *Stillbirth*. In addition, *Olderage* as well as the interaction effect between *%HigherEd* and *Smoked* were also found to be important predictors of *Stillbirth*.
- Chen (228) and Luo (278) found lower maternal education strongly related to the likelihood of *Stillbirth*. My finding that *%NoDip* was risk increasing for *Stillbirth* supports those conclusions. But my finding regarding the *Smoked***%HigherEd* interaction adds additional information, namely that the interaction effect between *Smoked* and *%HigherEd* was risk-increasing. Women who smoked had a higher risk than those who did not and that risk became greater as the DA level of *%HigherEd* increased.
- My findings of *Olderage* as a risk-increasing predictor support research by Gilbert (411) but contradict research by Bianco and colleagues (17), who found that *Olderage* (>40 years) had no association with rate of *Stillbirth*.
- Health Canada and CIHI concluded that foetal deaths may result from suboptimal maternal health and birthing care (401,412). While the current study did not include risk factors that reflected on birthing care, my finding that existing health problems was not a significant risk factor failed to support those prior conclusions.

- Research using small population areas in Calgary found that teenagers (<18) were at greatest risk of stillbirth and that women over 40 were second-greatest (36). *Teenage* was not a significant risk factor in the current study, but *Olderage* was.

4.2.5.2 *Stillbirth* Hotspot Group Results

Hotspot groups were not identified for *Stillbirth*. The 27 identified hotspots were widely dispersed across the province (Figure 4.4). The criterion of geographic proximity of hotspots and minimum counts of hotDAs (per confidentially requirements) could not be met. While *Stillbirth* is not by definition a rare disease (324), secondary analysis of *Stillbirth* hotspots suggested that hotspots for this outcome did appear to result from small numbers of events. For example some hotspots appeared to have been created based on as little as a single stillbirth in a DA surrounded by DAs with 0 stillbirths.

4.2.5.3. *Stillbirth* Regression Results Discussion

In spite of its sparseness, the *Stillbirth* model did present noteworthy findings. Ecologic variables demonstrate strong influence over the odds of a stillbirth outcome; two of the three main effects predictors were ecologic (*%NoDip* and *MedInc*). The effect of smoking was modified and amplified by the ecologic variable *%HigherEd*. The group at greatest risk of stillbirth was smokers living in an area with a high level of *%HigherEd*.

Exploratory research showed that *Olderage* had a strong collinear relationship with *%HigherEd* (Table 4.18). Table 4.18 shows that the percentage of older age mothers increased as the level of *%HigherEd* went up. We surmise that the interaction effect between *Smoked* and *%HigherEd* presented in Figure 4.26 resulted from *%HigherEd* acting as an indicator for *Olderage* and delayed childbirth (see Section 3.3.1 for further discussion). With these results in mind, Table 4.18 can be interpreted as demonstrating that

women living in DAs with higher proportions of older mothers (per my finding that *%HigherEd* is associated with older age mother*s*) who smoked were at greater risk of a stillbirth than women living in DAs with higher proportions of older mothers who did not smoke. An increasing level of *%HigherEd* possibly indicates a growing proportion of women in the DA who were older aged as well as a cultural norm that supported and reinforced older age childbearing. If these premises hold true, it follows that in DAs with higher levels of *%HigherEd*, *Smoked* would be a greater risk factor. The third column of Table 4.18 demonstrates that less than half of older age women in high *%HigherEd* DAs smoked compared to the lower *%HigherEd* DAs. Two other ecologic variables, *%NoDip* and *MedInc*, were also both significant predictors of *Stillbirth*. Low education and low income have been found to be predictors of stillbirths in a substantial amount of previous research (8,48,94,95,228,278,413-415).

Table 4.18 Breakdown of Older Age Mothers Across *%HigherEd*

Level %HigherEd	**All births % *Olderage* Mothers (i.e. >35 years)**	**Stillbirths % *Olderage* Mothers**	**Stillbirths % of *Olderage* mothers who smoked during pregnancy**
Low	15%	21.9%	31.3%
Mid	17.3%	23.1%	18%
High	27%	31.3%	15.4%

4.2.6. Comparison of Results Across Adverse Birth Outcomes

Up to this point all results, discussions and conclusions have been primarily within each adverse outcome. This section compares and contrasts those results and discussions for the different outcomes.

4.2.6.1. Full-Province Models Comparisons

Figure 4.27 summarizes the differences and similarities in the final regression models for the four adverse outcomes for the full province.

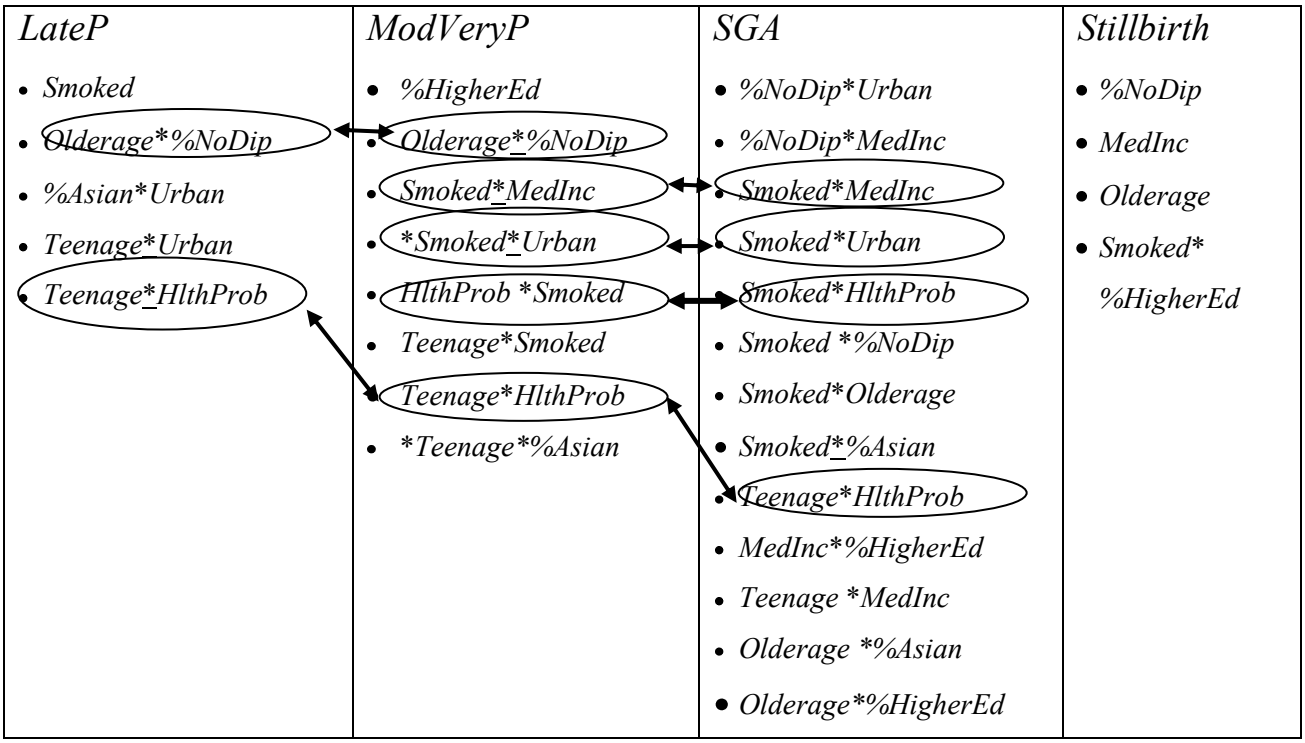


Figure 4.27 Summary Comparison of Full-Province Models

Drawing from all four models, the group at greatest risk of an adverse outcome was women who smoked, were older and lived in low-education areas. These predictors strongly correspond to previous understanding of risks for adverse birth outcomes. *Smoked* had the greatest presence in the four full-province models; it was a part of 12 significant predictors. Its influence included:

- a non-modified predictor in the late premature model;
- an interaction effect in four of seven predictors in the moderately to very premature births model;
- an interaction effect in six of 13 predictors in the SGA births model; and

- an interaction effect with *%HigherEd* in the *Stillbirth* model.

In the full province model *Smoked* consistently had a risk-increasing relationship in its interactions across all adverse outcomes; three of these interactions were shared between the *ModVeryP* and *SGA* models.

Olderage was also a part of each of the four full-province models, but its relationships with the different adverse outcomes were quite inconsistent. In the *Stillbirth* and East Toronto *SGA* models, where it was an unmodified predictor, it had opposite effects. In the former it increased risk, while in the later it decreased risk. In interactions with other factors that increase risk (e.g., *%NoDip* and *Smoked*), being older consistently further elevated risk. In interactions with protective factors (e.g., *%Asian* and *%HigherEd*), the effect was consistently reduced risk. This finding appears conceptually intriguing: older age seems to amplify risk effects, whether protective or damaging. In other words, being older confers both benefits and hazards to childbearing.

%NoDip was also influential in interaction effects in three of the four models, while in *Stillbirth* it was an unmodified predictor. It had a generally consistent risk-increasing relationship with all four outcomes except for a paradoxical interaction with *Smoked* in the *SGA* model, where it had a risk reducing relationship.

Teenage had a strong presence in three of the four provincial models (as well as in the hotspot group models); it consistently had a risk reducing, protective relationship in interactions with high risk factors (e.g., *Smoked* and *HlthProb*). In those interactions, teenage women were at lower risk of an adverse birth event than older women. Conversely, *Teenage* had a risk-increasing effect when interacting with generally protective variables (e.g., *%Asian* or higher *MedInc* levels).

Three *Smoked* interaction predictors as well as *%NoDip*Olderage* were common between the *ModVeryP* and *SGA* models. The *HlthProb *Teenage* interaction was common to the *SGA* and late premature (*LateP*) models.

4.2.6.2. Comparisons of Hotspot Group Models

At the hotspot group level of analysis the models were less complex, perhaps reflecting the greater homogeneity of these areas as well as smaller sample sizes. Figure 4.28 summarizes the final regression models for each of the hotspot groups within the three adverse outcomes where group analysis was completed.

LateP	ModVeryP	SGA	Stillbirth
Northern Toronto • *Olderage*%NoDip* **St Catharines** • *%NoDip*HlthProb* **SE of Ottawa** • *Olderage*%HigherEd*	**N Ottawa Valley:** • *MedInc* • *%HigherEd*Smoked* **Cambridge:** • *MedInc* %HigherEd* **Hamilton:** • *Smoked *%Asian* • *%NoDip *HlthProb* **S. Georgian Bay** • *MedInc*%HigherEd*	**East Toronto:** • *Teenage* • *Olderage* **London:** • *Smoked* **Northwest Toronto:** • *Teenage* • *Smoked*	There was no analysis of *Stillbirth* local groups.

Figure 4.28 Summary Comparison of Local Hotspot Group Models for All Adverse Outcomes

A comparison of the local group models suggests substantially different explanatory predictors. Noteworthy contrasts and commonalities were:

- *Olderage* was a primary influence in late premature births but was absent from *ModVeryP* hotspot group models
- *Smoked* and *MedInc* had the greatest influence in *ModVeryP* models but neither was present in the *LateP* hotspot group models.
- DA education level had a consistently strong influence across all *LateP* and *ModVeryP* group models. Both *%NoDip* and *%HigherEd* acted as indicators of DA education level except in Cambridge where it acted as an indicator of delayed childbearing.
- *Olderage* and *Smoked* were influential in the *SGA* models; however, neither was modified. DA education levels had no presence in the *SGA* models.
- Ecologic level variables had a strong presence in *LateP* and *ModVeryP* group models but none in *SGA* models.
- *Teenage* was influential in two of the *SGA* models but was not present in either of the *LateP* or *ModVeryP* local group models.
- St Catharines and Hamilton, two geographically close hotspot groups, shared a common predictor, *%NoDip*Morbidity*, across their *LateP* and *ModVeryP* outcome models.

4.2.6.3. Discussion

The full-province models showed marked differences across the four outcomes in complexity as well as in interaction effects. Only about one-third of the predictors were shared. *ModVeryP* and *SGA* shared the greatest number, four; *LateP* shared two; and *ModVeryP*, *SGA* and *Stillbirths* shared none. It is interesting to note that while *LateP* and *ModVeryP* represent a somewhat arbitrary categorization of prematurity, the two outcomes

have distinctly different risk profiles. This finding supports research discussed earlier that suggested later and earlier premature births have distinctly different profiles (2,8). The comparison of four adverse outcomes and nine risk factors for both provincial and diverse local area models in the current study allowed a more extensive assessment of risk than had been previously completed.

The large sample sizes for different adverse outcomes and the relatively small population areas within the big geographic area of Ontario, as well as the concurrent modeling of four different adverse birth outcomes used in the current study, allowed for findings that add to previous research. Specifically:

- *Teenage* was consistently risk reducing in its interaction effects with risk-increasing factors such as *Smoked*, *HlthProb*, or low *MedInc*.
- *MedInc* was not as influential a predictor of adverse outcomes as I had expected it to be. While it had a substantial presence in the *SGA* and *Stillbirth* models, it was absent from *LateP* and present in only one interaction effect (i.e., with *Smoked* in *ModVeryP*). In three of the four *SGA* predictors and in *Stillbirth*, *MedInc* had an inconsistent interaction effect; higher income did not equate to lower risk of an adverse birth outcome. This finding varies from a wide range of previous population-based studies (9,16,46,130,278,338).

The role of higher levels of *MedInc* as a risk-increasing factor may reflect growing numbers of women delaying childbirth in order to build income; but income did not interact with *Olderage* in any model. *MedInc* did interact with *%HigherEd* and *%NoDip* in the *SGA* full-province and in *ModVeryP* hotspot group level analyses. Still, with the exception of South Georgian Bay, the education variables in these interactions appeared to have greater

influence than *MedInc* over risk of an adverse birth outcome. Although smoking and low education have been found to be confounded by neighbourhood income levels in past research (8,16) I did not find evidence of this. As an ecologic level variable, *MedInc* was found to have less influence in adverse outcomes than education.

The relationship between *%HigherEd* and adverse birth outcomes differed depending on the model. Previous research has suggested that advanced university studies and career-building are important explanatory factors in delayed motherhood (9,373). The markedly different relationships *%HigherEd* had in the different models suggests that sometimes this factor acts to increase risk (i.e., representing delayed childbearing) and other times as a risk-decreasing indicator of higher area education levels. (This difference was explored in Section 2.5.3.1).

Overall, ecologic level risk factors strongly influenced the risk of adverse birth outcomes. They modified individual level variables 13 times, substantially more than the four times they modified ecologic level variables. Individual level variables modified individual ones seven times (Table 3.7.1). This finding supports research conclusions by Diez-Roux, O'Campo and others (78,146,345,395,416) that emphasized the importance of ecologic characteristics[28] in addition to individual characteristics in determining birth outcomes as well as health outcomes in general.

Research by the Canadian Institute of Health Information (CIHI) has suggested that biological factors (e.g., health problems and age) would have more influence on preterm births while social factors would have greater influence on SGA births (9). The provincial-level research in the current study was inconclusive on this point; ecologic and individual level variables had almost equal presence across the two preterm and SGA outcomes. My

[28] Note that four of five ecologic variables were compositional.

analysis of local hotspot groups allowed more extensive exploration of this finding; the three *SGA* local group models were made up entirely of individual level predictors (Table 3.7.2). This finding differs from the CIHI conclusions mentioned earlier.

For *LateP* and *ModVeryP* local group models, ecologic level risk factors had more influence in general. In the *LateP* models there was equal presence; however, every individual risk factor was modified by an ecologic one. In the *ModVeryP* model only three of the 11 risk factors were individual level, and all were modified by ecologic level risk factors.

At the provincial level, the complexity of the regression models (i.e., the number of predictors in the model and the interaction effects versus unmodified predictors) varied substantially across the different outcomes. While some of this variation may be explained in part by differences in sample sizes (see Table 4.2), I suggest that it may also reflect a more complex aetiology for the outcomes modeled. *LateP* represented a relatively narrow time period of prematurity (i.e., three weeks) compared with *ModVeryP*, which represented a minimum span of 12 weeks premature. Intrauterine growth restriction, indicated by the *SGA* measure, represents as complex and multifactorial a condition as preterm births (8). This possibility was supported by the models for *LateP* and *ModVeryP*; while both had approximately the same sample sizes, the *ModVeryP* model had almost double the number of predictors as *LateP*. It was also supported by findings for the *SGA* hotspot groups. SGA hotspot groups had larger counts of SGA events than either of the other outcomes, yet the models had no interaction effect predictors and only one or two total predictors.

The levels of complexity found in the full-province models were not represented in the local hotspot group models. While this discrepancy may again be explained in part by the smaller sample sizes for the hotspot groups, it may also be due to the use of a simpler

model to explain the adverse births in the spatially smaller and possibly culturally and socially more homogeneous areas. This suggestion is supported by the *SGA* hotspot group findings; sample sizes for those groups were among the largest (see Table 4.15) yet the models were among the simplest, with only three risk factors and no interactions. These areas were also possibly more homogeneous because of the shared characteristic of being hotspots.

Recalling that only a minority of the adverse outcomes occurred in the hotspot groups, hotspot and full-provincial models may have also differed because they were fitted to different samples. Provincial models were fitted to all adverse outcomes of a given type in the province. Although hotspot births were a subset of provincial births, they were not a representative sample; they appear to have arisen from a narrower set of etiological factors than would be required to explain adverse outcomes within hotspots, whereas a more diverse range of factors was required to explain all occurrences of an adverse outcome across the province.

The finding that hotspots for different adverse outcomes were largely spatially exclusive suggests that the aetiologies for the hotspots are not only sufficient to create significantly higher adverse birth outcomes within a given place but also that they are specific and hence insufficient to create significantly higher levels of other outcomes. Although the current study provided insights into the aetiologies sufficient to create hotspots, its findings do not explain why they were largely spatially exclusive. This question was beyond the scope of the current study.

Chapter 5. Conclusions, Contributions and Recommendations

The current study sought to identify the relative importance of different explanatory factors, especially ecologic ones, for four different adverse birth outcomes as well as the impact different local areas may have on explanatory models. This section includes:

- summary answers to the research questions;
- conclusions for each of the four outcomes and summary conclusions;
- observations on hypothesized relationships taken from the Schempf model (see Section 2.2);
- counterintuitive findings;
- strengths and limitations of this research;
- contributions to theory and the discipline of population health;
- suggested implications for possible interventions;
- recommendations for future research; and
- the author's statement of contribution.

5.1. Research Questions and Answers

The current study sought to answer three questions:

Question 1: Are there hotspots for the different adverse outcomes; if so, where are they? Clusters of DAs, each with significantly higher levels of one of the four different adverse outcomes were found. This finding indicates that certain geographic areas have aetiologies or patterns of risk factors sufficient to create significantly elevated levels of adverse

outcomes. It must be noted that these areas represent only a fraction[29] of all occurrences of the adverse outcomes.

While previous research has linked adverse birth outcomes to geographic areas (23,36,391) and geographic clustering has been shown (393,417), my analysis plan allowed me to concurrently identify and characterize a relatively large number of spatial hotspots for four different adverse birth outcomes for Ontario. This breadth allowed the current study to substantially add to the knowledge base from existing research (130,196,277,278,338) in several ways.

First, I demonstrated that individual level risk factors may have interacted with and have been amplified by contextual characteristics such that significantly higher levels of a given adverse birth outcome were created in relatively isolated areas. For example:

- In *LateP* hotspot models the risk effect of *Olderage* was amplified by DA levels of education, *%NoDip* and *%HigherEd*.
- In the *ModVeryP* hotspot group models the risk effects of *Smoked* and *Olderage* were amplified by education risk factors, *%NoDip* and *%HigherEd*.

Second, I found that the hotspots for the different outcomes were largely spatially exclusive. Spatial exclusiveness implies that while the aetiologies or patterns of risk factors found in the census dissemination areas were sufficient to create significantly higher levels of a given adverse outcome, they were specific to that outcome and were insufficient to create significantly higher levels of other adverse outcomes. This finding concurs with and adds additional strength to previous research findings that have suggested different risk profiles for different adverse outcomes (8,9,15,36,134,163,261) and that different adverse

[29] Between about 3.7% (*LateP*) and 20% (*SGA*). See Table 4.2.

outcomes are characterized by complex but different etiologic patterns (8,36). Previous findings neither observed nor explained mutual exclusivity of hotspots.

Previous research (7-9,16,48,95,130,185,231,400,418) has found neighbourhood and individual income (SES) and education levels to be strongly predictive of a range of adverse outcomes, but if this finding were a rule I would have expected to find numerous hotspots for the different outcomes sharing low income and/or low education areas; instead I found very few. These findings indicate that ecologic variables such as poor education or median income modify individual level variables but by themselves may have relatively low levels of influence.

It is important to repeat that the hotspots represent only a minority of births for any given adverse outcome (see Table 4.2). A large number of DAs likely had a more heterogeneous mix of adverse outcomes but not at sufficiently high levels to create a hotspot. Understanding the differences for the aetiologies between the two different types of DAs will be an important focus for future research.

Question 2: Are predictors for like adverse outcomes different between full-province and local hotspots? Substantial differences were found between full-province and local hotspot group models for the different adverse outcomes. These differences were more complex, and more nuanced, than expected. Provincial models consistently included more risk factors than the hotspot group models and also had a greater variety of interactions. Provincial models may have been more complex at least in part because they were explaining a larger population of adverse events spread over a much larger and diverse geographic area. Planning of local preventive interventions may benefit from understanding the narrower set of etiological factors operating in a local area.

Hotspot group models were striking for their simplicity, which we surmise was not merely due to small sample sizes. I suggest that they were also simpler because they were explaining more homogeneous subpopulations but also because they had characteristics and behaviours sufficient to create a significantly higher level of an adverse outcome.

Question 3: Do predictor variables for the same adverse outcomes differ between hotspots? The predictor variables for same adverse outcomes did vary between different hotspot groups. Specifically:

- The three *LateP* group models had more commonalities than differences. An education risk factor was common as an effect modifier in all three models, modifying *Olderage* in two and *HlthProb* in one. The risk effect of *Olderage* and *HlthProb* increased in DAs with lower levels of education.
- The *ModVeryP* group models shared the common factor of education in each of four models; but that common thread varied widely in its effects. Both education indicators acted counter to expectations (see Section 4.2.3.3). *MedInc* and *Smoked* delivered counterintuitive effects as well.
- *SGA* group models shared commonalities, yet again those commonalities acted against expectations. For example, *Teenage* had opposite effects in two different groups set relatively close to one another in Toronto.

I surmise that these paradoxical differences and variations in local models are evidence of differences in subpopulations and variations in local explanatory variables that were not included in the current study.

The noted differences between provincial and local models as well as the differences between local models suggest that when adverse outcomes are analyzed at a granular level, the models will become simpler because of the more homogenous

subpopulations but will also reflect substantial variations between the subpopulations. This relationship, in turn, implies that intervention planning should be based on local modeling of outcomes if it is to be effective.

5.2. LateP Conclusions

Five clear themes surfaced in this presentation of *LateP* analysis results:

1. *Smoked* presented a substantial increase in risk of late premature births at the provincial level. Of the five predictors included in the models, it represents the most easily modifiable risk factor.
2. Education, indicated by both *%NoDip* and *%HigherEd*, was a strong effect modifier; it amplified the risk effects of older age as well as health problems. I surmise that lower education as an ecologic variable acts as an indicator of neighbourhood deprivation and, in turn, as Holzman suggested (162), may be quite similar in its effect across diverse settings such as Southwest of Ottawa versus St Catharines.
3. *Teenage* had a consistent risk-decreasing relationship with late premature births, while *Olderage* had a strong risk-increasing one. Holzman's weathering hypothesis introduced the importance of accelerated aging as a possible causal pathway between high-risk areas and premature births. Therefore it seems plausible that *Teenage* is a corollary to the accelerated aging that puts older age women at greater risk; when faced with the same ecologic and individual risk factors, an older teenager may be biologically more capable of dealing with the effects of those factors and less likely to have a late premature birth than older women, especially those over age 35.
4. *%Asian* interacting with *Urban* had a strong risk-decreasing relationship with late premature births, possibly due primarily to the healthy immigrant effect

(47,194,196,282,284). Yet the contrast between *%Asian* in urban versus rural settings was striking. The markedly different risk relationship represented by a 2% increase in *%Asian* in urban versus rural settings suggests that the healthy immigrant effect differs by place and, possibly, that the effect of social capital decreases for immigrants in a rural area versus an urban one (194,283).

5. Models fitted to *LateP* hotspot groups shared the risk factors found most significant in the provincial final model but differed from that model in their simplicity and in the strong representation of ecologic indicators of education. Ecologic level education variables modified two strong individual risk factors, *Olderage* and *HlthProb*, in interaction effects that were found in all three hotspot groups. The effects of both risk factors were insignificant at high levels of education but were amplified at low levels, as shown by odds ratios larger than those found in the main effects. Low DA education levels appeared to be an important factor in the aetiology sufficient to create *LateP* hotspots.

My findings for late premature births shed light on the last two of the three research questions:

2) What are the predictors of the observed hotspots? and

3) Do predictor models differ within the same outcomes between those fitted to the full province and those fitted to hotspots, as well as between those fitted to geographically diverse hotspots?

Answers to question two are summarized in Table 4.10 and Figure 4.9. Regarding question two: models for late premature births fitted to the full-province and to local hotspot groups differ substantially from one another, as discussed above. An important part of explaining these noted differences is that the populations of the two different levels (i.e., full-province and hotspots) were markedly different. Full-province models were fitted to all

late premature births in the province but local hotspot models were fitted to subpopulations that were extreme by definition. It is important to remember that births in hotspots were not representative samples of the provincial births but were selected because they were in *LateP* hotspots. The existence of hotspots suggests aetiologies sufficient to create significantly higher levels of adverse outcomes; but those aetiologies are not likely to be the same as the provincial model.

The strong commonalities between the hotspot groups suggest that late premature births have roughly the same risk factors in hotspots across different geographic areas. This similarity may reflect the relatively homogenous population represented by births between 35 and 37 weeks' gestational age.

5.3. ModVeryP Conclusions

Five clear themes surfaced in the *ModVeryP* analysis results:

1. *Smoked* was highly influential as a risk-increasing factor in both the provincial and hotspot group models. Yet the effects of *Smoked* were highly modified with unexpected and sometimes perplexing results. These unexpected outcomes, especially from such a researched and influential predictor, suggest the need for additional research.
2. *%HigherEd* was an influential but inconsistent effect modifier. The seemingly identical interaction between *%HigherEd* and *MedInc* in two different local hotspot groups had opposite effects when the effect of *%HigherEd* was shown at different levels of *MedInc*. Yet the effect of *MedInc* at different levels of *%HigherEd* was the same for the two groups, giving a $\cap$-shaped trend line. While *%HigherEd* appears to be a valuable indicator, its effect varies greatly depending on interaction effects and also requires additional research.

3. The *Olderage*%NoDip* interaction had a strong effect on the risk of a moderate to very premature birth. Holzman's weathering hypothesis and the importance of accelerated aging introduced in the *LateP* discussion appears to be supported here.
4. *Teenage* had a consistent risk-decreasing relationship with moderate to very premature births; this finding was found in *LateP* results and continues here. My hypotheses that when faced with the same ecologic and/or individual risk-increasing factors, an older teenager will show less risk of an adverse birth outcome than non-teenage women, appears to be supported here.
5. Models fitted to the hotspot groups shared the risk factors found most significant in provincial main effects but differed from the full-province model in their simplicity and in their strong representation of ecologic indicators of education. Ecologic level education variables modified two strong individual risk factors, *Smoked* and *HlthProb*, in interaction effects found in all four hotspot groups. While their presence was consistently strong, the effects from their interactions were almost as consistently paradoxical. Several of those effects will need further research to explain them.

My findings for moderately to very premature births shed light on the last two of the three research questions:

2) What are the predictors of the observed hotspots?

3) Do predictor models differ within the same outcomes between those fitted to the full-province and those fitted to hotspots, as well as between those fitted to geographically diverse hotspots?

Answers to question two are summarized in Table 4.13 and Figures 4.15 and 4.16. Regarding question three: models for late premature births fitted to the full-province and to local hotspot groups differ substantially from one another, as discussed in Section 4.2.3.4

above. Models for moderately to very premature births fitted both to the full-province and local hotspot groups differ substantially from one another in terms of the predictors found within them as well as in the effects of the risk factors that make up those predictors. An important part of explaining these noted differences is that the full province and hotspots populations were markedly different, as discussed above. The existence of hotspots indicates aetiologies sufficient to create significantly higher levels of adverse outcomes; these aetiologies are not likely to be mirror images of the provincial model.

Differences between hotspot group models suggest that:

- there were different predictors of ostensibly the same adverse outcomes in different geographic areas;
- the births grouped together in the current study as "moderately to very premature" may represent a collection of different events with different risk profiles; and
- identical predictors may act differently in different places. I surmise that modifiers and confounders outside the range of the current study may explain the observed differences in predictor effects.

5.4. SGA Conclusions

Four clear themes seemed to surface in the *SGA* analysis results:

1. Smoking substantially increases the risk of an SGA birth; it was the most influential of the risk factors in the provincial model and present in two of the three hotspot groups. It represents the one most easily modified of the nine risk factors.

2. The socioeconomic indicators of median household income and education have a strong influence in the *SGA* provincial model, with a presence in six of the 12 full-province model predictors. Both acted as clear effect modifiers in their interaction effects, although several of the interaction effects with *MedInc* were counterintuitive. I surmise that lower DA income and education levels serve to amplify individual level risk factors (e.g., *Smoked* and *Teenage*) through exposure to pollution, higher crime rates, available foods and other stressors endemic to low-income/low-education, high-deprivation neighbourhoods.
3. *Teenage* continued to present inconsistent effects as a risk factor and/or predictor of SGA births. These inconsistencies are explained in part by the hypothesis presented in Section 4.2.2.3, that older teenage women will have a lower risk of adverse birth outcome than older women when interacting with risk- increasing settings, such as area poverty or low education, and individual characteristics such as *Smoked* or *HlthProb*, was supported in the full-province model.
4. Hotspot group models were starkly different from the provincial model in the character of the risk factors represented: they included no risk modifiers and no ecologic level variables. Although it is difficult to understand how those predictors were sufficient to create a hotspot, exploratory research supported the findings nonetheless.

My findings for SGA births shed light on questions 2 and 3 of the three research questions:

2) What are the predictors of the observed hotspots?

3) Do predictor models differ within the same outcomes between those fitted to the full-province and those fitted to hotspots, as well as between those fitted to geographically diverse hotspots?

Answers to question two are summarized in Table 4.16 and Figure 4.24. Regarding question 3, models for SGA births fitted to the full province and to local hotspot groups differ substantially from one another both in terms of predictors found in the provincial model but missing from the hotspot group models, and the character of the predictors. An important part of explaining these noted differences is that the populations of the two different levels, full-province and hotspots, were markedly different.

The striking differences between the hotspot group models suggest that SGA births can have markedly different predictors in hotspots in different geographic locations. The complexity shown in the full-province model may be due to variability in associations between risk factors and SGA birth outcomes across the full province. Previous research has suggested that SGA births are among the most complex to explain, at least in part because these births represent different outcomes measured by the one indicator. The local hotspot group models support that SGA outcomes vary by geographic area and the characteristics of the populations that reside in them.

5.5. Stillbirth Conclusions

Four clear themes surfaced in this presentation of *Stillbirth* analysis results:

1. *Smoked* was linked to a substantial increase in risk of *Stillbirth* and, as shown in previous analysis sections, did so in an interaction by amplifying the effect of *%HigherEd* (and, I surmise, the related *Olderage*) and delayed childbearing.

2. The socioeconomic indicators of DA median household income and education, *%NoDip*, had a small but significant influence in the *Stillbirth* model. I surmise that lower DA income and education levels may amplify a variety of individual level risk factors that are not represented in the model developed in this study (e.g., diet, exercise and early natal care, as well as the stressors endemic to low-income and low-education neighbourhoods).
3. *Olderage* was shown to be influential as a predictor of stillbirths. Although some previous studies have suggested that *Olderage* did not represent a hazard after other factors are adjusted for, it was shown to be a significant, independent risk factor in my model.
4. *%HigherEd* had an interesting relationship with *Stillbirth*. In this model I surmise that it was acting as an indicator of delayed childbearing and *Olderage*, whereas in other adverse outcomes models it has acted as an indicator of education. Further research will be needed to fully understand and make effective use of this variable.

The second and third research questions were not answered for stillbirths. While *Stillbirth* hotspots were identified, regression analysis could not be completed due to requirements of confidentiality and statistical rigour.

5.6. Overall Conclusions

In this section I summarize four conclusions made for the full research study.

1. Both ecologic and individual level risk factors play an important role in understanding adverse birth outcomes at both provincial and local levels. Both should be included in any effort to model these outcomes and to develop interventions. Ecologic level risk factors made up a consistent, substantial and important portion of the provincial-level

regression models for all four adverse outcomes and for local-level models for *LateP* and *ModVeryP* (local models for *SGA* were made up only of individual level predictors). The effects of all individual level risk factors *Olderage*, *Smoked*, *HlthProb* and *Teenage* were modified and amplified by ecologic level risk factors. Different ecologic level risk factors modified different individual level ones, with striking and sometimes paradoxical inconsistencies in effects in the different local models. This was observed at both the provincial and local hotspot group levels.

2. To effectively understand the aetiologies of adverse birth outcomes they should be analyzed at relatively small spatial scales. Large-scale models may not accurately represent any given local area. The finding of hotspots for the different adverse outcomes offered initial support for this conclusion, and the markedly different models fitted for the same outcomes in diverse hotspots sustained it. The inconsistencies in local area models, inconsistencies that I surmise were due in part to postulated local risk factors, further corroborate this finding. While there were common risk factor threads running through the models there were also substantially different interaction effects. A more effective understanding of adverse outcomes requires both identification and analysis of risk factors, both known and unknown, at local levels. In addition, the general approach to modeling adverse outcomes at broad geographic scales requires reconsideration.
3. Adverse birth outcomes (e.g., preterm and SGA) should be analyzed as multifaceted phenomena if they are to be effectively understood. Both SGA and moderate to very premature births represent complex factors which should be broken into sub-facets (e.g., stages of gestational age) in order to be more parsimoniously modeled (8,419). I surmise that the treatment of these outcomes as homogenous events at least in part

explains the complex provincial level models for each of those two outcomes and may explain some of the paradoxical local hotspot group models.

4. Ecologic levels of education were a more influential and more consistent risk factor than median household income of adverse birth outcomes. While education and median income have often been grouped together as indicators of socioeconomic status, I found that education is a more effective and more consistent risk factor. Further evaluation is needed of measures of education and of the compositional versus contextual effects; the consistently stronger presence and influence of education in predicting adverse outcomes suggest that it should not be grouped together with median income but instead considered as a separate, important risk factor.

5.7. Hypothesized Relationships

The model discussed in Chapter 2 (and shown below as Figure 5.1) suggests a variety of relationships between different levels of predictors for adverse birth outcomes (43). The current study focused on these relationships (Figure 5.1).

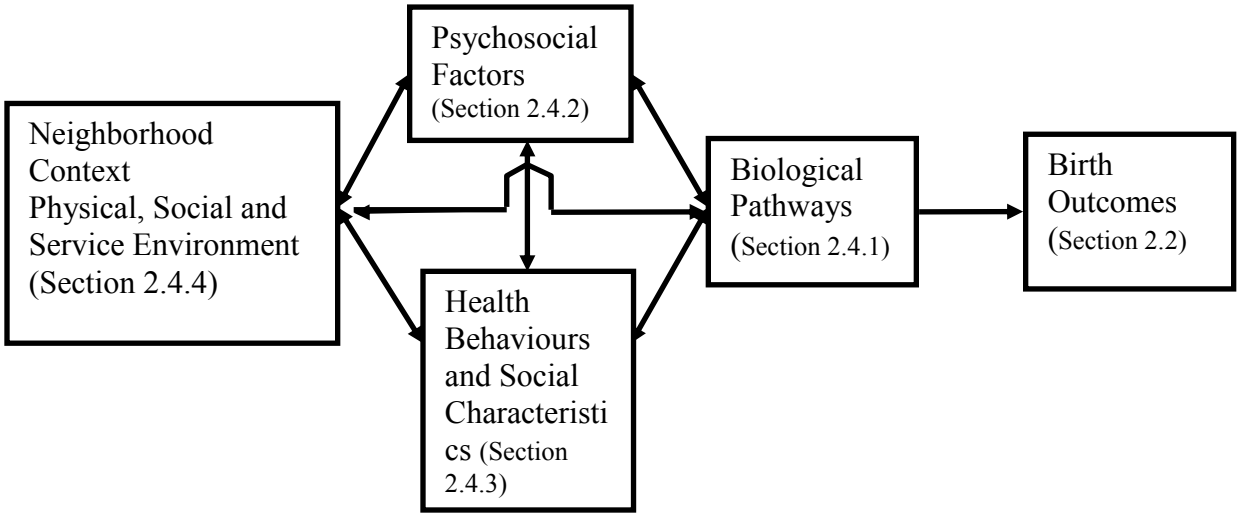


Figure 5.1 A Biopsychosocial Multilevel Conceptual Model of Birth Outcomes

My findings of suggest a more complex, textured model then Shempf envisioned (even with the modification of the link arrows from one to two way). Namely:

1. Neighborhood context variables interact extensively. Within the full-province models for *LateP*, *%Asian* and *Urban* had a significant interaction effect. For *SGA* outcomes, education (*%NoDip*) with *Urban* and education (*%NoDip*) with low income had significant interaction effects. Within local hotspot models, education (*%HigherEd*) and median income interacted in two different models of moderate to very premature births.
2. Biologic pathways variables interacted extensively. Maternal age (*Teenage*) and health issues interacted in provincial-level models for *LateP*, *ModVeryP* and SGA outcomes. Within local hotspot models, maternal age (*Olderage*) and health issues were part of both *LateP* and *ModVeryP* models for two different groups.

While there was only one health behaviour factor in the independent research variables of the current study and psychosocial factors were not represented, my findings suggest that those variables likely interact extensively as well.

In response to these findings, I suggest the model be modified. The varying relationships between the levels of factors found in the models used in the current study suggest that the hypothesized relationships between contextual and individual level variables are highly dynamic, more so than a simple two-way arrow would suggest. I propose that the interaction effects would be better represented by mutually intersecting spheres of influence strengthened by a loose application of Bhopal's original concentric circle model (422); this representation would include layers of arrows representing influence and, possibly, causation (although I do not suggest that the current study identified causal relationships). In this proposed model (Figure 5.2), dotted arrows indicate psychosocial factors that were not included in the current study and dot-dashed arrows are used to show links to biologic pathways. An individual adverse outcome would reside in the center the biologic pathways that form the final pathway(s) to the birth outcome. Circular arrows within the three different areas suggest that factors within those areas interact as well they are not included in the psychosocial area because variables from that area, e.g. stress or anxiety, were not included in this study).

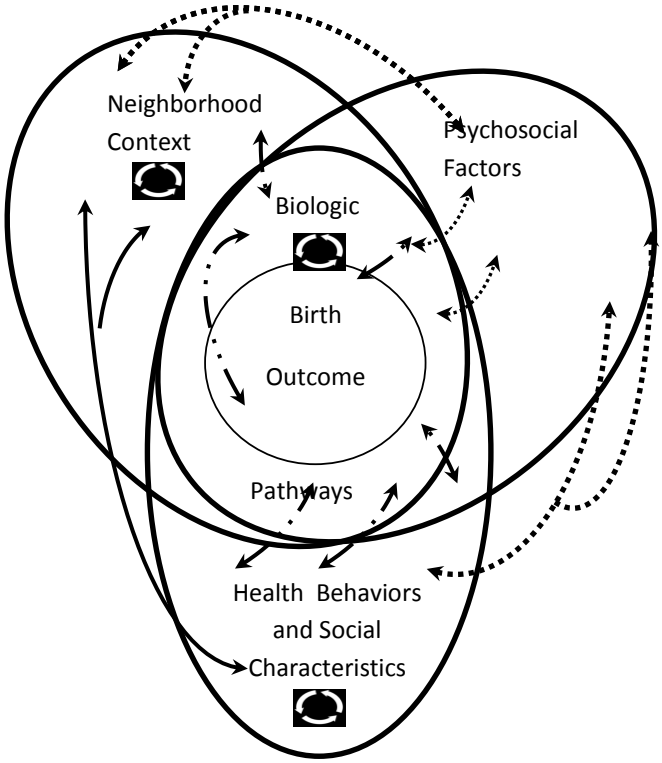


Figure 5.2 A Modified Biopsychosocial Model

The goal in revising the model is to better reflect the strength of the interaction effects that influence birth outcomes; for example, physical overlaps suggest stronger interactions than single arrows. My analysis strongly suggests that interaction effects between the different levels of factors, neighbourhood and individual, are important in explaining adverse outcomes; as previously stated, these relationships are not only highly complex but also dynamic beyond what can be suggested by a two-way arrow. Moreover, the sequences of the relationships are not clear; for example, I would not suggest that neighbourhood factors existed before social characteristics for the individual women. Hence in the proposed model the different categories of factors equally overlap to represent all-way interaction between the different factors. I recognize that the social ecology paradigm suggests that the different levels (e.g., individual, social, meso and macro) are

layered; the goal here was to represent the different interactions that predict adverse birth outcomes.

5.8. Counterintuitive Findings

While a substantial number of individual findings were counterintuitive, five were found consistently across the different models:

1. Hotspots for different adverse outcomes were found to be largely spatially exclusive. This finding was corroborated using a number of GIS and statistical analysis tools. This seems to contradict findings from a large number of previous research findings which suggested that common ecologic level variables (e.g., median household income and education levels) would broadly predict all four adverse outcomes. While the finding of exclusive hotspots does not preclude the importance of any given predictor, it does suggest that local ecologic and individual level variables will have greater influence over and stronger associations with adverse birth outcomes than broad socioeconomic variables alone. This insight results from the ability within the current study to examine these outcomes on a smaller geographic scale than has previously been used.
2. *Teenage* had a protective/risk reducing relationship in most of the interactive relationships in which it played a part. For women with a pre-existing health condition or who smoked, lived in a rural area or in a low-income DA, older teenagers had a lower risk of adverse birth outcome than older women. Without those effect modifiers, however, *Teenage* was a risk- increasing factor for most adverse outcomes.

3. Median household income was found to not have a major presence in the *LateP* and *ModVeryP* regression models. Where it was present in the *SGA* and *Stillbirth* models its role was inconsistent; higher levels of income did not consistently predict lower risk of adverse outcomes.
4. *%HigherEd* was shown to be an influential risk factor, yet its role was inconsistent. Higher education was included in the current study as a risk factor because of findings that have suggested it would be an effective indicator of delayed childbearing and the risks that accompany it; yet, the majority of the time it was found to act as an indicator of DA education level and had a risk reducing relationship with the adverse outcome(s).
5. Identical predictors, whether non-modified risk factors or in interaction effects, could have opposite effects in different hotspot group models. The *Teenage* risk factor in the *SGA* hotspot group models and the *MedInc*%HigherEd* predictor in the *ModVeryP* group models presented completely opposite risk effects on the same adverse outcomes. This disparity suggests that there were local risk factors not included in the analysis that would explain these outcomes. Such contradictory predictors were not found in the provincial models.

As counterintuitive as each of these findings seems, plausible explanations were put forward in most cases. Our use of a very large sample linked to small population areas allowed for these results and, as counter intuitive as some may seem, we suggest that they present a consistently more accurate reflection of the complex explanations of adverse birth outcomes than has been offered to date.

5.9. Strengths of this Research

Areas of strength in the current study were:

1. The birth event database was large, approximately 636,000 births. The count of geographic units was also large, approximately 15,800. These sizes allowed the power to carry out extensive hotspot analysis as well as hierarchical regression analysis with considerable confidence in the outcomes.
2. The concurrent analysis of all four adverse outcomes at both the full-province and local-area geographic scales allowed for a broader understanding of the different outcomes as well as the distinct character of the different regression models created to explain them.
3. The use of GIS hotspot analysis to logically identify "at risk" local areas and/or communities represents a more statistically rigorous technique for prioritizing areas on which to focus analysis than are commonly used (such as rank-ordering by risk factors or by size of outcome).
4. The use of DAs as small population areas allowed for a far more granular understanding of hotspots of different adverse outcomes as well as the ecologic predictors of adverse outcomes. I surmise that my use of small population areas within the larger context of Ontario allowed for a number of the unexpected findings in the current study, for example exclusivity of hotspots and the contradictory roles of like predictors in different geographic areas.
5. The BORN Ontario Niday database allowed linkage of the known individual risk factors of smoking, existing health conditions and maternal age directly to individual birth outcomes for a very large sample of births across Ontario. These individual variables and the link to individual births are not available in alternative sources.

6. Use of data from the 2006 Statistics Canada long census allowed for timely, accurate and reliable ecologic level variables to be developed and linked to the DAs. These data will not be available again for the foreseeable future.

5.10. Limitations of this Research

The perceived limitations lie principally in five areas:

1. This was an observational cross-sectional study that as such was subject to possible biases:
    - Selection bias. The selection of study subjects was not based on random selection and therefore possibly not representative of the population (420,421). The BORN Ontario Niday database represented about 90% of all births in Ontario during the 2004–2009 period, ranging from 82% in 2004–5 to 97% in 2009–10 (see Appendix 10). It is difficult to know how the births not included in the current study from one year to the next might have affected/biased the representativeness of the population. Specific information about the non-participation by hospital or area is not readily available.

      The bias that may have been introduced would have been the under-reporting of births for different areas in the 2004–2009 time-frame. While my analysis was based on proportions of adverse outcomes per DA, which should have allowed for the rate of adverse outcomes per DA to be reasonably accurately represented, I recognize that small at-risk populations per DA may have affected the validity of the cluster analysis tool and suggest that the corrections allowed by the conditional Monte Carlo tool should have adequately adjusted for this possible inaccuracy.

The alternative Ontario vital statistics database has been documented as biased due to selective under-reporting. The alternative discharge abstract databases have several limitations, including the need to derive adverse birth outcomes from ICD/ICC codes and the lack of maternal health and behavioural characteristics (see Section 3.2.1).

- Information bias. Errors in measurement or classification are kept to a minimum in part by the nature of how observations are made for the BORN Ontario Niday database. There is no imprecision due to lag between event and data gathering; data are gathered at the time of birth.
- Measurement bias. Rigorous quality control and assurance steps by BORN Ontario staff (as well as previously by the Niday Date Base managers, the Perinatal Partnership Program of Eastern and Southeastern Ontario) minimize errors due to missing or invalid answers (167,363).

2. This analysis was limited by the number of risk factors included. Psychosocial factors such as stress and/or anxiety, ethnic background, parity and others were not included because individual level, observational data were not available for these variables. The BORN Ontario Niday database allowed for the analysis of remarkably high-quality observational data on birth outcomes as well as maternal health characteristics and behaviours. This ability allowed me to answer the research questions and also to investigate interactions not explored before with a large sample spread over a large geographic area.
3. Spatial cluster identification is not an exact science. While the concept is well known, each of the different statistical tools has its own strengths and weaknesses (see Chapter

2). The different tools have been shown in various applications to identify slightly different clusters (322-324). The local Moran's I tool was selected because of its tendency towards conservative hotspot identification (309) and because it has been found to identify smaller, more core clusters rather than larger clusters (322,323). Hanson and Wieczorek suggested the use of a multi-method approach to cluster identification to adjust for this challenge (322). We suggest that multiple methods as well as a careful evaluation of their outcomes would be a valuable addition to future research. Careful comparison of the identified hotspots as well as the characteristics of those hotspots, such as the clinical relevance of the degree of heightened levels of adverse outcomes, should be undertaken.

4. Local groups of hotspots were not representational of all hotspots; they were selected empirically for hypothesis generation purposes. While there were criteria for their selection, they were not a random sample and therefore cannot be said to represent all births or hotspots of a given adverse outcome. This phase of the analysis was principally for hypothesis generation; the goal was to compare and contrast regression models for like and different adverse outcomes for the full province and diverse local areas.
5. My purposeful use of small areas (i.e., census dissemination areas) engages the risk of the small number problem, whereby a single event may spuriously increase local risk (34). This effect was illustrated with stillbirth outcomes, where individual stillbirth events increased average local rates significantly. It is important to recognize that adverse birth outcomes, especially preterm and SGA, are not rare events; this recognition decreases the risk of the small number problem affecting the outcomes of the current study as much as for an event such as cancer.

The small number problem represents a trade-off in that the use of larger geographic units would reduce the affect of the small number problem, but at a loss of local information (34). Reassuringly, Thiell (51) found that when the number of groups was large (>459), the presence of groups with less than five observation did not affect the outcomes of hierarchical regression analysis. This finding in addition to the relatively non-rare rate of adverse birth outcomes and the value of the information gained by using DAs made the trade-offs favor use of the smaller areas.

5.11. Contributions to Population Health

5.11.1. Theoretical Contributions

My findings are strongly supportive of the social ecology perspective which suggests that broader physical and social contexts and the interdependencies among contexts that surround women play an important part in predicting adverse birth outcomes (71,72). The seemingly inconsistent roles of various risk factors (e.g., area education level and mother's age) are better understood when one considers their interactive relationships with the social and physical environment that surrounds the women (12,28,401,422). These variables can and will have different effects in different places (71-73,96,97). I surmise that several of the more paradoxical findings for local area analysis were due to local variables not included in my analysis.

As discussed in Section 6.6, I found that the layered model by which the social ecology paradigm is often depicted does not fit my findings well. The inner circle which usually depicts the individual is usually separated from neighbourhood or community setting by rings representing interpersonal relationships. Results of the current study suggest that there may be a more direct interaction between individual and neighbourhood

effects (e.g., maternal age and neighbourhood income levels) than is represented in those models. Tobler's First Law of Geography, which states that "Everything is related to everything else, but near things are more related than distant things" (301,423,424), was supported by my finding of hotspots and hotspot groups, and that spatially close hotspots are more alike in prediction models than those further apart.

The weathering hypothesis was supported and expanded upon by my findings and explanations. I expanded this hypothesis to explain the consistently risk decreasing affect of (older) teenage women. This paradoxical outcome gave remarkable insight into the risks associated with teenage mothers.

5.11.2. Methodological Contributions

The methodological contributions of this dissertation to population health are in its:

1. Advancement of the understanding of geographical patterns of non-communicable morbidities patterns such as adverse birth outcomes. This was done for large spatial areas using predictor and outcome variables aggregated to small population areas and provided insights into the inconsistencies of predictors across distance and, conversely, the importance of local modeling of adverse outcomes.
2. Development of a stronger appreciation of the importance of small population areas and the variables linked to them. My findings suggest that analysis of small population areas within the context of a larger geographic space and the ability to compare different regression models across that large area are important to a full understanding of possible determinants and the variation between them.
3. Advancement of the consideration of adverse birth outcomes as a more accurate alternative indicator of population health for a given place than some of the more

common indicators now in use (e.g. levels of cancer or heart disease). I make this suggestion because:

a. The gestational cycle for a baby is nine months, compared to decades for heart disease or cancer (300). This relatively short cycle time would allow for more accurate estimates of ecologic variables effects in modeling; for example, compared with longer cycle time morbidities there is a much greater likelihood that the area where the mother lived at the birth was the one lived in throughout the pregnancy. In addition to a shorter gestational cycle, women are less mobile during pregnancy than the population as a whole and those who move tend to stay within the same community (425).
b. Descriptive data were gathered for the great majority of births, adverse as well as normal, for administrative purposes and birth registration statistics. These data allow for better representation of the population and more effective regression analysis. In addition, adverse birth outcomes can better be compared with healthy ones within like areas. Even with the potential limitations, data available for birth outcomes are still more likely to be representative of the population and more effective for analysis purposes than those for other morbidities.
c. Adverse births represent a health issue with a greater impact on society; a newborn child can be assumed to have many more affected life-years ahead of it than older cancer or heart disease victims.
d. Birth outcomes reflect a more direct barometer of the health of the surrounding population. While an individual woman gives birth to a baby, my findings strongly suggest that the health of the baby is strongly associated with both contextual and individual risk factors.

4. Underscoring of the dynamic, complex character of contextual risk factors in their relationship with health outcomes. Even neighbourhood median income, which has arguably been one of the most consistently supported risk-increasing factors, was found to have different relationships with adverse outcomes in different places.

5.12. Practical Implications for Possible Interventions

My findings suggest possible up-stream interventions at three different levels: macro, meso and micro.

At the macro level:

1. Increased recognition that education is a health policy issue. The present study has shown low levels of education to be a consistent risk-increasing predictor in all four adverse birth outcomes; it is far more influential than median household income. A stronger etiologic understanding of education (both at the ecologic and individual level) as a health determinant is needed, as are alternatives to "keep the kids in school". Older women long past the age of "staying in school" clearly benefit from higher ecologic levels of educations; possibly there are alternative ways to gain those same benefits for those who were not inclined to complete their formal education.
2. Recognition by local public health authorities of small area geographic hotspots of adverse birth outcomes and their diversity. Additional information should be gathered or assessed (if already available) that could help to further explain these local findings. My finding that different areas can have markedly different models suggests that each public health region should individually analyze their service areas, using small population areas, and then intervene accordingly.

3. Strengthen smoking reduction efforts in general. Of course, considerable evidence of the health hazards of smoking is already in place. My findings reinforce this evidence.

At the meso level provincial or regional wellness campaigns should be customized for local populations in order to optimize effectiveness. My finding of substantial differences between local hotspot groups in predictors for like adverse outcomes suggest that even in an area as relatively small as metropolitan Toronto, differences in predictors of adverse birth outcomes can be substantial. Local public health units should work with education systems to better understand the population base and to develop educational offerings directed at all women of childbearing age. The avoided cost of adverse birth outcomes could at least partially offset extra costs incurred.

At the micro level: Increased individual level contact by public health nurses to offer education and guidance on pre-pregnancy and pre-natal health behaviours. These contact efforts should focus on women in high-deprivation areas.

5.13. Recommendations for Future Research

The findings presented here seemingly pose more questions than they answer. This research demonstrates the power of a small population area spatial analysis to both answer questions as well as to generate new venues of inquiry. A few of the suggested areas for future research are:

1. Expand on the use of small-scale GIS analysis to better understand local-area patterns of health inequities as well as their predictors. This analysis should include local ecologic as well as individual level variables and address the nature of the interactions between them in areas with high levels of adverse outcomes.

2. Expand the use of GIS spatial cluster analysis in exploring and understanding predictors of adverse birth outcomes. Hotspots of recognized predictors could be identified and act as a "topographical" map for local health agencies. Additional analysis could also be carried out to determine the degree that predictor hotspots spatially correlate with outcome hotspots.
3. Expand on the risk factors used in local regression analysis. My research demonstrated the presence of unknown local variables that modified the risk factors in my analysis to the extent that they had opposite effects on the same adverse outcome. Other social, natural and built environment variables are available and could be linked to census boundary files for hypothesis building and in exploratory analysis.
4. Further investigate the finding of spatially exclusive hotspots. My findings lent insight into this important question but much more extensive analysis is needed.
5. Expand upon the understanding of higher education as a predictor of adverse birth outcomes. My findings suggest the presence of confounding relationships that should be better understood in order to effectively utilize this risk factor in research.
6. Additional research in the ecologic role of education may be valuable. Research questions might be:
    - Is the ecologic effect solely compositional or is there an independent, contextual effect?
    - If there are contextual effects can those effects be created without individual level intervention?
7. I surmise that the marked differences in model complexity between the different adverse outcomes were due at least in part to multifaceted birth outcomes analyzed as a

homogenous event. Future regression analysis of adverse outcomes should explore multiple facets of the outcomes, for example four to five levels of preterm birth (8) and several facets of intra-uterine growth restriction, such as premature versus full-term or symmetrical versus asymmetrical growth-restricted (419).[30]

8. Explore cluster analysis and identification using alternative cluster analysis tools, such as the Spatial Scan statistic.

5.14. Statement of contribution

I, David N Williams, take full responsibility for this research project. I completed all stages of the research from data grooming to geographic analysis to hierarchical regression analysis to final conclusions. I am the sole author of this dissertation.

I was supported by members of my dissertation committee, Drs Ian McDowell, Eric Crighton, Tim Ramsey and Mark Walker. Ian McDowell provided guidance on epidemiological research design and execution as well as dissertation crafting. Eric Crighton offered guidance on GIS analysis and the geographic perspective. Tim Ramsey lent support on research design and statistical issues.

Other contributors included:

- Kathryn A Williams, MSc Statistics. Ms Williams provided guidance in large database analysis as well as in hierarchical logistic regression.
- Perry Ghioureliotis, BSc, contributed to the creation of GIS data bases, guidance in the derivation of key spatial variables and outcome maps.
- Jean Dumais, MSc Statistics, contributed to the formulation of DA-level median income estimates.

[30] Symmetrical vs. asymmetrical would require information not currently available in the BORN Ontario database.

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Appendix 1: Niday Database Pre-existing Maternal Health Problems

Morbidities

- Chronic Hypertension
- Diabetes insulin dependant
- Diabetes non-insulin dependant
- Heart disease
- Thyroid disease
- Lupus
- Alcohol dependence syndrome/Alcoholism
- Asthma
- HIV
- Other
- Hepatitis B

Substance Use

- Drug & Medication Use-Opioides
- Drug & Medication Use-Narcotics
- Drug & Medication Use-Cocaine
- Drug & Medication Use-Hallucinogens
- 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

Appendix 2: GLIMMIX code for hierarchical regression analysis

Below is an example of code for the hierarchical analysis carried out. This example was used to calculate odds ratios for late premature births; this same code was used with only minor variations for all odds ratio generation. A line by line explanation of the component parts follows.

1. **proc glimmix** data=key9_11.Ndaycensus621750format order=formatted;
2. class dauid *Teenage HlthProb Olderage Urban Smoked*;
3. model *LateP*(event='1')= *HlthProb Teenage Olderage Urban Smoked %NoDip*
   %Asian
4. *Teenage*Urban*
5. *%Asian*Urban*
6. *Olderage* %NoDip*
7. *HlthProb*Teenage*
8. / solution dist=binary link=logit ddfm=bw
9. oddsratio (diff=all at *%Asian*=7 at *%NoDip*=**.3**
10. unit *%Asian %NoDip* = 2 .1);
11. random intercept / subject=dauid solution;
12. lsmeans *Teenage*Urban HlthProb*Teenage*
13. /or cl DIFF;
14. **run**;

Line(s):

1. The SAS procedure and database (*data=*) are defined.
2. The "*class*" statement instructs the procedure to treat the variables, *HlthProb, Olderage, Urban,* and *Smoked*, as classification, that is binary, variables.
3. through 7. The "*model"* command identifies the variable, in this case *LateP*, that is to be fitted in the GLIMMIX procedure
   - (event='1') specifies that *LateP* is to be modeled when it equals 1 (indicating a late premature birth)
   - The predictors that are to be used in the modeling are defined. All individual risk factors, such as *Hlthprob* and *Teenage,* are required to be included when they are part of an interaction effect, for example *Teenage*Hlthprob*.
8. The *solution* term requests that fixed effects parameters be produced. These parameters were presented as tables in each of the regression results chapters to illustrate the final model.
   - "*dist=binary"* specifies that the conditional probability distribution of the data was binary.
   - *"link = logit"* specifies that the link function in the generalized linear mixed model was logit. A logit option is required in order that odds ratios be generated.
   - "*ddfm=bw*" specifies the method by which degrees of freedom are determined. The "*bw*" option was chosen because we were processing by

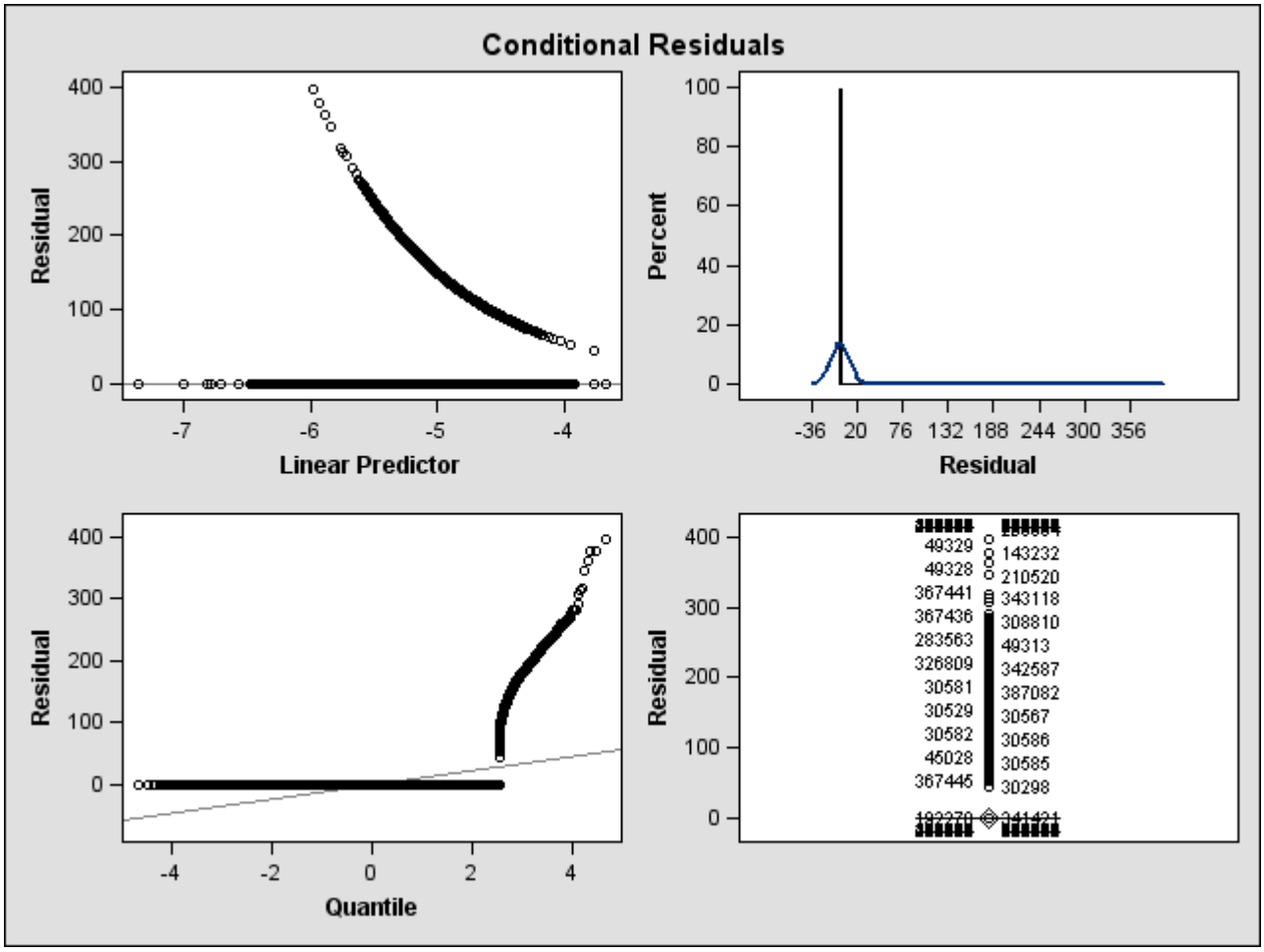
DA. The selected "*bw*" option functions by dividing the residual degrees of freedom into between-subject and within-subject portions. It then determines whether a fixed effect changes within any DA.

9. "*oddsratio"* requests that estimates of odds ratios and confidence intervals be generated for main effects and continuous variable interactions in the model statement.
    - "*diff=all*" specifies that odds ratios for main effects be produced on all pairwise differences.
    - "*at…*" specifies the reference values for continuous variables used in the model. For example *%Asian*=7 specifies that 7% will be used as the reference value for *%Asian* in generating odds ratios. It was the "*at*" values that were changed when odds ratios for different levels of the continuous variables, high, mid, and low, were generated for presentation in the various results figures.
10. "*unit…*" specifies the units in which the effect of the continuous variables in the model are assessed. For example *%Asian* will be assessed at a 2% change from the reference value of 7% (given in the "at" option statement above – e.g. 7% level was compared to the 9% level). See Appendixes 4-7 for an example of the output.
11. The *"random intercept/subject=dauid / solution*" specified that the linear predictor(s) contains an intercept term that randomly varies at the level of the DA effect.
12. "*lsmeans*" requests the least-squares means for the binary*binary interactions, such as *Teenage***Urban*. The "*or cl and DIFF*" options requests odds ratios, confidence intervals and pairwise differences (and their significance) between the variables being displayed.
13. The *"ods"* statement requests that least-squares means related graphics are produced via ODS Graphics; "exclude" specifies that the solution (random effects solution vector) table not be generated as this would duplicate the output requested by the *solution* command mentioned in line 8 above. (139)
14. "*run*" commands the code be executed.

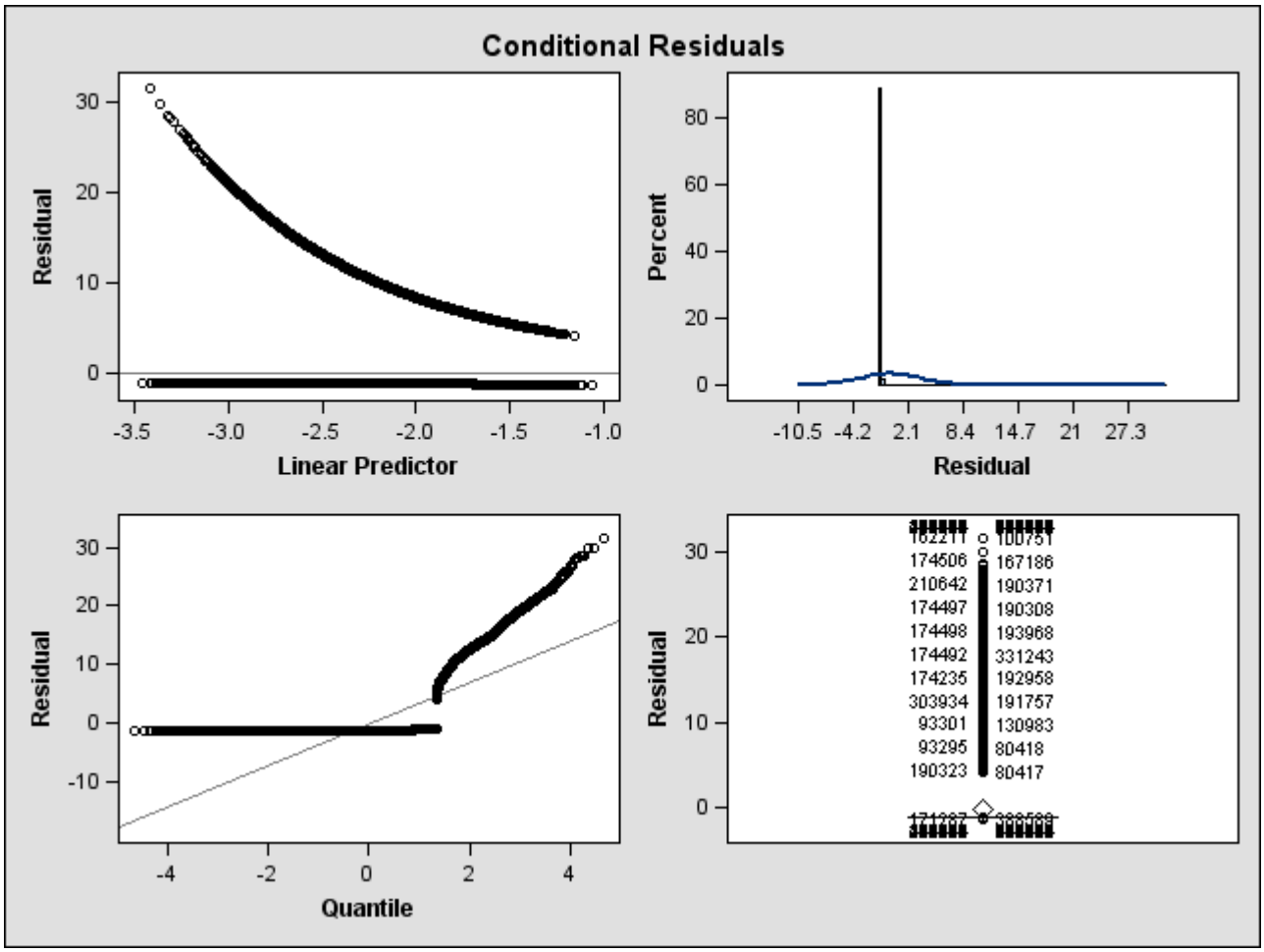
Appendix 3: Conditional Residual Plots

Residuals in logistic regression can be defined as the differences between observed and expected, fitted, values (386); residuals allow for evaluating the fit of the model. In logistic regression the term "conditional" is used to denote that the residuals are estimated based on predictors of the random effects (347). This allows for a more accurate estimate of residual values vs. observed values (386). Within SAS GLIMMIX, the panel of conditional residuals is constructed from $y - \mathbf{x}'\hat{\boldsymbol{\beta}} - \mathbf{z}'\hat{\boldsymbol{\gamma}}$; where $\hat{\boldsymbol{\gamma}}$represents an estimated distribution based on random-effects solutions (347).

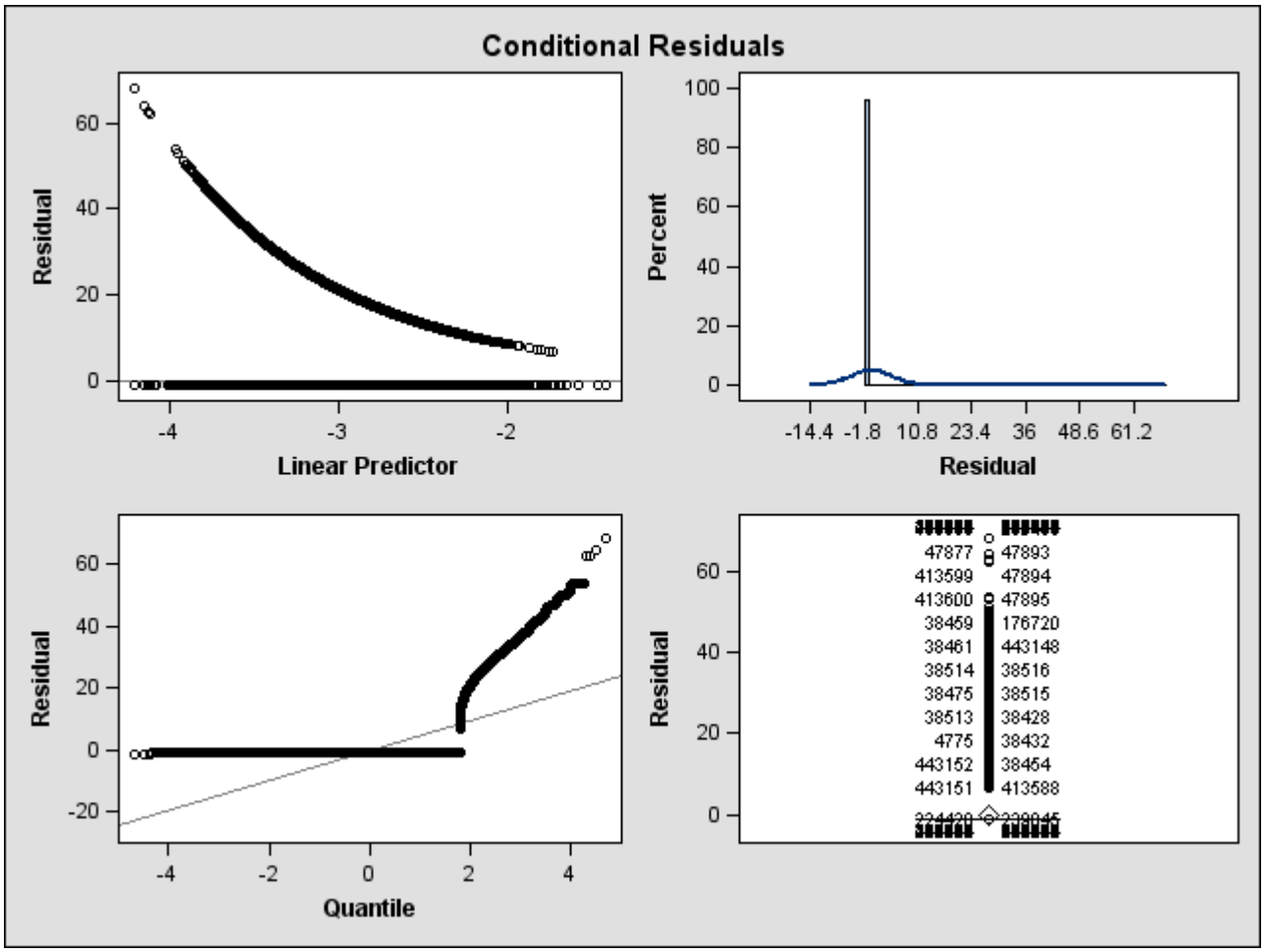
1. Stillbirth Mortalities Full-Provincial Model



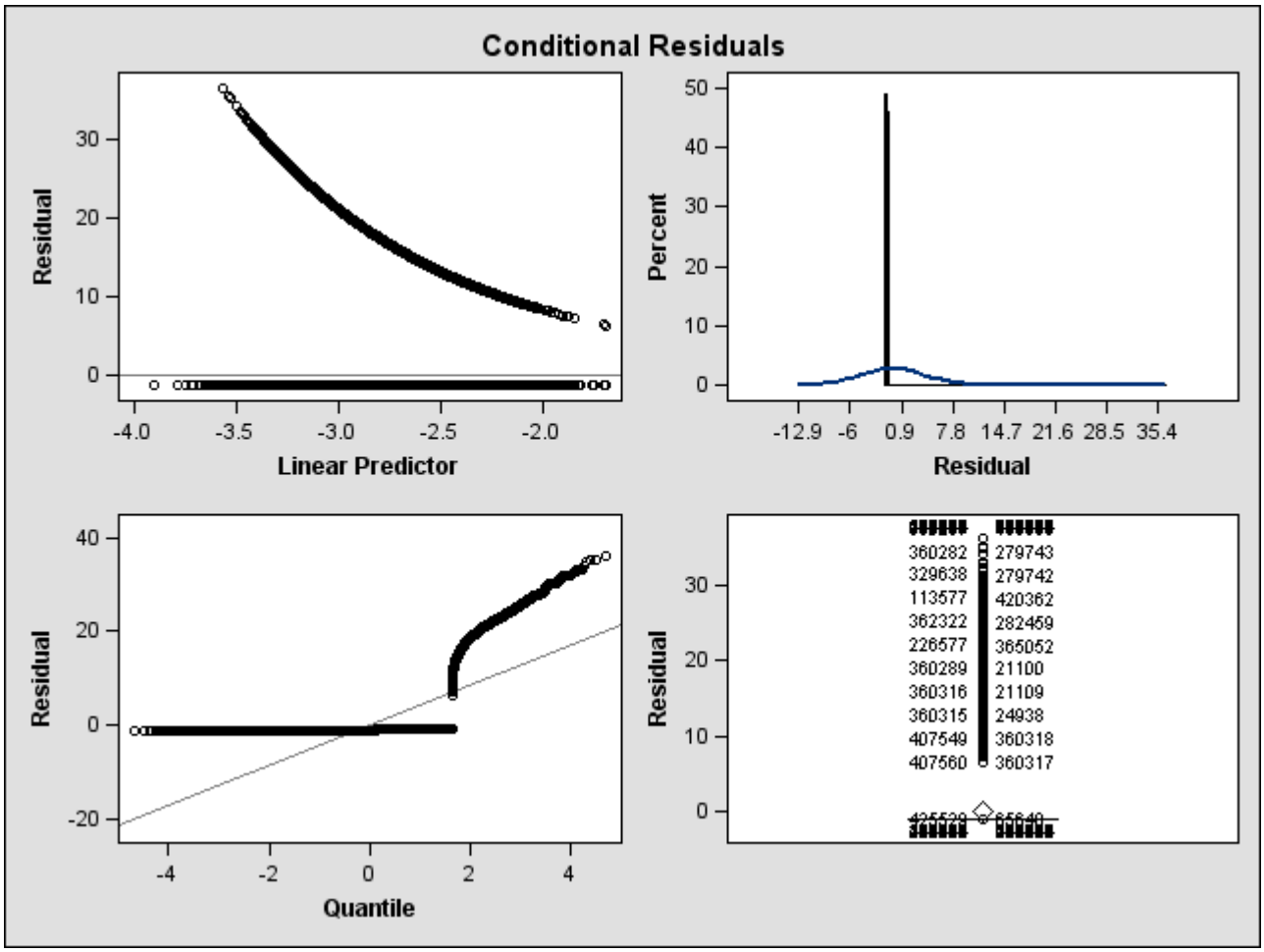
2. Small for Gestational Age Full-Provincial Model



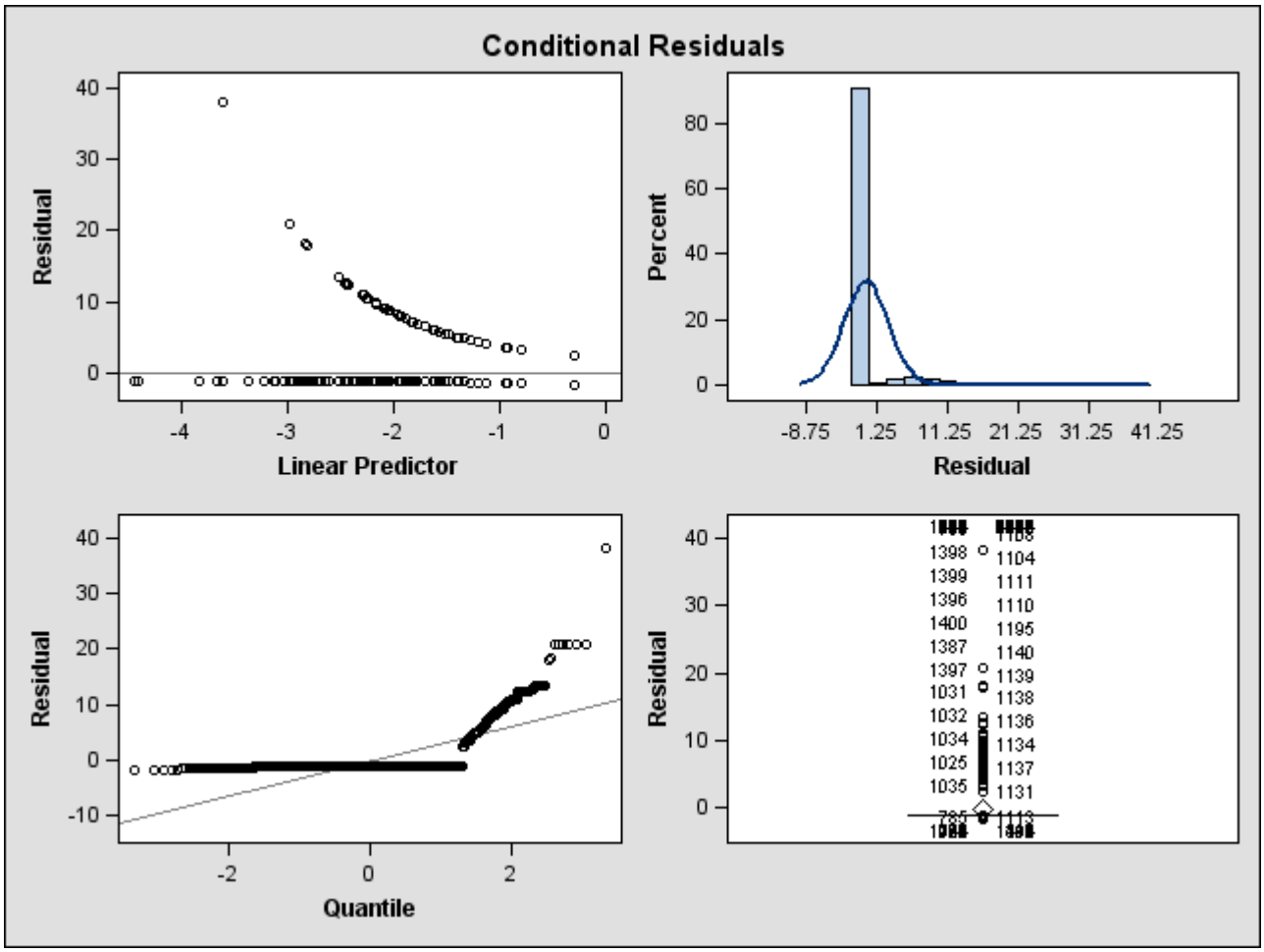
3. Moderate to Very Premature Full-Provincial Model



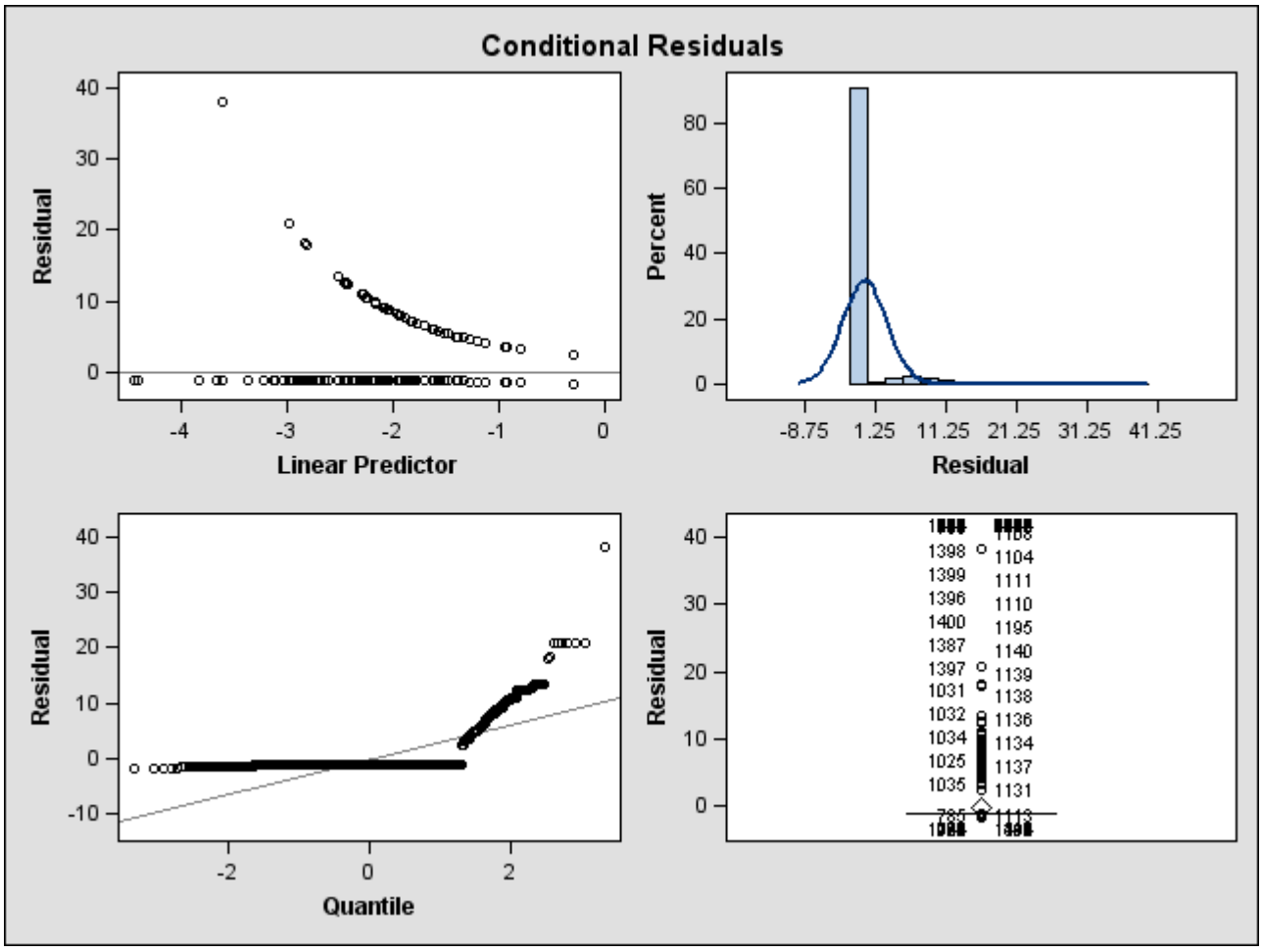
4. Late Premature Full-Provincial Model



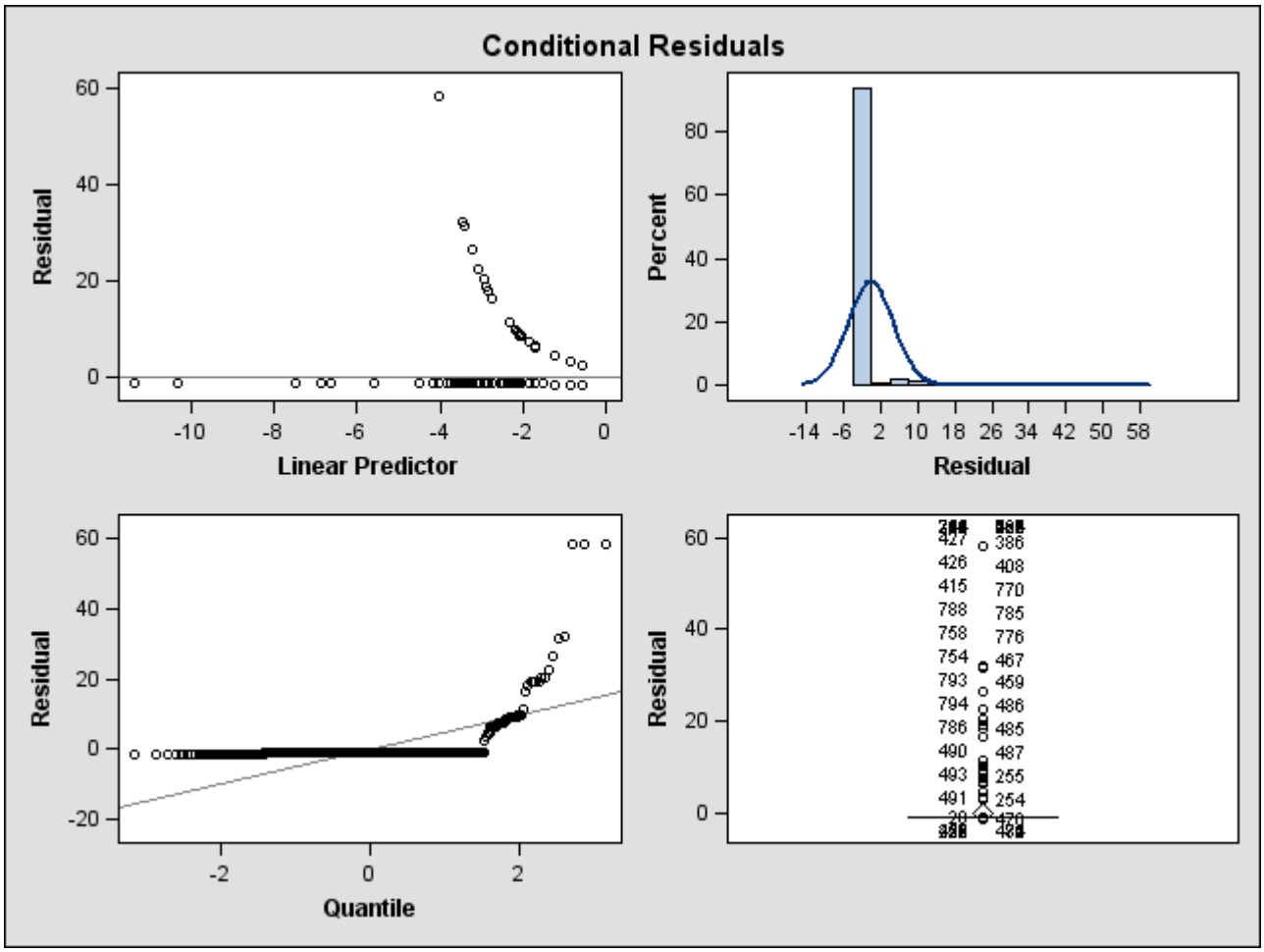
5. Late Premature Cambridge



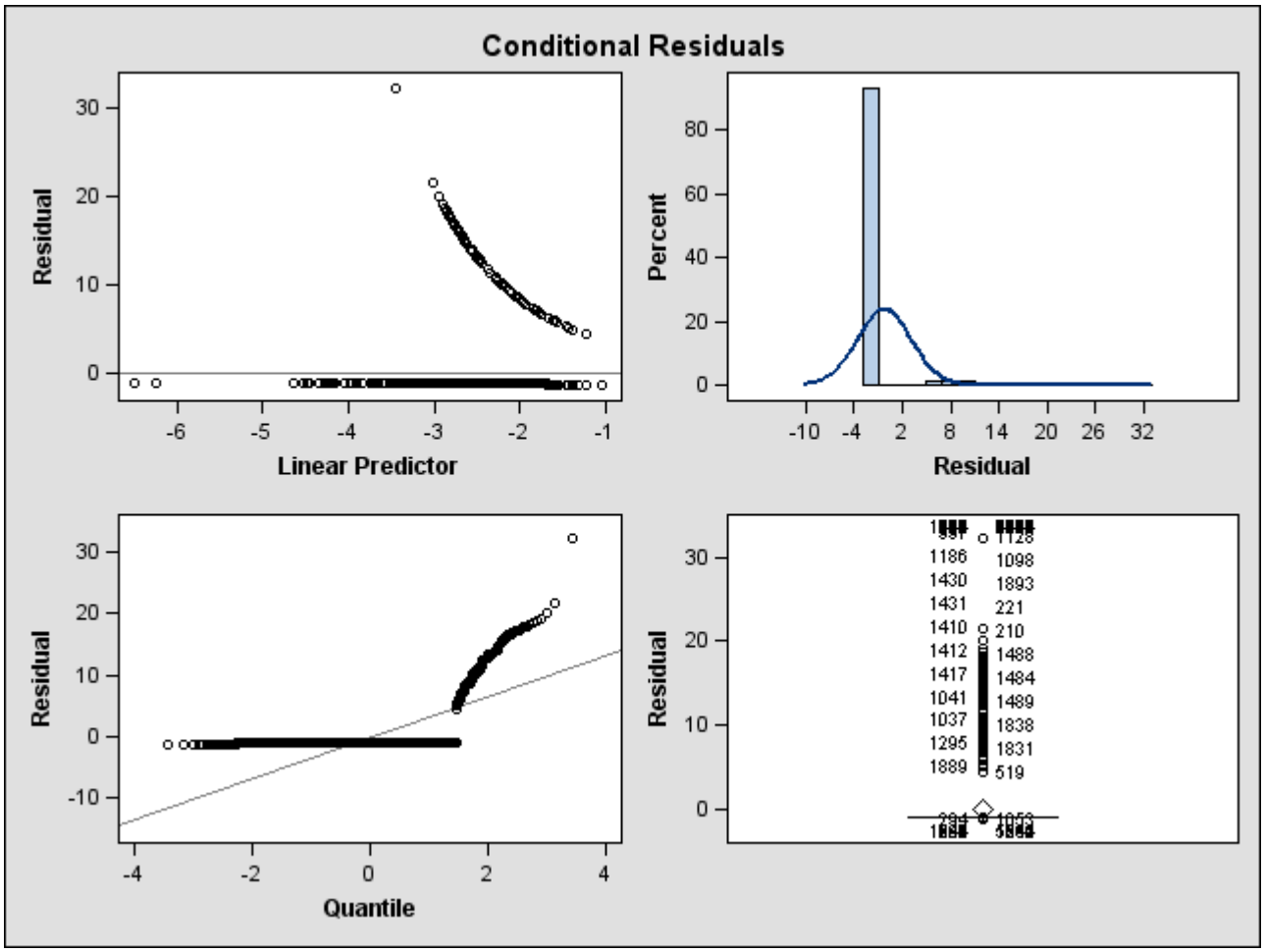
6. Moderately to Very Premature Births South Georgian Bay



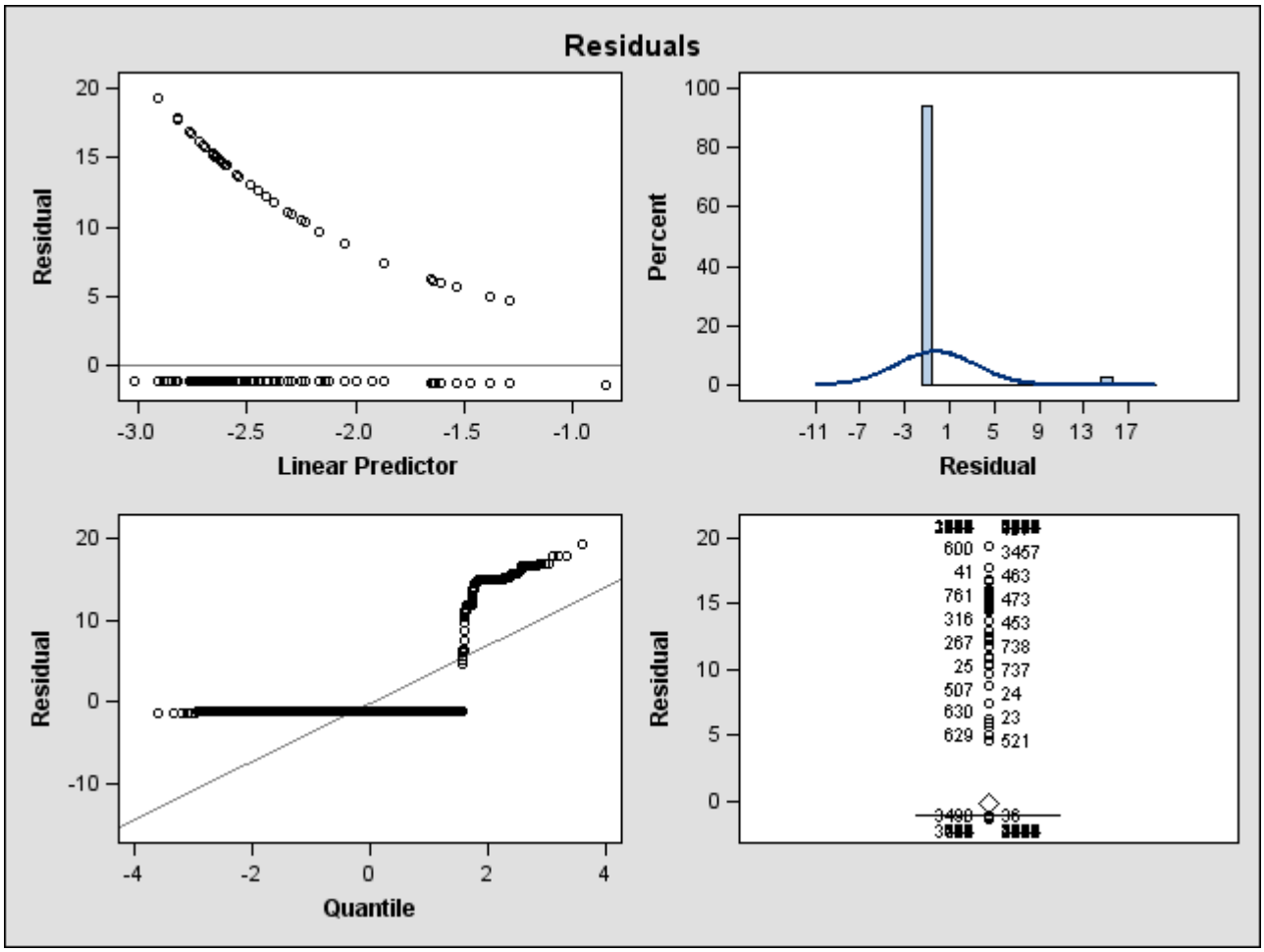
7. Moderately to Very Premature Births North Ottawa Valley



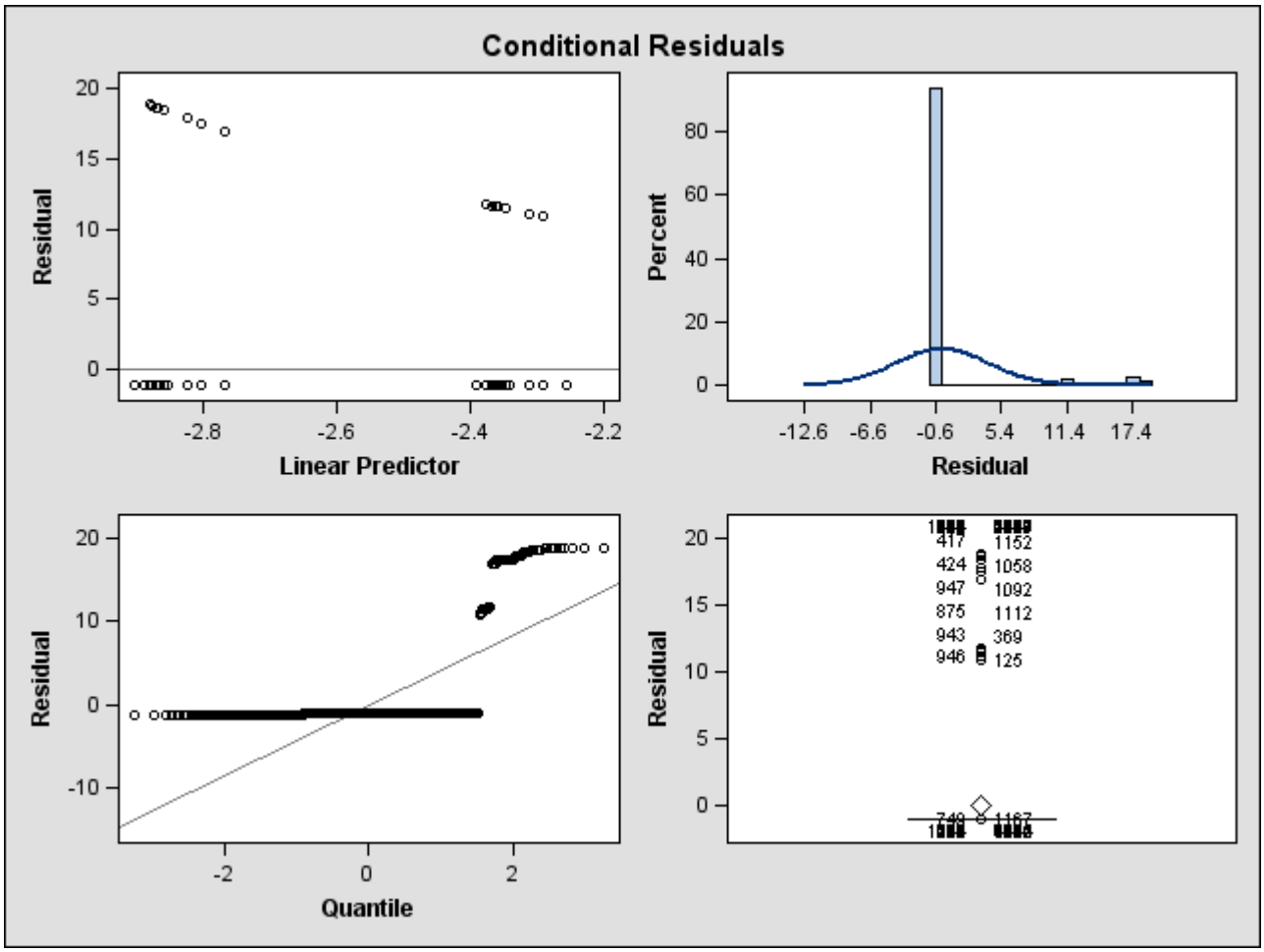
8. Moderately to Very Premature Births Hamilton



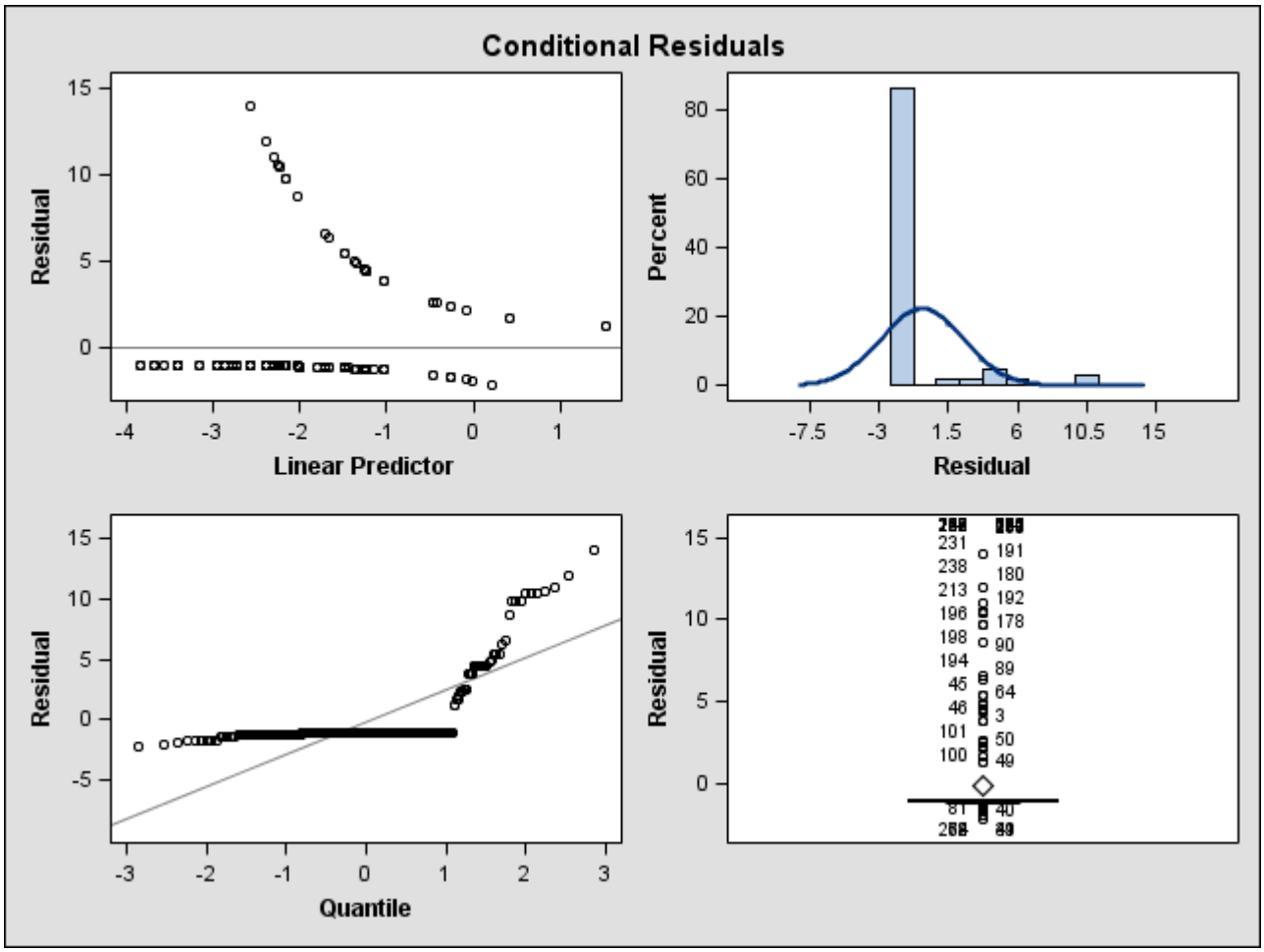
9. Late Premature Births North Toronto



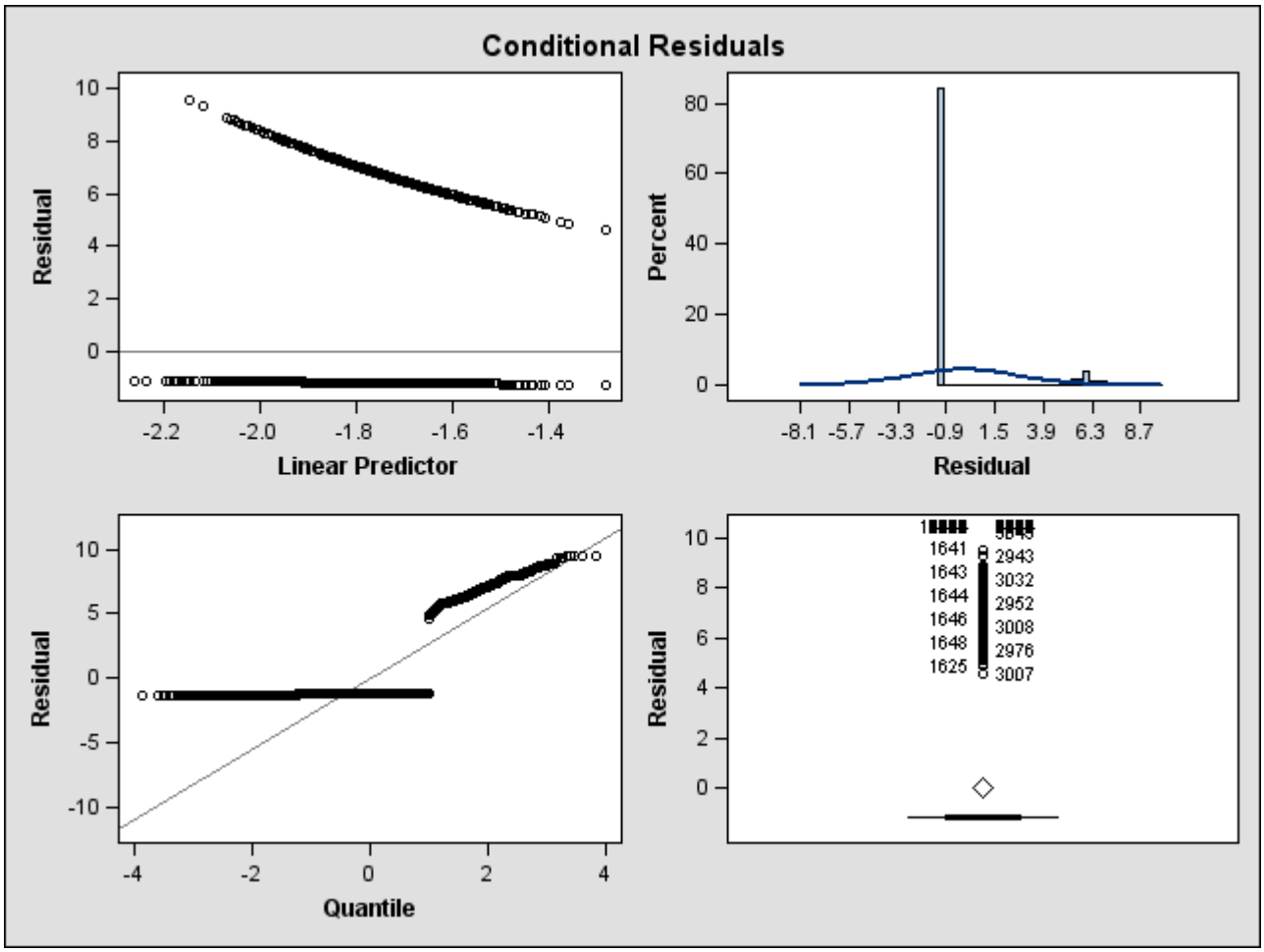
10. Late Premature Births SW of Ottawa



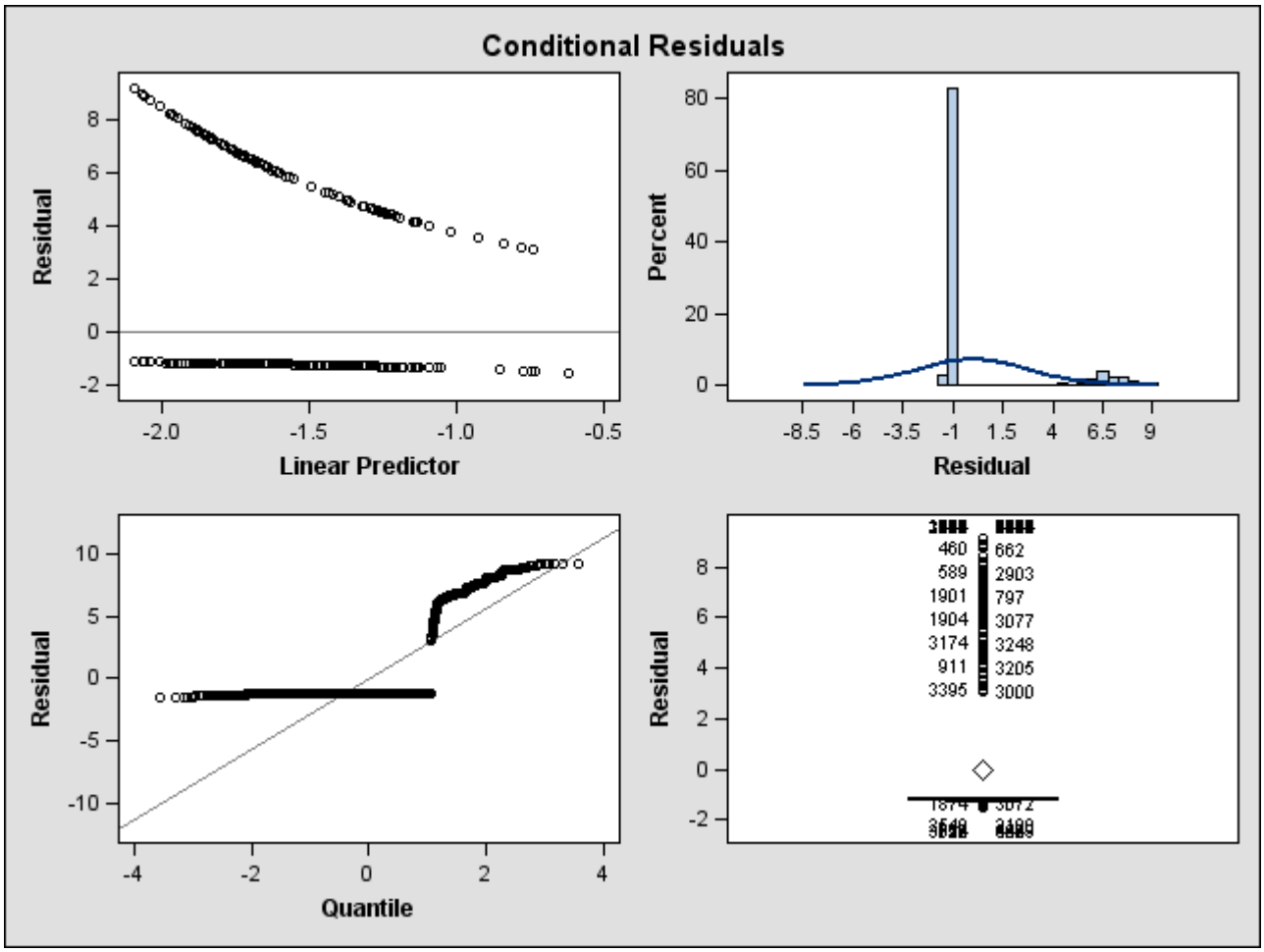
11. Late Premature Births St. Catharines



12. Small for Gestational Age Births East Toronto



13. Small for Gestational Age Births NW Toronto



Appendix 4: Late Premature Births Final Model Odds Ratio Estimates

Full Province Regression Models

4.1 Predictor Variable Distribution Characteristics
4.2 Main effects
4.3 Continuous*Binomial Regression Tables
4.4 Binomial*Binomial Risk Factor Regression Tables
4.5 Goodness of Fit Statistics

Hotspot Cluster Models

4.6 St. Catharines
4.7 Southwest of Ottawa
4.8 Northern Toronto

4.1 Full Province Late Premature Births Predictor Variable Distribution Characteristics									
Risk Factor	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
HlthProb	485666	0.12	0.33	0	0	0	1.00	0	1.00
Teenage	621688	0.04	0.18	0	0	0	0	0	1.00
Olderage	621688	0.21	0.41	0	0	0	1.00	0	1.00
Urban	621750	0.91	0.28	1.00	1.00	1.00	1.00	0	1.00
Smoked	548480	0.12	0.32	0	0	0	1.00	0	1.00
%NoDip	619622	0.18	0.12	0.16	0.09	0.25	0.35	0	1.00
%Asian	619347	5.8	9.77	1.86	0	7.07	17.22	0	80.46

4.2 Full Province Late Premature Births Main Effects Odds Ratios Estimates (Presented in Figure 4.5)

Predictor	Reference Value							Assessment Value							Estimate	DF	95% Confidence Limits	
	Teen Age	Hlth Prob	Older Age	*Urban*	*Smoked*	%No Dip	% Asian	Teen Age	Hlth Prob	Older Age	*Urban*	*Smoked*	%No Dip	% Asian				
Teenage	indep					0.18	5.167	ref					0.18	5.17	0.92	6895	0.85	0.98
Olderage			indep			0.18	5.17			ref			0.18	5.17	1.21	14416	1.17	1.25
%NoDip						0.28	5.17						0.18	5.17	0.998	15735	0.98	1.01
%Asian						0.18	7.17						0.18	5.17	0.99	15735	0.99	0.99
Urban				indep		0.18	5.17				ref		0.18	5.17	0.97	15735	0.91	1.03
Smoked					indep	0.18	5.17					ref	0.18	5.17	1.20	11578	1.15	1.25
HlthProb		indep				0.18	5.17		ref				0.18	5.17	1.38	12871	1.32	1.43

Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.

Linking Appendices Tables to Figures in text.

Odds ratio and confidence interval estimates presented in Table 4.6 were taken from three tables found in this appendix: models 4.3a – 4.3c. Model 4.3a presents odds ratio estimates for *%NoDip*Olderage* where *%NoDip* is set at a low level, 0.1 (that is 0.1, or 10%, of women 20 years or older did not have a high school diploma). The first row for the predictor *%NoDip*Olderage* can be read as: older aged women ("indep" Reference Value columns) living in a low (.1) *%NoDip* DA have an estimated odds ratio of 1.19 (CI 1.15-1.24) greater risk of a late premature birth than younger women ("ref" Assessment Value). Columns under "Reference Value" present target values (binomial or continuous) that are compared with those presented in the columns under "Assessment Value".

The following Appendix table 4.3b shows that older women living in a mid *%NoDip* level DA, 0.2 (20%), have an estimated odds ratio of 1.22 (CI 1.18-1.26) of a late premature birth compared with younger women. Table 4.3c shows that older women living in a high *%NoDip* area, .3 (30%) have an estimated odds ratio of 1.26 (CI 1.2-1.32). Odds ratios and confidence intervals presented in figures throughout Chapter 4 were taken from their respective appendixes as shown in this example.

4.3a Full Province Late Premature Births Low-Range Binomial*Continuous Odds Ratio Estimates (Presented in Figure 4.6)																		
Predictor	Reference Value							Assessment Value							Estimate	DF	95% Confidence Limits	
	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian				
HlthProb		indep				0.1	2		ref				0.1	2	1.23	12871	1.11	1.36
Teenage	indep					0.1	2	ref					0.1	2	0.74	6894	0.64	0.85
%NoDip Olderage*			indep			0.1	2			ref			0.1	2	1.19	14416	1.15	1.24
%NoDip Olderage*			indep			0.2	2			indep			0.1	2	1.02	431E3	0.99	1.04
%NoDip Olderage*			ref			0.2	2			ref			0.1	2	0.99	431E3	0.98	1.01
%Asian Urban*				indep		0.1	2				ref		0.1	2	0.98	15734	0.82	1.17
%Asian Urban*				indep		0.1	4				indep		0.1	2	0.99	15734	0.99	0.99
%Asian Urban*				ref		0.1	4				ref		0.1	2	1.19	15734	1.03	1.38
Smoked					indep	0.1	2					ref	0.1	2	1.20	11578	1.16	1.25

4.3b Full Province Late Premature Births Mid-Range Binomial*Continuous Odds Ratio Estimates (Presented in Figure 4.6)																	
Predictor	Reference Value							Assessment Value							Estimate	DF	95% Confidence Limits	
	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian				
HlthProb		indep				0.18	3.8		ref				0.18	3.8	1.23	12871	1.11	1.35
Teenage	indep					0.18	3.8	ref					0.18	3.8	0.74	6894	0.64	0.85
%NoDip Olderage*			indep			0.18	3.8			ref			0.18	3.8	1.22	14416	1.18	1.26
%NoDip Olderage*			indep			0.28	3.8			indep			0.18	3.8	1.02	431E3	0.99	1.04
%NoDip Olderage*			ref			0.28	3.8			ref			0.18	3.8	0.99	431E3	0.98	1.0
%Asian Urban*				indep		0.18	3.8				ref		0.18	3.8	0.83	15734	0.62	1.1
*%Asian*Urban*				indep		0.18	5.8				indep		0.18	3.8	0.99	15734	0.99	0.99
%Asian Urban*				ref		0.18	5.8				ref		0.18	3.8	1.19	15734	1.027	1.38
Smoked					indep	0.18	3.8					ref	0.18	3.8	1.20	11578	1.15	1.2

4.3c Full Province Late Premature Births High-Range Binomial*Continuous Odds Ratio Estimates (Presented in Figure 4.6)																	
Predictor	Reference Value							Assessment Value							Estimate	DF	95% Confidence Limits	
	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian	Teen Age	Hlth Prob	Old erage	Urb an	Smo ked	%No Dip	% Asian				
HlthProb		indep				0.3	7		ref				0.3	7	1.228	12871	1.11	1.35
Teenage	indep					0.3	7	ref					0.3	7	0.739	6894	0.65	0.84
%NoDip Olderage*			indep			0.3	7			ref			0.3	7	1.260	14416	1.20	1.32
%NoDip Olderage*			indep			0.4	7			indep			0.3	7	1.020	431E3	0.99	1.04
%NoDip Olderage*			ref			0.4	7			ref			0.3	7	0.992	431E3	0.98	1.00
%Asian Urban*				indep		0.3	7				ref		0.3	7	0.626	15734	0.38	1.04
*%Asian*Urban*				indep		0.3	9				indep		0.3	7	0.994	15734	0.99	0.99
%Asian Urban*				ref		0.3	9				ref		0.3	7	1.189	15734	1.03	1.37
Smoked					indep	0.3	7					ref	0.3	7	1.204	11578	1.16	1.25

4.4a Full Province Late Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Teenage*	*Urban*	*_Teenage*	*_Urban*	Estimate	95% Confidence Limits	
*Teenage*Urban*	indep	indep	indep	ref	0.89	0.57	1.37
*Teenage*Urban*	indep	indep	ref	indep	0.89	0.80	0.99
*Teenage*Urban*	indep	ref	ref	ref	0.61	0.49	0.77
*Teenage*Urban*	ref	indep	ref	ref	0.61	0.42	0.88

4.4b Full Province Late Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Teenage*	*HlthProb*	*_Teenage*	*_HlthProb*	Estimate	Lower Odds Ratio	Upper Odds Ratio
*Teenage*HlthProb*	indep	indep	indep	ref	1.08	0.89	1.32
*Teenage*HlthProb*	indep	indep	ref	indep	0.65	0.53	0.80
*Teenage*HlthProb*	indep	ref	ref	ref	0.84	0.74	0.94
*Teenage*HlthProb*	ref	indep	ref	ref	1.39	1.34	1.44

4.5. Full Province Late Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	2602889
Generalized Chi-Square	414188.6
Gener. Chi-Square / DF	0.93

Hotspot Cluster Models

St. Catharines

4.6a St. Catharines Hotspot Cluster Late Premature Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
HlthProb	285	0.15	0.36	0	0	0	1.00	0	1.00
%NoDip	316	0.15	0.1	0.12	0.08	0.21	0.30	0	0.43

4.6b St. Catharines Hotspot Cluster Late Premature Births Predictor Main Effects Odds Ratios Estimates								
Risk Factors	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
HlthProb	indep	0.15	ref	0.15	3.76	18	1.58	8.92
%NoDip		0.25		0.15	0.95	23	0.60	1.5
Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.								

4.6c St. Catharines Late Premature Low-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*HlthProb*	*%NoDip*	*_HlthProb*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
HlthProb%NoDip*	indep	0.09	ref	0.09	1.25	18	0.34	4.56
HlthProb%NoDip*	indep	0.14	indep	0.09	1.59	258	1.05	2.41
HlthProb%NoDip*	ref	0.14	ref	0.09	0.75	258	0.55	1.01

4.6d St. Catharines Late Premature Mid-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*HlthProb*	*%NoDip*	*_HlthProb*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
HlthProb%NoDip*	indep	0.147	ref	0.146	2.95	18	1.04	8.32
HlthProb%NoDip*	indep	0.196	indep	0.146	1.6	258	1.05	2.41
HlthProb%NoDip*	ref	0.197	ref	0.146	0.74	258	0.55	1.01

4.6e St. Catharines Late Premature High-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*HlthProb*	*%NoDip*	*_HlthProb*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
HlthProb%NoDip*	indep	0.17	ref	0.17	4.21	18	1.53	11.6
HlthProb%NoDip*	indep	0.22	indep	0.17	1.59	258	1.06	2.41
HlthProb%NoDip*	ref	0.22	ref	0.17	0.74	258	0.55	1.01

4.6f St. Catharines Late Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	1441.86
Generalized Chi-Square	227.71
Gener. Chi-Square / DF	0.81

Southwest of Ottawa

4.7a. Southwest of Ottawa Hotspot Cluster Late Premature Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
Olderage	1173	0.2003410	0.40	0	0	0	1.00	0	1.00
%HigherEd	1173	0.0726718	0.04	0.08	0.03	0.11	0.11	0	0.16

4.7b Southwest of Ottawa Hotspot Cluster Late Premature Births Main Effects Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictor	*Olderage*	*%HigherEd*	*_Olderage*	*_%HigherEd*	Estimate	DF	95% Confidence Limits	
Olderage	indep	0.07	ref	0.07	1.67	12	0.93	3.00
%HigherEd		0.17		0.07	1.1	12	0.57	2.10
Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.								

4.7c Southwest of Ottawa Hotspot Cluster Late Premature Births Low-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictor	*Olderage*	*%HigherEd*	*_Olderage*	*_%HigherEd*	Estimate	DF	95% Confidence Limits	
Olderage%HigherEd*	indep	0.04	ref	0.04	3.18	12	1.57	6.46
Olderage%HigherEd*	indep	0.09	indep	0.04	0.45	1157	0.25	0.83
Olderage%HigherEd*	ref	0.09	ref	0.04	1.42	1157	0.99	2.01

4.7d Southwest of Ottawa Hotspot Cluster Late Premature Births Mid-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictor	*Olderage*	*%HigherEd*	*_Olderage*	*_%HigherEd*	Estimate	DF	95% Confidence Limits	
Olderage%HigherEd*	indep	0.08	ref	0.08	1.28	12	0.64	2.54
Olderage%HigherEd*	indep	0.13	indep	0.08	0.45	1157	0.25	0.83
Olderage%HigherEd*	ref	0.13	ref	0.08	1.42	1157	0.99	2.01

4.7e. Southwest of Ottawa Hotspot Cluster Late Premature Births Mid-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictor	*Olderage*	*%HigherEd*	*_Olderage*	*_%HigherEd*	Estimate	DF	95% Confidence Limits	
Olderage%HigherEd*	indep	0.11	ref	0.11	0.64	12	0.24	1.72
Olderage%HigherEd*	indep	0.16	indep	0.11	0.45	1157	0.25	0.83
Olderage%HigherEd*	ref	0.16	ref	0.11	1.42	1157	0.99	2.01

4.7f Southwest of Ottawa Late Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	6733.69
Generalized Chi-Square	1155.86
Gener. Chi-Square / DF	0.99

North Toronto

4.8a North Toronto Hotspot Cluster Late Premature Predictor Variable Distribution Characteristics									
Predictor	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
%NoDip	3836	0.09	0.05	0.086	0.08	0.09	0.14	0	0.42

4.8b North Toronto Late Premature Main Effects Odds Ratio Estimates								
Predictor	*Olderage*	*%NoDip*	*_Olderage*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
Olderage	indep	0.09	ref	0.09	1.37	62	1.02	1.85
%NoDip		0.19		0.09	1.18	62	0.88	1.6

4.8c North Toronto Late Premature Births Low-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*Olderage*	*%NoDip*	*_Olderage*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
Olderage%NoDip*	indep	0.05	ref	0.05	1.08	62	0.74	1.56
Olderage%NoDip*	indep	0.15	indep	0.05	1.58	3657	1.09	2.29
Olderage%NoDip*	ref	0.15	ref	0.05	0.89	3657	0.59	1.34

4.8d North Toronto Late Premature Births Mid-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*Olderage*	*%NoDip*	*_Olderage*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
Olderage%NoDip*	indep	0.1	ref	0.1	1.43	62	1.06	1.94
Olderage%NoDip*	indep	0.2	indep	0.1	1.58	3657	1.09	2.29
Olderage%NoDip*	ref	0.2	ref	0.1	0.89	3657	0.59	1.33

4.8e North Toronto Late Premature Births High-Range Odds Ratio Estimates								
	Reference Value		Assessment Value					
Predictors	*Olderage*	*%NoDip*	*_Olderage*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
Olderage%NoDip*	indep	0.12	ref	0.12	1.61	62	1.15	2.24
Olderage%NoDip*	indep	0.22	indep	0.12	1.58	3657	1.09	2.29
Olderage%NoDip*	ref	0.22	ref	0.12	0.89	3657	0.6	1.34

4.8f North Toronto Late Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	21351.27
Generalized Chi-Square	3541.42
Gener. Chi-Square / DF	0.95

Appendix 5: Moderately to Very Premature Births Model Odds Ratio Estimates

Full Province Regression Models

Hotspot Cluster Models

Full-Province Model

5.1. Full Province Moderately to Very Premature Births Predictor Variable Distribution Characteristics

Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
%NoDip	619622	0.18	0.13	0.16	0.09	0.25	0.35	0	1.000
MedInc	621750	65959.74	27143.57	64275.00	45840.00	83658.00	98494.00	0	551293.00
%HigherEd	619622	0.08	0.07	0.06	0.03	0.18	0.17	0	1.000
%Asian	619347	5.8	9.77	1.86	0	7.07	17.223	0	80.46

5.2 Full Province Moderately to Very Premature Births Main Effects Odds Ratios Estimates

	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits	
	Olderage	*Smoked*	*Hlth Prob*	*Teenage*	*Urban*	*%Asian*	*Med Inc*	*%No Dip*	*%Hi Ed*	*Olderage*	*Smoked*	*Hlth Prob*	*Teenage*	*Urban*	*%Asian*	*Med Inc*	*%No Dip*	*%Hi Ed*				
Teenage	indep					65.81	0.18	0.08	5.167	ref					65.81	0.18	0.08	5.17	1.029	6895	0.95	1.11
Olderage		indep				65.81	0.18	0.08	5.167		ref				65.81	0.18	0.08	5.17	1.323	14416	1.27	1.37
MedInc						65.81	0.18	0.08	5.167						65.81	0.18	0.08	5.17	1.014	15733	1.00	1.02
%NoDip						65.81	0.18	0.08	5.167						65.81	0.18	0.08	5.167	1.004	15733	0.99	1.02
%HigherEd						65.81	0.18	0.08	5.167						65.81	0.18	0.08	5.17	0.961	15733	0.93	0.98
%Asian						65.81	0.18	0.08	7.167						65.81	0.18	0.08	5.17	0.990	15733	0.98	0.99
Urban			indep			65.81	0.18	0.08	5.167			ref			65.81	0.18	0.078	5.17	1.014	15733	0.95	1.09
Smoked				indep		65.81	0.18	0.08	5.167				ref		65.81	0.18	0.08	5.167	1.306	11578	1.25	1.37
HlthProb					indep	65.81	0.18	0.08	5.167					ref	65.81	0.18	0.08	5.17	1.234	12871	1.18	1.29

Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.

5.3a Full Province Moderately to Very Premature Births Low-Range Binomial*Continuous Odds Ratio Estimates																					
Predictors	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits	
	Old rage	*Sm ked*	*Hlt Pro*	*Tee age*	*Urb an*	*%Asian*	*Med Inc*	*%No Dip*	*%Hi Ed*	*Olde rage*	*Smo ked*	*Hlth Prob*	*Teen age*	*Urb an*	*%As ian*	*Med Inc*	*%No Dip*	*%Hi Ed*				
Olderag* *%NoDip*	indep					2	35	0.1	0.03	ref					2	35	0.1	0.03	1.29	14416	1.24	1.35
Olderag* *%NoDip*	indep					2	35	0.2	0.03	indep					2	35	0.1	0.03	1.03	431E3	1.00	1.06
Olderag* *%NoDip*	ref					2	35	0.2	0.03	ref					2	35	0.1	0.03	0.99	431E3	0.98	1.01
Smoked MedInc*		indep				2	35	0.1	0.03		ref				2	35	0.1	0.03	1.14	11577	1.03	1.27
Smoked MedInc*		indep				2	25	0.1	0.03		indep				2	35	0.1	0.03	1.03	431E3	1.01	1.05
Smoked MedInc*		ref				2	25	0.1	0.03		ref				2	35	0.1	0.03	1.01	431E3	1.00	1.02
HlthProb			indep			2	35	0.1	0.03			ref			2	35	0.1	0.03	1.01	12871	0.89	1.17
%Higher Ed						2	35	0.1	0.08						2	35	0.1	0.03	0.98	15733	0.97	0.99
Teenage %Asian*				indep		2	35	0.1	0.03				ref		2	35	0.1	0.03	0.89	6895	0.79	1.00
Teenage %Asian*				indep		4	35	0.1	0.03				indep		2	35	0.1	0.03	1.02	431E3	0.99	1.05
Teenage %Asian*				ref		4	35	0.1	0.03				ref		2	35	0.1	0.03	0.990	431E3	0.98	0.99
Urban					indep	2	35	0.1	0.03					ref	2	35	0.1	0.03	1.05	157	0.97	1.14

5.3a Full Province Moderately to Very Premature Births Mid-Range Binomial*Continuous Odds Ratio Estimates																					
Predictors	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits
	Olderage	*Smoked*	*HlthProb*	*Teenage*	*Urban*	*%Asian*	*MedInc*	*%NoDip*	*%HiEd*	*Olderage*	*Smoked*	*HlthProb*	*Teenage*	*Urban*	*%Asian*	*MedInc*	*%NoDip*	*%HiEd*			
Olderage %NoDip*	indep					3.8	65	0.2	0.08	ref					3.8	65	0.2	0.08	1.34	14416	1.29 1.39
Olderage %NoDip*	indep					3.8	65	0.3	0.08	indep					3.8	65	0.2	0.08	1.03	431E3	1.00 1.06
Olderage %NoDip*	ref					3.8	65	0.3	0.08	ref					3.8	65	0.2	0.08	0.99	431E3	0.98 1.01
Smoked MedInc*		indep				3.8	65	0.2	0.08		ref				3.8	65	0.2	0.08	1.07	11577	0.96 1.19
Smoked MedInc*		indep				3.8	55	0.2	0.08		indep				3.8	65	0.2	0.08	1.03	431E3	1.01 1.05
Smoked MedInc*		ref				3.8	55	0.2	0.08		ref				3.8	65	0.2	0.08	1.01	431E3	1.00 1.02
HlthProb			indep			3.8	65	0.2	0.08			ref			3.8	65	0.2	0.08	1.01	12871	0.89 1.14
%Higher Ed						3.8	65	0.2	0.08						3.8	65	0.2	0.08	0.98	15733	0.97 0.99
Teenage %Asian*				indep		3.8	65	0.2	0.08				ref		3.8	65	0.2	0.08	0.91	6895	0.81 1.03
Teenage %Asian*				indep		5.8	65	0.2	0.08				indep		3.8	65	0.2	0.075	1.018	431E3	0.99 1.05
Teenage %Asian*				ref		5.8	65	0.2	0.08				ref		3.8	65	0.2	0.075	0.990	431E3	0.98 0.99

5.3a Full Province Moderately to Very Premature Births Mid-Range Binomial*Continuous Odds Ratio Estimates																					
Predictors	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits
Urban					indep	3.8	65	0.2	0.08					ref	3.8	65	0.2	0.075	1.051	15733	0.97	1.14

5.3a Full Province Moderately to Very Premature Births High-Range Binomial*Continuous Odds Ratio Estimates																						
Predictors	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits	
	Olderage	*Smoked*	*Hlth Prob*	*Teenage*	*Urban*	*%Asian*	*MedInc*	*%NoDip*	*%HiEd*	*Olderage*	*Smoked*	*Hlth Prob*	*Teenage*	*Urban*	*%Asian*	*MedInc*	*%NoDip*	*%HiEd*				
Olderage %NoDip*	indep					7	80	0.25	0.11	ref					7	80	0.25	0.11	1.36	14416	1.30	1.42
Olderage %NoDip*	indep					7	80	0.35	0.11	indep					7	80	0.25	0.11	1.03	431E3	1.00	1.06
Olderage %NoDip*	ref					7	80	0.35	0.11	ref					7	80	0.25	0.11	0.99	431E3	0.98	1.01
Smoked MedInc*		indep				7	80	0.25	0.11		ref				7	80	0.25	0.11	1.03	11577	0.91	1.16
Smoked MedInc*		indep				7	70	0.25	0.11		indep				7	80	0.25	0.11	1.03	431E3	1.01	1.05
Smoked MedInc*		ref				7	70	0.25	0.11		ref				7	80	0.25	0.11	1.01	431E3	1.00	1.02
HlthProb			indep			7	80	0.25	0.11			ref			7	80	0.25	0.11	1.01	12871	0.89	1.14

5.3a Full Province Moderately to Very Premature Births High-Range Binomial*Continuous Odds Ratio Estimates																					
Predictors	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits	
%Higher Ed						7	80	0.25	0.16						7	80	0.25	0.11	0.98	15733	0.97	0.99
Teenage %Asian*				indep		7	80	0.25	0.11				ref		7	80	0.25	0.11	0.95	6895	0.83	1.09
Teenage %Asian*				indep		9	80	0.25	0.11				indep		7	80	0.25	0.11	1.02	431E3	0.99	1.05
Teenage %Asian*				ref		9	80	0.25	0.11				ref		7	80	0.25	0.11	0.99	431E3	0.98	0.99
Urban					indep	7	80	0.25	0.11					ref	7	80	0.25	0.11	1.05	15733	0.97	1.14

5.4a Full Province Moderately to Very Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*HlthProb*	*Teenage*	*_HlthProb*	*_Teenage*	Estimate	95% Confidence Limits	
*HlthProb*Teenage*	indep	indep	indep	ref	0.78	0.62	0.98
*HlthProb*Teenage*	indep	indep	ref	indep	0.85	0.67	1.07
*HlthProb*Teenage*	indep	ref	ref	ref	1.2	1.13	1.27
*HlthProb*Teenage*	ref	indep	ref	ref	1.11	1.00	1.22

5.4b Full Province Moderately to Very Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Smoked*	*Teenage*	*_Smoked*	*_Teenage*	Estimate	95% Confidence Limits	
*Smoked*Teenage*	indep	indep	indep	ref	0.84	0.71	0.98
*Smoked*Teenage*	indep	indep	ref	indep	0.96	0.80	1.15
*Smoked*Teenage*	indep	ref	ref	ref	1.18	1.1	1.28
*Smoked*Teenage*	ref	indep	ref	ref	1.03	0.89	1.19

5.4c Full Province Moderately to Very Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Smoked*	*HlthProb*	*_Smoked*	*_ HlthProb*	Estimate	95% Confidence Limits	
*Smoked*HlthProb*	indep	indep	indep	ref	0.94	0.82	1.08
*Smoked*HlthProb*	indep	indep	ref	indep	0.99	0.87	1.14
*Smoked*HlthProb*	indep	ref	ref	ref	1.14	1.03	1.27
*Smoked*HlthProb*	ref	indep	ref	ref	1.08	0.96	1.23

5.4d Full Province Moderately to Very Premature Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Smoked*	*Urban*	*_Smoked*	*_Urban*	Estimate	95% Confidence Limits	
*Smoked*Urban*	indep	indep	indep	ref	1.13	1.00	1.28
*Smoked*Urban*	indep	indep	ref	indep	1.15	1.04	1.27
*Smoked*Urban*	indep	ref	ref	ref	0.99	0.85	1.15
*Smoked*Urban*	ref	indep	ref	ref	0.98	0.90	1.05

5.5 Full Province Moderately to Very Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	2722684
Generalized Chi-Square	388242.5
Gener. Chi-Square / DF	0.87

Hotspot Cluster Models

Southern Georgian Bay Hotspot Cluster

5.6a Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Predictor Variable Distribution Characteristics

Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
*MedInc*2	1434	56459.20	19446.85	50910.00	42857.14	67196.00	88849.00	18407.00	99912.00
%HigherEd	1434	0.05	0.04	0.04	0.03	0.06	0.10	0	0.16

5.6b Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Predictor Main Effects Odds Ratios Estimates

	Reference Value		Assessment Value					
Predictors	*MedInc*	*%HigherEd*	*_MedInc*	*_%HigherEd*	Estimate	DF	95% Confidence Limits	
MedInc	76459	0.05	56459	0.05	0.54	77	0.38	0.76
%HigherEd	56459	0.10	56459	0.05	1.24	77	0.86	1.78

Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.

Interaction Effects between Continuous Risk Factors

The interaction between two continuous variables requires a total of six GLIMMIX tables in order to show the odds ratios for three levels of each variable, high, mid- and low range. Two interaction effects are shown below, requiring 12 total tables.

5.6v Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Low-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	40000	0.09	40000	0.04	1.708	76	1.042	2.80

6d Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Mid-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	55000	0.09	55000	0.04	1.18	76	0.82	1.70

6e. Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births High-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	65000	0.09	65000	0.04	0.93	76	0.57	1.5

5.6f Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	35000	0.03	55000	0.03	1.86	77	1.32	2.63

5.6g Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	35000	0.05	55000	0.05	2.07	76	1.44	2.99

5.6h Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	35000	0.07	55000	0.07	1.86	77	1.32	2.63

5.6i Southern Georgian Bay Hotspot Cluster Moderately to Very Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	7640.66
Generalized Chi-Square	1152.27
Gener. Chi-Square / DF	0.81

Cambridge Hotspot Cluster

5.7a Cambridge Hotspot Cluster Moderately to Very Premature Births Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
*MedInc*2	1623	73493.07	25519.59	75333.33	56571.43	88673.00	103688.00	0	145564.00
%HigherEd	1607	0.09	0.07	0.07	0.03	0.16	0.18	0	0.27

5.7b Cambridge Moderately to Very Premature Births Predictor Main Effects Odds Ratios Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc	44225	0.09	74225	0.088	1.34	83	1.03	1.72
%HigherEd	74225	0.13	74225	0.088	1.14	83	0.97	1.34
Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.								

Interaction Effects between Continuous Risk Factors

The interaction between two continuous variables requires a total of six GLIMMIX tables in order to show the odds ratios for three levels of each variable, low, mid- and high range. Two interaction effects are shown below, requiring 12 total tables.

5.7c Cambridge Hotspot Cluster Moderately to Very Premature Births Low-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	50000	0.14	50000	0.09	1.03	82	0.84	1.26

5.7d Cambridge Hotspot Cluster Moderately to Very Premature Births Mid-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	75000	0.14	75000	0.09	1.17	82	0.99	1.39

5.7e Cambridge Hotspot Cluster Moderately to Very Premature Births High-Range Continuous*Continuous Odds Ratio Estimates

Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	90000	0.14	90000	0.09	1.26	82	1.02	1.56

5.7f Cambridge Hotspot Cluster Moderately to Very Premature Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	60000	0.16	90000	0.16	1.34	83	1.03	1.724

5.7g Cambridge Hotspot Cluster Moderately to Very Premature Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	60000	0.03	90000	0.03	1.34	83	1.03	1.72

5.7h Cambridge Hotspot Cluster Moderately to Very Premature Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	60000	0.09	90000	0.09	1.44	82	1.10	1.89

5.7i Cambridge Hotspot Cluster *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	8683.18
Generalized Chi-Square	1484.68
Gener. Chi-Square / DF	0.93

Hamilton Hotspot Cluster

5.8a Hamilton Hotspot Cluster Moderately to Very Premature Births Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
%NoDip	2464	0.3	0.14	0.27	0.2	0.39	0.50	0.04	0.67
%Asian	2452	2.05	3.73	0	0	3.02	6.37	0	25.16

5.8b Hamilton Moderately to Very Premature Births Main Effects Odds Ratios Estimates												
Predictors	Reference Value				Assessment Value				Estimate	DF	95% Confidence Limits	
Smoked	indep		0.29	2.02	ref		0.29	2.02	1.78	108	1.23	2.59
%NoDip			0.69	2.02			0.29	2.02	0.76	113	0.42	1.38
%Asian			0.29	3.02			0.29	2.02	0.97	113	0.91	1.04
HlthProb		indep	0.29	2.02		ref	0.29	2.02	0.80	112	0.52	1.22
Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.												

5.8c Hamilton Moderately to Very Premature Births Mid-Range Binomial*Continuous Odds Ratio Estimates												
Predictor	Reference Value				Assessment Value				Estimate	DF	95% Confidence Limits	
	Smoked	*Hlth Prob*	*%No Dip*	*%Asian*	*Smoked*	*Hlth Prob*	*%No Dip*	*%Asian*				
Smoked%Asian*	indep		0.16	1.3	ref		0.16	1.3	1.82	108	1.24	2.66
Smoked%Asian*	indep		0.16	2.3	indep		0.16	1.3	0.84	1862	0.72	0.99
Smoked%Asian*	ref		0.16	2.3	ref		0.16	1.3	1.01	1862	0.94	1.08
HlthProb%NoDip*		indep	0.16	1.3		ref	0.16	1.3	1.24	112	0.73	2.12
HlthProb%NoDip*		indep	0.2	1.3		indep	0.16	1.3	0.85	1862	0.74	0.97
HlthProb%NoDip*		ref	0.2	1.3		ref	0.16	1.3	0.99	1862	0.93	1.07

5.8d Hamilton Moderately to Very Premature Births High-Range Binomial*Continuous Odds Ratio Estimates												
Predictor	Reference Value				Assessment Value				Estimate	DF	95% Confidence Limits	
	Smoked	*Hlth Prob*	*%No Dip*	*%Asian*	*Smoked*	*Hlth Prob*	*%No Dip*	*%Asian*				
Smoked%Asian*	indep		0.2	2	ref		0.2	2	1.60	108	1.01	2.41
Smoked%Asian*	indep		0.2	3.5	indep		0.2	2	0.78	1862	0.61	0.99
Smoked%Asian*	ref		0.2	3.5	ref		0.2	2	1.01	1862	0.91	1.12
HlthProb%NoDip*		indep	0.2	2		ref	0.2	2	1.05	112	0.66	1.68
HlthProb%NoDip*		indep	0.26	2		indep	0.2	2	0.80	1862	0.67	0.96
HlthProb%NoDip*		ref	0.26	2		ref	0.2	2	0.99	1862	0.90	1.1

5.8e Hamilton Hotspot Cluster *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	7640.66
Generalized Chi-Square	1152.27
Gener. Chi-Square / DF	0.81

North Ottawa Valley Hotspot Cluster

5.9a North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births Predictor Variable Distribution Characteristics

Risk Factor	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
MedInc	899	46747.67	14635.78	45882.35	34313.00	54222.22	60933.00	14905.66	112727.00
%HigherEd	899	0.02	0.03	0.01	0	0.02	0.04	0	0.14

5.9b North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births Main Effects Odds Ratio Estimates

Risk Factor	Reference Value			Assessment Value			Estimate	DF	95% Confidence Limits	
Smoked	indep	46944	0.02	ref	46944	0.02	0.45	25	0.21	0.97
MedInc		36944	0.02		46944	0.02	1.51	26	1.09	2.09
%HigherEd		46944	0.12		46944	0.02	4.08	26	0.8	20.89

Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.

5.9c North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births Low-Range Binomial*Continuous) Odds Ratio Estimates										
Predictor	Reference Value			Assessment Value			Estimate	DF	95% Confidence Limits	
	Smoked	*MedInc*	*%HigherEd*	*Smoked*	*MedInc*	*%HigherEd*				
MedInc		20000	0.005		35000	0.01	1.91	26	1.17	3.12
*Smoked*HigherEd*	indep	35000	0.005	ref	35000	0.01	0.59	25	0.27	1.32
Smoked%HigherEd*	indep	35000	0.01	indep	35000	0.01	0.78	767	0.52	1.16
Smoked%HigherEd*	ref	35000	0.01	ref	35000	0.005	1.099	767	1.013	1.19

5.9d North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births Mid-Range Binomial*Continuous Odds Ratio Estimates										
Predictor	Reference Value			Assessment Value			Estimate	DF	95% Confidence Limits	
	Smoked	*MedInc*	*%HigherEd*	*Smoked*	*MedInc*	*%HigherEd*				
MedInc		30000	0.015		45000	0.015	1.91	26	1.17	3.12
Smoked%HigherEd*	indep	45000	0.015	ref	45000	0.015	0.29	25	0.09	0.93
Smoked%HigherEd*	indep	45000	0.025	indep	45000	0.015	0.60	767	0.27	1.33
Smoked%HigherEd*	ref	45000	0.025	ref	45000	0.015	1.21	767	1.03	1.42

5.9e North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births High-Range Binomial*Continuous Odds Ratio Estimates										
Predictor	Reference Value			Assessment Value			Estimate	DF	95% Confidence Limits	
	Smoked	*MedInc*	*%HigherEd*	*Smoked*	*MedInc*	*%HigherEd*				
MedInc		40000	0.02		55000	0.02	1.91	26	1.17	3.12
Smoked%HigherEd*	indep	55000	0.02	ref	55000	0.02	0.21	25	0.05	0.92
Smoked%HigherEd*	indep	55000	0.03	indep	55000	0.02	0.60	767	0.27	1.33
Smoked%HigherEd*	ref	55000	0.03	ref	55000	0.02	1.21	767	1.03	1.42

5.9f North Ottawa Valley Hotspot Cluster Moderately to Very Premature Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	4645.99
Generalized Chi-Square	705.89
Gener. Chi-Square / DF	0.89

Appendix 6: Small for Gestational Age Births Model Odds Ratio Estimates

Full Province Regression Models

- 6.1 Predictor Variable Distribution Characteristics
- 6.2 Main Effects
- 6.3 Continuous*Binomial Regression Tables
- 6.4 Continuous*Continuous Regression Tables
- 6.5 Binomial*Binomial Risk Factor Regression Tables
- 6.6 Goodness of Fit Statistics

Hotspot Cluster Models

- 6.7 Eastern Toronto
- 6.8 London
- 6.9 Northwest Toronto

Full Province Model

6.1 Full Province Small for Gestational Age Births Predictor Variable Distribution Characteristics									
Outcome	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
%NoDip	619622	0.18	0.12	0.17	0.09	0.25	0.35	0	1.00
MedInc	621750	65959.74	27143.57	64275.00	45840.00	83658.00	98494.00	0	551293.00
%HigherEd	619622	0.08	0.07	0.06	0.03	0.18	0.18	0	1.00
%Asian	619347	5.8	9.77	1.86	0	7.07	17.22	0	80.46

6.2 Full Province *SGA* Births Main Effects Odds Ratios Estimates

Predictor	Reference Value									Assessment Value									Estimate	DF	95% Confidence Limits	
	Teenage	*Oldage*	*Urban*	*Smoked*	*HlthProb*	*MedInc*	*%NoDip*	*%HiEd*	*%Asian*	*Teenage*	*Oldage*	*Urban*	*Smoked*	*HlthProb*	*MedInc*	*%NoDip*	*%HiEd*	*%Asian*				
Teenage	Indep A					65808	0.18	0.08	5.17	ref					65808	0.18	0.08	5.17	1.18	6862	1.12	1.238
Olderage		indep				65808	0.18	0.08	5.17		ref				65808	0.18	0.08	5.17	0.91	14340	0.89	0.94
MedInc						55808	0.18	0.08	5.17						65808	0.18	0.08	5.17	1.02	15733	1.01	1.02
%NoDip						65808	0.18	0.08	5.17						65808	0.18	0.08	5.17	1.05	15733	1.04	1.06
%HigherEd						65808	0.18	0.08	5.17						65808	0.18	0.08	5.17	0.97	15733	0.96	0.99
%Asian						65808	0.18	0.08	5.17						65808	0.18	0.08	5.17	0.97	15733	0.97	0.97
Urban			indep			65808	0.18	0.08	5.17			ref			65808	0.18	0.08	5.17	1.43	15733	1.36	1.5
Smoked				indep		65808	0.18	0.08	5.17				ref		65808	0.18	0.08	5.17	1.75	11502	1.7	1.80
HlthProb					indep	65808	0.18	0.08	5.17					ref	65808	0.18	0.08	5.17	0.98	12781	0.95	1.01

Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value.

SGA Continuous*Binomial Regression Tables

Due to a SAS application "bug" the following Continuous*Binomial Odds Ratio Tables were required to be run separately; the pieces across the following tables complete a full table (as seen in above appendixes). The bug discovered and reported limited the GLIMMIX application's capability to run same variables in more than one interaction at a time. All adjustments were made but are not displayed here in order to save space; cell values have been blanked where they are not applicable to the interaction being displayed. See the Main Effects table for Reference and Assessment values for cells that have been cleared.

6.3a Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates

Predictor	Reference Value										Assessment Value						Esti mate	DF	95% Confidence Limits	
Smoked%NoDip*	indep			0.1							ref				0.2		2.22	11501	2.07	2.38
Smoked%NoDip*	indep			0.2							indep				0.2		0.99	414E3	0.97	1.02
Smoked%NoDip*	ref			0.2							ref				0.2		1.04	414E3	1.03	1.06

6.3b Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates

Predictor	Reference Value									Assessment Value							Estimate	DF	95% Confidence Limits	
*Smoked*MedInc*	indep		35,000							ref		35,000					2.18	11501	2.04	2.34
*Smoked*MedInc*	indep		25,000							indep		35,000					1.04	414E3	1.02	1.05
*Smoked*MedInc*	ref		25,000							ref		35,000					1.03	414E3	1.02	1.04

6.3c Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value									Assessment Value						Estimate	DF	95% Confidence Limits	
Smoked%Asian*	indep					2				ref					2	1.78	11502	1.72	1.83
Smoked%Asian*	indep					4				indep					2	1.00	414E3	0.99	1.01
Smoked%Asian*	ref					4				ref					2	1.03	414E3	1.03	1.03

6.3d Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates																			
Predictor	Reference Value								Assessment Value							Estimate	DF	95% Confidence Limits	
Urban%NoDip*	indep			35	0.1	0.03	2			ref			35	0.1	0.03	2	1.26	15731	1.18	1.35
Urban%NoDip*	indep			35	0.2	0.03	2			indep			35	0.1	0.03	2	1.06	15731	1.05	1.07
Urban%NoDip*	ref			35	0.2	0.03	2			ref			35	0.1	0.03	2	0.98	15731	0.95	1.01

6.3e Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value									Assessment Value								Estimate	DF	95% Confidence Limits	
*%HigherEd*Olderage*	indep						0.03	2		ref						0.03	2	1.08	14340	1.03	1.13
*%HigherEd*Olderage*	indep						0.08	2		indep						0.03	2	0.97	414E3	0.97	1.00
*%HigherEd*Olderage*	ref						0.08	2		ref						0.03	2	1.019	414E3	1.01	1.03

6.3f Full Province *SGA* Births Low-Range Binomial*Continuous Odds Ratio Estimates																	
Predictor	Reference Value									Assessment Value					Estimate	DF	95% Confidence Limits	
*MedInc*HlthPrb*	indep	35								ref	35				0.95	12781	0.91	0.99
*MedInc*HlthPrb*	indep	25								indep	35				1.008	414E3	0.99	1.02
*MedInc*HlthPrb*	ref	25								ref	35				1.021	414E3	1.015	1.026

6.3g Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value										Assessment Value						Estimate	DF	95% Confidence Limits	
Smoked%NoDip*	indep			0.2							ref			0.2			1.97	11501	1.88	2.07
Smoked %NoDip*	indep			0.3							indep			0.2			1.02	414E3	0.99	1.04
Smoked %NoDip*	ref			0.3							ref			0.2			1.07	414E3	1.06	1.08

6.3h Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value										Assessment Value						Estimate	DF	95% Confidence Limits	
*Smoked*MedInc*	indep			65							ref			65			1.97	11501	1.88	2.07
*Smoked*MedInc*	indep			55							indep			65			1.02	414E3	0.99	1.04
*Smoked*MedInc*	ref			55							ref			65			1.07	414E3	1.06	1.08

6.3i Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value									Assessment Value							Estimate	DF	95% Confidence Limits	
Smoked%Asian*	indep					3.8				ref					3.8		1.73	11502	1.68	1.78
Smoked%Asian*	indep					5.8				indep					3.8		1.00	414E3	0.99	1.01
Smoked%Asian*	ref					5.8				ref					3.8		1.03	414E3	1.03	1.03

6.3j Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value									Assessment Value							Estimate	DF	95% Confidence Limits	
Urban%NoDip*	indep				0.2					ref				0.2			1.37	15731	1.3	1.45
Urban%NoDip*	indep				0.3					indep				0.2			1.06	15731	1.05	1.07
Urban%NoDip*	ref				0.3					ref				0.2			0.98	15731	0.95	1.01

6.3k Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value								Assessment Value								Estimate	DF	95% Confidence Limits	
*%HigherEd*Olderage*	indep						0.075			ref						0.08		1.03	14340	0.99	1.08
*%HigherEd*Olderage*	indep						0.125			indep						0.08		0.99	414E3	0.97	1.01
*%HigherEd*Olderage*	ref						0.125			ref						0.08		1.02	414E3	1.01	1.03

6.3l Full Province *SGA* Births Mid-Range Binomial*Continuous Odds Ratio Estimates												
Predictor	Reference Value					Assessment Value					Estimate	DF	95% Confidence Limits	
*MedInc*HlthProb*	indep	65				ref	65				0.98	12781	0.95	1.02
*MedInc*HlthProb*	indep	55				indep	65				1.01	414E3	0.99	1.02
*MedInc*HlthProb*	ref	55				ref	65				1.021	414E3	1.02	1.03

6.3m Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates																		
Predictor	Reference Value							Assessment Value						Estimate	DF	95% Confidence Limits	
Smoked%NoDip*	indep			0.25				ref			0.25			1.80	11501	1.676	1.93
Smoked%NoDip*	indep			0.35				indep			0.25			1.03	414E3	1.01	1.06
Smoked%NoDip*	ref			0.35				ref			0.25			1.08	414E3	1.01	1.1

6.3n Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates																	
Predictor	Reference Value						Assessment Value						Estimate	DF	95% Confidence Limits	
*Smoked*MedInc*	indep		80				ref		80				1.833	11501	1.71	1.96
*Smoked*MedInc*	indep		70				indep		80				1.022	414E	1.01	1.03
*Smoked*MedInc*	ref		70				ref		80				1.010	414E	1.00	1.01

6.3o Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates																				
Predictor	Reference Value									Assessment Value						Estimate	DF	95% Confidence Limits	
Smoked%Asian*	indep					7				ref					7	1.65	11502	1.59	1.72
Smoked%Asian*	indep					9				indep					7	1.00	414E3	0.99	1.01
Smoked%Asian*	ref					9				ref					7	1.03	414E3	1.03	1.03

6.3p Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates																			
Predictor	Reference Value									Assessment Value						Estimate	DF	95% Confidence Limits	
Urban%NoDip*	indep				0.25					ref				0.25			1.43	15731	1.36	1.50
Urban%NoDip*	indep				0.35					indep				0.25			1.06	15731	1.05	1.07
Urban%NoDip*	ref				0.35					ref				0.25			0.98	15731	0.95	1.01

6.3q Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates																			
Predictor	Reference Value									Assessment Value							Estimate	DF	95% Confidence Limits	
*%HigherEd*Olderage*	indep						0.11			ref						0.11		0.90	14340	0.88	0.93
*%HigherEd*Olderage*	indep						0.16			indep						0.11		0.99	414E3	0.97	1.00
*%HigherEd*Olderage*	ref						0.16			ref						0.11		1.03	414E3	1.02	1.04

6.3r Full Province *SGA* Births High-Range Binomial*Continuous Odds Ratio Estimates													
Predictor	Reference Value					Assessment Value					Estimate	DF	95% Confidence Limits	
*MedInc*HlthProb*	indep	80				ref	80				0.99	429E3	0.95	1.03
*MedInc*HlthProb*	indep	70				indep	80				1.01	429E3	0.99	1.02
*MedInc*HlthProb*	ref	70				ref	80				1.02	429E3	1.02	1.03

Continuous*Continuous Risk Factors

The interaction between two continuous variables requires a total of six GLIMMIX tables in order to display the odds ratios for three levels of each variable, high, mid- and low range. Two interaction effects are shown below, requiring 12 total tables. While only the risk factors of interest are shown, all other factors are held constant.

6.4a Full Province *SGA* Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
%HigherEd MedInc*	40	0.12	40	0.07	0.98	414E3	0.96	0.99

6.4b Full Province *SGA* Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
%HigherEd MedInc*	65	0.12	65	0.07	0.99	414E3	0.97	1.00

6.4c Full Province *SGA* Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
%HigherEd MedInc*	80	0.12	80	0.07	1.00	414E3	0.98	1.02

6.4d Full Province *SGA* Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	45	0.0	65	0.0	1.05	15731	1.04	1.07

6.4e Full Province *SGA* Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	45	0.03	65	0.03	1.05	15731	1.04	1.06

6.4f Full Province *SGA* Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%HigherEd*	45	0.17	65	0.17	1.02	15731	1.01	1.04

6.4g Full Province *SGA* Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
*%NoDip *MedInc*	40	.27	40	0.07	1.03	15731	1.02	1.05

6.4h Full Province *SGA* Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
*%NoDip *MedInc*	65	.27	65	0.17	1.06	15731	1.05	1.07

6.4i Full Province *SGA* Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
*%NoDip *MedInc*	100	.27	65	0.17	1.1	15731	1.07	1.12

6.4j Full Province *SGA* Births Low-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%NoDip*	45	0.04	65	0.4	1.08	15731	1.06	1.1

6.4k Full Province *SGA* Births Mid-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%NoDip*	45	0.16	65	0.16	1.05	15731	1.04	1.06

6.4l Full Province *SGA* Births High-Range Continuous*Continuous Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
MedInc%NoDip*	45	0.35	65	0.35	1.01	15731	0.99	1.03

Binomial*Binomial Regression Tables

6.5a Full Province *SGA* Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Urban*	*Smoked*	*_Urban*	*_Smoked*	Estimate	95% Confidence Limits	
*Urban*Smoked*	indep	indep	indep	ref	1.86	1.77	1.96
*Urban*Smoked*	indep	indep	ref	indep	1.06	0.97	1.15
*Urban*Smoked*	indep	ref	ref	ref	1.52	1.43	1.62
*Urban*Smoked*	ref	indep	ref	ref	2.68	2.43	2.95

6.5b Full Province *SGA* Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Smoked*	*HlthProb*	*_Smoked*	*_HlthProb*	Estimate	95% Confidence Limits	
*Smoked*HlthProb*	indep	indep	indep	ref	0.95	0.87	1.03
*Smoked*HlthProb*	indep	indep	ref	indep	2.34	2.15	2.55
*Smoked*HlthProb*	indep	ref	ref	ref	2.13	2.00	2.26
*Smoked*HlthProb*	ref	indep	ref	ref	0.86	0.8	0.93

6.5c Full Province *SGA* Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
Predictor	*Olderage*	*Smoked*	*_Olderage*	*_Smoked*	Estimate	95% Confidence Limits	
*Olderage*Smoked*	indep	indep	indep	ref	2.52	2.300	2.76
*Olderage*Smoked*	indep	indep	ref	indep	1.15	1.062	1.24
*Olderage*Smoked*	indep	ref	ref	ref	0.90	0.875	0.93
*Olderage*Smoked*	ref	indep	ref	ref	1.98	1.867	2.09

6.5d Full Province *SGA* Births Binomial*Binomial Odds Ratio Estimates							
	Reference Value		Assessment Value				
	Teenage	*HlthProb*	*_Teenage*	*_HlthProb*	Estimate	95% Confidence Limits	
*Teenage*HlthProb*	indep	indep	indep	ref	0.81	0.70	0.93
*Teenage*HlthProb*	indep	indep	ref	indep	0.98	0.85	1.12
*Teenage*HlthProb*	indep	ref	ref	ref	1.23	1.16	13
*Teenage*HlthProb*	ref	indep	ref	ref	1.01	0.98	1.05

Goodness of Fit Statistics

6.6 Full-Province *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	2300640
Generalized Chi-Square	410304.2
Gener. Chi-Square / DF	0.96

Hotspot Cluster Models

Eastern Toronto

6.7a Eastern Toronto Hotspot Cluster *SGA* Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
Teenage	10732	0.04	0.19	0	0	0	0	0	1.00
Olderage	10732	0.21	0.41	0	0	0	1.00	0	1.00

7.7b East Toronto Hotspot Cluster *SGA* Births Odds Ratio Estimates								
Predictors	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
Olderage		indep		ref	0.81	199	0.70	0.93
Teenage	indep		ref		0.72	131	0.52	0.98

7.7c East Toronto Hotspot Cluster *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	50503.74
Generalized Chi-Square	10212.39
Gener. Chi-Square / DF	0.98

London

7.8a London Hotspot Cluster *SGA* Predictor Variable Distribution Characteristics								
N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
1318	0.29	0.45	0	0	1.00	1.00	0	1.00

7.8b London Hotspot Cluster *SGA* Births Odds Ratio Estimates						
Predictor	Reference Value	Assessment Value	Estimate	DF	95% Confidence Limits	
Smoked	indep	ref	2.025	48	1.41	2.90

7.8c London Hotspot Cluster *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	6513.64
Generalized Chi-Square	1264.00
Gener. Chi-Square / DF	1.00

Northwest Toronto

7.9a Northwest Toronto Hotspot Cluster *SGA* Predictor Variable Distribution Characteristics									
Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
Teenage	5002	0.033	0.18	0	0	0	0	0	1.00
Smoked	3575	0.034	0.18	0	0	0	0	0	1.00

7.9b Northwest Toronto Hotspot Cluster *SGA* Births Odds Ratio Estimates								
Predictor	Reference Value		Assessment Value		Estimate	DF	95% Confidence Limits	
Smoked	indep		ref		1.61	45	1.00	2.58
Teenage		indep		ref	1.68	45	1.04	2.69

7.9c Northwest Toronto Hotspot Cluster *SGA* Births Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	17077.34
Generalized Chi-Square	3368.16
Gener. Chi-Square / DF	0.97

Appendix 7: Stillbirth Model Odds Ratio Estimates

Full Province Regression Models

7.1 Predictor Variable Distribution Characteristics
7.2 Main Effects
7.3 Non-modified and Continuous*Binomial Regression Table
7.4 Goodness of Fit Statistics

7.1 Full Province Stillbirth Predictor Variable Distribution Characteristics

Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
MedInc	621750	65959.74	27143.57	64275.00	45840.00	83658.00	98494.00	0	551293.00
%HigherEd	619622	0.08	0.07	0.06	0.03	0.18	0.18	0	1.00
%NoDip	619622	0.18	0.12	0.16	0.09	0.25	0.35	0	1.00

7.2 Full Province Stillbirths Main Effects Odds Ratios Estimates														
Risk Factor	Reference Value					Assessment Value					Estimate	DF	95% Confidence Limits	
	Older Age	*Smok Ed*	*Med Inc*	*%High erEd*	*%No Dip*	*Older Age*	*Smok Ed*	*Med Inc*	*%High erEd*	*%No Dip*				
Olderage	Indep		66226	0.08	0.18	ref		66226	0.08	0.18	1.42	14812	1.31	1.55
MedInc			56226	0.08	0.18			66226	0.08	0.18	1.04	15755	1.02	1.06
%HigherEd			66226	0.02	0.18			66226	0.08	0.18	1.09	15755	1.02	1.16
%NoDip			66226	0.08	0.08			66226	0.08	0.18	0.96	15755	0.93	0.99
Smoked		indep	66226	0.08	0.18		ref	66226	0.08	0.18	1.36	12211	1.23	1.51
Effects of continuous variables are assessed as offsets from the mean. The AT suboption modifies the reference value (347).														

7.3a Full Province Stillbirths Low-Range Odds Ratio Estimates													
Olderage	*Smoked*	*MedInc2*	*%HigherEd*	*%NoDip*	*_Olderage*	*_Smoked*	*_MedInc2*	*_%HigherEd*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
indep		65000	0	0.3	ref		65000	0	0.3	1.43	14812	1.31	1.55
		55000	0	0.3			65000	0	0.3	1.04	15755	1.02	1.06
		65000	0	0.4			65000	0	0.3	1.04	15755	1.00	1.07
	indep	65000	0	0.3		ref	65000	0	0.3	1.24	12211	1.08	1.42

7.3a Full Province Stillbirths Low-Range Odds Ratio Estimates													
Olderage	*Smoked*	*MedInc2*	*%HigherEd*	*%NoDip*	*_Olderage*	*_Smoked*	*_MedInc2*	*_%HigherEd*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
	indep	65000	0.02	0.3		indep	65000	0	0.3	1.02	531E3	0.98	1.05
	ref	65000	0.02	0.3		ref	65000	0	0.3	0.98	531E3	0.97	0.99

7.3b Full Province Stillbirths Mid-Range Odds Ratio Estimates													
Olderage	*Smoked*	*MedInc2*	*%HigherEd*	*%NoDip*	*_Olderage*	*_Smoked*	*_MedInc2*	*_%HigherEd*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
indep		65000	0.075	0.3	ref		65000	0.075	0.3	1.43	14812	1.31	1.55
		55000	0.075	0.3			65000	0.075	0.3	1.04	15755	1.02	1.06
		65000	0.075	0.4			65000	0.075	0.3	1.04	15755	1.00	1.07
	indep	65000	0.075	0.3		ref	65000	0.075	0.3	1.42	12211	1.28	1.58
	indep	65000	0.095	0.3		indep	65000	0.075	0.3	1.02	531E3	0.98	1.05
	ref	65000	0.095	0.3		ref	65000	0.075	0.3	0.98	531E3	0.97	0.99

7.3c Full Province Stillbirths High-Range Odds Ratio Estimates													
Olderage	*Smoked*	*MedInc2*	*%HigherEd*	*%NoDip*	*_Olderage*	*_Smoked*	*_MedInc2*	*_%HigherEd*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
indep		65000	0.11	0.3	ref		65000	0.11	0.3	1.43	14812	1.31	1.55
		55000	0.11	0.3			65000	0.11	0.3	1.04	15755	1.02	1.06
		65000	0.11	0.4			65000	0.11	0.3	1.04	15755	1.00	1.07
	indep	65000	0.11	0.3		ref	65000	0.11	0.3	1.51	12211	1.32	1.74
	indep	65000	0.13	0.3		indep	65000	0.11	0.3	1.02	531E3	0.98	1.05
	ref	65000	0.13	0.3		ref	65000	0.11	0.3	0.98	531E3	0.97	0.99

7.3d Full Province Stillbirths Regression Model Goodness of Fit Statistics	
-2 Res Log Pseudo-Likelihood	4354831
Generalized Chi-Square	458234.5
Gener. Chi-Square / DF	0.84

Appendix 8: *MedInc* Confounding with %NoDip and other variables

Stillbirth model check for confounding of *MedInc*. *ModVP* and *SGA* models were too complex (i.e. *MedInc* interacts with too many variables) to check for confounding. In *LateP* it was not significant as a fixed effect and therefore confounding is rejected.

Stillbirth*: odds ratio estimates with *MedInc													
Olderage	*Smoked*	*MedInc2*	*%HigherEd*	*%NoDip*	*_Olderage*	*_Smoked*	*_MedInc2*	*_%HigherEd*	*_%NoDip*	Estimate	DF	95% Confidence Limits	
indep		65000	0.075	0.3	ref		65000	0.075	0.3	1.43	14812	1.31	1.55
		55000	0.075	0.3			65000	0.075	0.3	1.04	15755	1.02	1.06
		65000	0.075	0.4			65000	0.075	0.3	1.04	15755	1.00	1.07
	indep	65000	0.075	0.3		ref	65000	0.075	0.3	1.42	12211	1.28	1.58
	indep	65000	0.095	0.3		indep	65000	0.075	0.3	1.02	531E3	0.98	1.05
	ref	65000	0.095	0.3		ref	65000	0.075	0.3	0.98	531E3	0.98	0.99

Appendix 9: Comparison of Cambridge and South Georgian Bay *MedInc*/*%HigherEd* Characteristics

Variable	N	Mean	Std Dev	Median	25th Pctl	75th Pctl	90th Pctl	Minimum	Maximum
Cambridge									
MedInc	1623	73493.07	25519.59	75333.33	56571.43	88673.00	103688.00	0	145564.00
%HigherEd	1607	0.09	0.067	0.07	0.022	0.157	0.182	0	0.267
North Georgian Bay									
MedInc	1434	56459.20	19446.85	50910.00	42857.14	67196.00	88849.00	18407.00	99912.00
%HigherEd	1434	0.05	0.037	0.045	0.029	0.064	0.105	0	0.16

Appendix 10: Ontario birth data submitted to BORN Database 2005-9

BORN Represented Births as a Proportion of Total Ontario Hospital Births

Source	2004-5	2005-6	2006-7	2007-8	2009-10	Grand total
BORN	113,220	120,803	125,724	136,980	139,278	636,005
DAD[31]	137,996	139,159	141,173	144,240	142,896	705,464
% captured by BORN	0.82	0.87	0.89	0.95	0.97	0.90

BORN Ontario (2011). Perinatal Health Report.

[31] Discharge Abstract Database (DAD): captures administrative, clinical and demographic information on hospital discharges (13).

Appendix 11: Estimates of Coefficient and Associated Standard Error

In these tables the cells containing the "indep" term identify the predictor(s) of interest. For each predictor, there is a coefficient estimate that indicates the effect of each on the log odds, the standard error of that estimate and the hypothesis test of the null being the coefficient equal to zero.

11.1 Full Province Late Premature Births: Estimates of Coefficient and Associated Standard Error										
Effect	***Teenage***	***HlthProb***	***Olderage***	***Urban***	***Smoked***	**Estimate**	**Standard Error**	**DF**	**t Value**	**Pr > |t|**
Intercept						-2.60	0.09	15,734	-27.01	<.01
HlthProb		indep				-0.08	0.09	12,871	-0.82	0.42
Teenage	indep					0.24	0.09	6,894	2.54	0.01
Olderage			indep			-0.15	0.03	14,416	-5.39	<.01
Urban				indep		-0.34	0.12	15,734	-2.91	0.01
Smoked					indep	-0.19	0.02	11,578	-9.06	<.01
%NoDip						0.2	0.12	15,734	1.65	0.09
%Asian						-0.01	0.01	15,734	-3.13	0.01
Teenage Urban*	indep			indep		0.37	0.12	6,894	3.13	0.01
%Asian Urban*				indep		0.09	0.04	15,734	2.39	0.02
%NoDip Olderage*			indep			-0.28	0.13	431,E3	-2.11	0.04
Teenage HlthProb*	indep	indep				-0.25	0.1	1,178	-2.44	0.02

11.2 Full Province Moderate to Very Premature Births: Estimates of Coefficient and Associated Standard Error										
Effect	***Olderage***	***Smoked***	***HlthProb***	***Teenage***	***Urban***	**Estimate**	**Standard Error**	**DF**	**t Value**	**Pr > |t|**
Intercept						-3.27	0.05	15,733	-64.25	<.01
Olderage	indep					0.22	0.03	14,416	6.73	<.01
Smoked		indep				0.32	0.08	11,577	3.83	0.01
HlthProb			indep			0.25	0.02	12,871	10.0	<.01
%Asian						-0.01	0.01	15,733	-4.33	<.01
MedInc						-0.01	0.01	15,733	-2.54	0.01
%NoDip						-0.05	0.09	15,733	-0.56	0.58
%HigherEd						-0.37	0.14	15,733	-2.56	0.01
Teenage				indep		0.13	0.06	6,895	2.17	0.03
Urban					indep	-0.02	0.04	15,733	-0.64	0.52
*%Asian*Teenage*				indep		0.01	0.01	431E3	2.11	0.04
*HlthProb*Teenage*			indep	indep		-0.35	0.12	1,178	-2.83	0.01
*Smoked*Urban*		indep			indep	0.15	0.07	11,577	2.24	0.02
*Smoked*Teenage*		indep		indep		-0.21	0.09	1,805	-2.41	0.02
*MedInc*Smoked*		indep				-0.01	0.01	431,E3	-2.28	0.02
*Smoked*HlthProb*		indep	indep			-0.14	0.06	4,149	-2.57	0.01
*%NoDip*Olderage*	indep					0.37	0.15	431,E3	2.45	0.01

11.3 Full Province SGA Births: Estimates of Coefficient and Associated Standard Error

Effect	*Teenage*	*Olderage*	*Urban*	*Smoked*	*HlthProb*	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept						-2.84	0.05	15,731	-55.08	<.01
Teenage	indep					0.04	0.07	6,862	0.53	0.6
Olderage		indep				0.03	0.02	14,340	1.38	0.17
MedInc						-0.01	0.01	15,731	-6.64	<.01
%NoDip						0.12	0.14	15,731	0.90	0.37
%HigherEd						-0.06	0.23	15,731	-0.27	0.78
Urban			indep			0.47	0.03	15,731	15.48	<.01
Smoked				indep		1.1	0.07	11,501	15.11	<.01
HlthProb					indep	-0.08	0.04	12,781	-1.86	0.06
%Asian						0.017	0.01	15,731	22.83	<.01
*%NoDip*Smoked*				indep		-0.46	0.12	414,E3	-3.79	0.01
*MedInc*Smoked*				indep		-0.002	0.01	414,E3	-2.27	0.02
*Urban*Smoked*			indep	indep		-0.34	0.05	11,501	-7.35	<.01
*%Asian*Smoked*				indep		-0.01	0.01	414,E3	-4.96	<.01
*%Asian*Olderage*		indep				-0.01	0.01	414,E3	-5.52	<.01
MedInc%NoDip*						0.01	0.01	15,731	3.92	<.01
MedInc%HigherEd*						0.01	0.01	15,731	2.81	0.01

11.3 Full Province SGA Births: Estimates of Coefficient and Associated Standard Error										
Effect	***Teenage***	***Olderage***	***Urban***	***Smoked***	***HlthProb***	**Estimate**	**Standard Error**	**DF**	**t Value**	**Pr > |t|**
*MedInc*Teenage*	indep					0.01	0.01	414,E3	2.53	0.011
*%HigherEd*Olderage*		indep				-0.77	0.18	414,E3	-4.27	<.01
*Teenage*HlthProb*	indep				indep	-0.18	0.08	1,165	-2.46	0.01
*Smoked*HlthProb*				indep	indep	0.09	0.038	4,075	2.48	0.01
*Olderage*Smoked*		indep		indep		0.2	0.04	3,071	5.26	<.01
*%NoDip*Urban*			indep			0.77	0.17	15,731	4.59	<.01

11.4 Full Province Stillbirths: Estimates of Coefficient and Associated Standard Error

Effect	*Olderage*	*Smoked*	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept			-5.11	0.08	15,755	-63.75	<.01
Olderage	indep		0.36	0.04	14,812	8.17	<.01
MedInc2			-4.02E-6	0	15,755	-7.2	<.01
Smoked		indep	0.22	0.07	12,211	3.06	0.01
%HigherEd			-1.04	0.33	15,755	-0.19	0.76
%NoDip			0.37	0.17	15,755	2.19	0.03
*%HigherEd*Smoked*		indep	1.82	0.84	531,E3	2.15	0.03

Appendix 12: Summary of BORN Ontario (Niday) Quality Assurance Methods

BORN Ontario carries out a quality assurance audit every five years or less. The *Data Quality Management Framework* developed by the Ontario Ministry of Health and Long Term Care Health Results Team for Information Management (HRT-IM) is used to guide their audit. The main objectives of the audit were to evaluate data quality (timeliness, validity, reliability and usability) as well as the process of data collection and entry. Two methods were used to address these objectives:

- re-abstraction of information from patient records and
- surveys of stakeholders (hospitals, public health units, decision makers and other database users).

Re-abstraction of information from the patient record was carried out to assess concordance between the data in the Niday database and the charts for the mother and infant. This allowed for determination of the validity (accuracy and completeness) of the data. The patient chart was found to be the only source of information and multiple sources, such as patient, hospital staff, other documents, may have been used in the original data entry.

A representative sample of Ontario hospitals was taken from the five provincial regions. Random samples of 100 maternal chart numbers (and matched baby cases) were generated for each hospital site from existing cases that had been entered into the Niday database. A subset of 33 of the 90 Niday variables was chosen for re-abstraction. Criteria for selection were: that the variable was a mandatory reporting variable, that the variable was non-mandatory with <10% missing data (variables with greater than 10% missing were not released for analysis) and that it addressed a practice issue of interest.

The random samples of charts for each hospital were obtained from the records department of each hospital. Data from each chart was reviewed and re-abstracted by trained, independent auditors using standardized data entry procedures. Postal codes and maternal age were taken from the admission record. Other variables were obtained from the labour record, delivery record, discharge summary, nurses' notes, post-partum screening and other records kept by each hospital.

Percent agreement, Cohen's kappa and Intra-class Correlation Coefficient (ICC) between the variables were used to compare hospital chart/record entries and data entered into the Niday database. Percent agreement was calculated for all variables. Adjustments were made to allow for these tools to be applied to categorical as well as continuous variables.

The survey of stakeholders relied on a self-completed questionnaire to gather information about the data collection and entry process used by the hospitals. Data entry personnel, data users and decision makers from hospitals, health units and other settings made up the population. Data Entry and Data User survey questionnaires were designed and tested for validity. A qualitative descriptive analysis was carried out to search for themes, patterns and to identify issues related to data collection, entry and use.

Results for the four key variables: timeliness, validity, reliability and usability, were reported. In 2008, the Niday Perinatal Database either fully or partially met expectations in all attributes assessed (167, 363).