The Significance of Local Area Ecologic and Individual-Level Risk Factor Interactions in Understanding Social Determinants of Health

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Abstract
The ability to link state/province-wide individual data with census aggregate data at local geographic areas allows for granular results and the identification of interactions between ecologic and individual risk factors as these form social determinants of health. Using adverse birth outcomes as a health problem that is only partially predicted from individual risk factors we used two-way interaction tests and contrasts within hierarchical models to explore the relationship between ecologic and individual risk factors. Far too often, subgroup analyses of risk factors have ignored the importance of broader effects that apply across the subgroups, and also the possible heterogeneity among the subgroups. Using data from Ontario, Canada, we show how local area census socio-economic data alter the effect that individual factors such as maternal age and smoking have on birth outcomes. A useful visual representation of interactions advancing on the valuable forest plot was developed. The results suggest that complex spatial and regression analyses of ecologic and individual variables will help inform community-based health intervention efforts.

Key Words: adverse birth outcomes, social determinants of health, hierarchical regression, spatial analysis, geographic hotspots, ecologic and individual risk factor interactions

1. Background

The percentage of premature births increased steadily in Canada and in Ontario from the early 1980s until 2007, from about 6.0% to 8.1%, 8.3% in Ontario[3] (1). Between 2009 and 2012 the proportions decreased slightly and remained stable at about 7.8% (2-4); 8.1% in Ontario (3). While the prevalence of known risk factors such as smoking and teenage births has declined (5,6), other factors increased: births to women over age 40 (7,8), obstetric interventions due to fetal distress (8), and mothers living in low socio-economic status environments (9). Percentages of small-for-gestational-age (SGA) singleton births decreased across Canada in the decade prior to 2009 to 8.1% (8.9% in Ontario), but increased to 8.7% or 9.0% in Ontario, by 2011-2012 (2).

Our research identified neighborhood hotspots that exhibited statistically elevated rates for three different adverse birth outcomes. There were 132 hotspots for preterm births at

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[3] Estimates are accurate to +/-15% of the estimate, 95% of the time. To improve readability, confidence intervals (CI) are included where this general rule does not hold.

35 – 36.9 weeks' gestation ('Prem≥35'); 152 for those <35 weeks ('Prem<35') and 257 for SGA. Hotspots for the different outcomes were found to be largely spatially exclusive. The finding of hotspots demonstrated patterns of adverse birth outcomes that suggest that higher order risk factors may likely play a role rather than a more random distribution we should have seen if these outcomes were attributable only to individual factors (14). We surmise that one or more risk factors concentrated in certain places to produce significantly higher percentage of a given outcome (11). The finding that the hotspots were geographically exclusive implies different etiologies for each adverse outcome; the combinations of risk factors and their interactions that are sufficient to create a hotspot for one adverse outcome are insufficient for another (10). It also suggests that models for the different hotspots should be able to differentiate sufficiently between the outcomes to explain this finding.

In this paper we explore the etiology for the two adverse outcomes: Prem<35 and Prem≥35. The goal is to explore the role and significance of interactions between ecologic and individual level risk factors in explaining health outcomes, in particular adverse birth outcomes.

2. Methods

Individual birth outcome and pre-existing maternal health problem and behavior observations were taken from the BORN Ontario neonatal database (12). Our study included observations for 621,750 births registered between April 1, 2004, and March 31, 2009, about 90% of births for that timeframe. Individual birth outcome and maternal characteristics were linked to 18,922 census dissemination areas (DAs) via the postal code for mother's residence. DAs are geographic areas established by Statistics Canada with a median population of 540 (inter-quartile range: 450–711); they are the smallest standard geographic area for which census data are disseminated (13). DA level factors were derived from Statistics Canada 2006 census data files and census boundary files.

Four individual level risk factors were created from the BORN database for each birth: maternal age over 35 years, labeled "Older" for the rest of this report; maternal age under 20 years, "Teenage," existing maternal health problems, "HlthProb," and whether
Four individual level risk factors were created from the BORN database for each birth: maternal age over 35 years, labeled "Older" for the rest of this report; maternal age the mother smoked at any time during pregnancy, "Smoked." Five known ecologic-level risk factors were created for each DA: median household income, "MedInc," percent of women over 25 with less than a high school degree, "%NoDip," percent with greater than a bachelor's degree, "%HigherEd," whether the DA was urban or rural in character, "Urban," and percentage of southern and eastern Asian immigrants,"%Asian." Boundary files served to spatially define census dissemination areas.

Confidentiality and statistical analysis requirements did not allow for individual hotspots to be analyzed; groupings of geographically close hotspots were created (Tables 1 and 2) for each adverse outcome. Groupings were based on close geographic proximity and sufficient adverse birth event counts (e.g. about 50 or more) to meet analysis and confidentiality requirements.

Hierarchical models for the full-province and for each of the different local area hotspot groups were created for Prem≥35 and Prem<35 births. Following identification of significant main effects, a modified forward-selection/backward-selection stepwise approach was used to create final models. The final full-province models retained predictors with a P<0.07; *P*<0.10 was used for local area models due to the relatively small *n*'s. This allowed for creation of parsimonious models and minimized risk of over-fitting. All two-way interactions were considered in order of main effects ranking, three way interactions were also considered although none were found to be significant. The resulting full-province and hotspot group models were contrasted. SAS Proc Glimmix (14) was used to carry out hierarchical regression analysis.

3. Results

Models for the same adverse birth outcomes differed markedly between local area 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. Significant interactions were found.

Figure 1 illustrates how the Prem≥35 hotspots are distributed across Ontario.

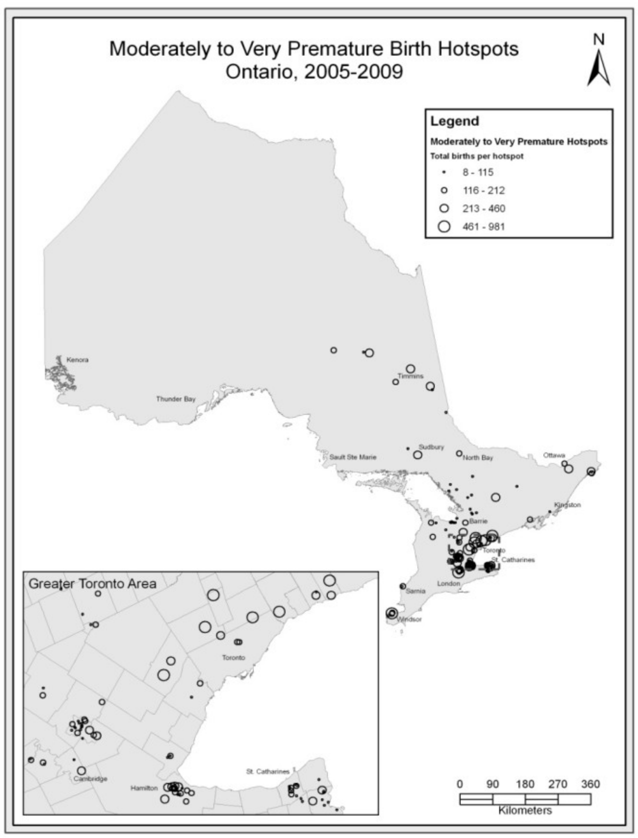

Figure 1: Prem≥35 hotspots in Ontario

Full-province models for Prem≥35 and Prem<35 births are presented in Tables 1 and 2 respectively. Interaction effects were significant for the large majority of predictors; only Smoked in Prem≥35 and %HigherEd in Prem<35 were found in the full-province model and MedInc in a local hotspot group model to have significant, non-modified relationships.

	Estimated Odds Ratio (OR)	***95% CI***
Smoked	1.21	1.15-1.2
Teenage*Urban	0.61	0.49-0.77
%Asian*Urban	1.19	1.027-1.38
Olderage*%NoDip	1.22	1.18-1.26
Teenage*HlthProb	0.65	0.53-0.80

Table 1: Full-Province Prem≥35 Final Model

	Estimated Odds Ratio (OR)	**95% CI**
%HigherEd	0.98	0.97-0.99
Teenage*%Asian	0.91	0.81-1.03
HlthProb*Teenage	0.78	0.62-0.98
Smoked*Urban	1.15	1.04-1.27
Smoked*Teenage	0.84	0.71-0.98
Smoked*MedInc	1.07	0.96-1.19
Smoked *HlthProb	0.94	0.82-1.08
Olderage*%NoDip	1.34	1.29-1.39

Table 2: Full-Province Prem<35 Final Model

Odds ratios presented are for the mid-range values of continuous variables. Because our analysis included continuous variable values, the OR estimate presented in these tables may appear insignificant at mid-range yet may be significantly risk increasing or decreasing when the full range of values is considered.

Tables 3 and 4 present regression models for each of the Prem≥35 and Prem<35 hotspot groups.

	Odds Ratio at mid-range	**95% CI**
Northern Toronto: 218 (6%) Prem≥35 births		
Olderage*%NoDip	1.43	1.06-1.94
Southwest of Ottawa: 73 (6%) Prem≥35 births		
Olderage*%HigherEd	1.28	0.64-2.54
St Catharines: 40 (13%) Prem≥35 births		
HlthProb*%NoDip	2.95	1.04-8.32

Table 3: Final Models for Three Prem≥35 Hotspot Groups

Prem<35 births	**Odds Ratio at mid-range**	**95% CI**
Cambridge: 131 (8.1% Prem<35 births)		
MedInc*%HigherEd	1.44	1.10-1.89
Hamilton: 192 (7.8% Prem<35 births)		
HlthProb*%NoDip	1.24	0.73-2.12
Smoked*%Asian	1.82	1.24-2.66
South Georgian Bay: 135 (9.5% Prem<35 births)		
MedInc*%HigherEd	1.18	0.82-1.7
North Ottawa Valley: 60 (6.7% Prem<35 births)		
MedInc	1.91	1.17-3.12
Smoked *%HigherEd	0.29	0.09-0.93

Table 4: Final Models for Four Prem<35 Hotspots Groups

These results present two groups of model comparisons for discussion: within like-outcomes and across the two different outcomes. Models for the full-province and for hotspot groups are contrasted.

Contrasting Prem≥35 full-province and hotspot group models (Tables 1 and 3) suggests that:

- while ecologic variables have a clear role in the full-province model, three of the five predictors include individual factors modified by ecologic ones; their presence in the hotspot group models is even stronger: every predictor is made up of an individual level factor modified by an ecologic level one. In the full-province model, both Smoked and Teenage*HlthProb reflect the clear role of individual level variables but in the hotspot group models the ecologic level factor low education (indicated by both %NoDip and %HigherEd[4]) is universal in its modification of the individual level factors Olderage and HlthProb.
- the majority of risk factors found significant at the province level were not significant at local levels: Smoked, Teenage, %Asian and Urban did not appear in the hotspot group models.

A comparison of the Prem<35 full-province and individual level models suggests that individual level risk factors had a stronger presence in the provincial level model than in the local hotspot group models. Three of the eight predictors in the full-province model were made up of interaction effects between individual factors; Smoked is present in four interaction effects. In hotspot group models ecologic-level factors are dominant; two of the models are made up solely of interaction effects between ecologic variables, in a third

[4] Both %NoDip and %HigherEd were found to act as indicators of education; increased education levels reduced the risk of an adverse outcome. %HigherEd was included as a risk increasing factor representing the percentage of women that delayed child bearing in order to complete schooling; in all but one model it represents a risk decreasing factor; as the percentage increases risk of an adverse outcome decreases. Only in the Cambridge hotspot group model was %HigherEd found positively associated with risk of an adverse outcome.

median income is an unmodified predictor and in the fourth individual level factors are modified by ecologic level ones.

A comparison of the full-province models for Prem≥35 and Prem<35 (Table 5) shows that:

- while Smoked has a strong presence in both, its effects in Prem<35 are inconsistent. While a more extensive discussion of the models is beyond the scope of this paper, a review of Table 2 shows that in interaction effects the risk of Smoked is moderated by both ecologic as well as individual level factors, that those effects are inconsistent and, in the case of Smoked*HlthProb, counter intuitive. It is interesting to note that while Smoked is commonly cited as having one of the strongest associations with premature birth, the interaction effect %NoDip*Olderage was found to have a greater estimated association with both Prem≥35 and Prem<35.
- two interaction predictors were shared.
- the model for Prem<35 was substantially more complex with eight predictors compared with five for ≥35. The greater complexity of the Prem<35 model suggests that those births may represent a more complex, heterogeneous array of outcomes than ≥35weeks.

Prem≥35	**Prem<35**
Smoked	*%HigherEd*
Olderage%NoDip*	*Olderage*%NoDip*
*%Asian*Urban*	*Smoked*MedInc*
*Teenage*Urban*	*Smoked*Urban*
*Teenage*HlthProb*	*HlthProb *Smoked*
	*Teenage*Smoked*
	*Teenage*HlthProb*
	Teenage%Asian*

Table 5: Contrasting Prem≥35 and Prem<35 full-province models

A comparison of the hotspot group models for the two adverse outcomes (Table 6) presents several similarities as well as striking differences:

- while education (represented by both %NoDip and %HigherEd) was a common thread across all hotspot group models for both outcomes, the risk factors that are modified by those education variables are different. Olderage and HlthProb are modified in the Prem≥35 models while MedInc, Smoked and HlthProb are modified in the Prem<35 models. St. Catharines and Hamilton share the predictor, HlthProb * %NoDip, possibly because they are geographically close. The Cambridge model is the only example of where increasing percentages of higher education, which is the percentage of women with a post-graduate degree, represents a risk increasing factor. Figure 2 using a forest plot is presents a good visualization of these findings.
- MedInc and Smoked each have strong interactive effect roles in the Prem<35 hotspot group models but neither appears in any of the Prem≥35 models.
- Olderage is present in two of the Prem≥35 models but does not appear in any of the Prem<35 models.

Prem≥35	Prem<35
Northern Toronto • Olderage*%NoDip **St Catharines** • HlthProb*%NoDip **SE of Ottawa** • Olderage*%HigherEd	**N Ottawa Valley** • MedInc • Smoked * %HigherEd **Cambridge** • MedInc* %HigherEd **Hamilton** • Smoked*%Asian • HlthProb * %NoDip **S. Georgian Bay** • MedInc*%HigherEd

Table 6: Contrasting Prem≥35 and Prem<35 hotspot group models

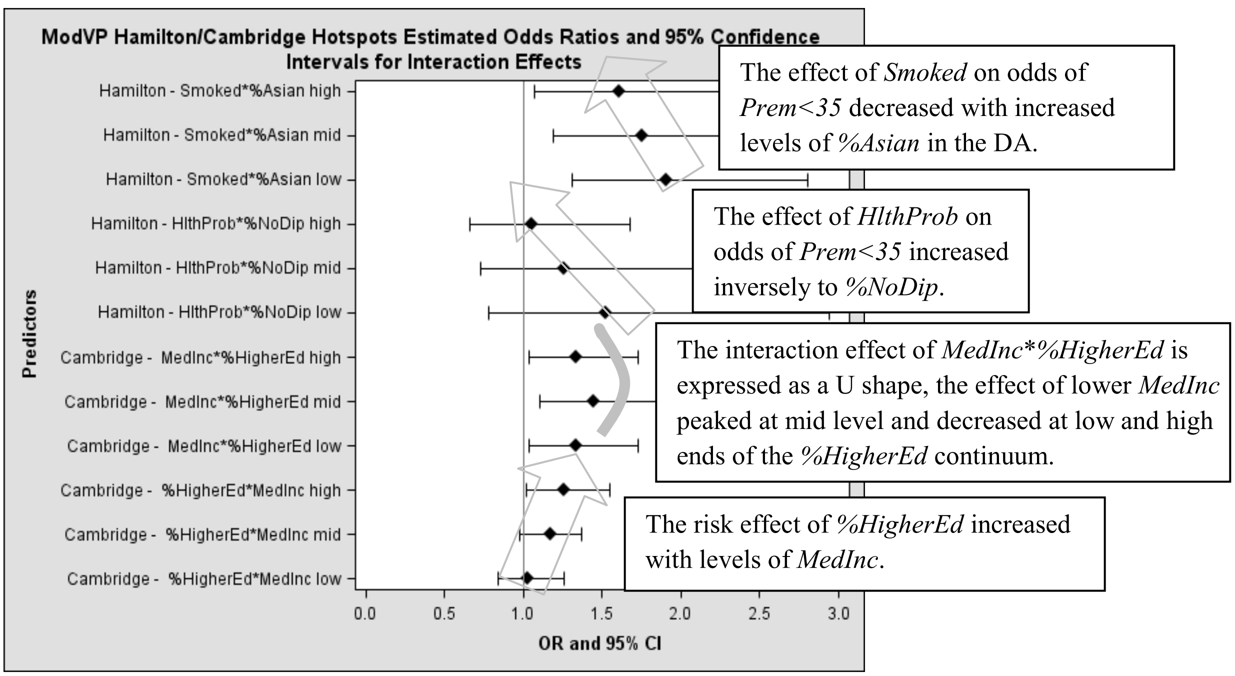

Figure 2: Hamilton and Cambridge Prem<35 Hotspot Interaction Effects

4. Discussion

The consistently stronger presence of ecologic level variables in hotspot group models supports the conjecture that higher order risk factors play a stronger role in hotspot areas than they do for the full province. While the smaller sample sizes represented by local hotspot groups likely account for some of the differences, the consistency of the risk factors patterns across the models reinforces this possible conclusion. This corroborates 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 (9,16,21-25).

The differences in the models for the two birth outcomes at both the full-province and hotspot group levels seem to suggest that different etiologies are at play. The hotspot group models clearly support this. The striking differences between models for both adverse outcomes at the different scales of analysis suggests that even these partial models are capable of differentiating between the two birth outcomes as well as between those for hotspots and for the full province.

The presence of education in interaction effects in each of the hotspot group models suggests that this ecologic level variable may serve to amplify the effects of a range of individual and ecologic level variables. This is supportive of the weathering hypothesis (275,276) which suggests that women living in high-deprivation areas develop accelerated aging that increases risk of preterm birth. Women with risk increasing individual characteristics such as Olderage and HlthProb and Smoked that live in low income and low education areas were shown to have significantly higher odds of an adverse outcome. The consistently strong risk-decreasing effect of *Teenage* in interactions with *HlthProb* and *Smoked* appears to further support the weathering hypothesis: when faced with a risk increasing factor, such as *Smoked* or *HlthProb*, teenage mothers are less likely to have a preterm birth outcome compared with older women. It should be noted that an estimated 98% of teenage mothers were 18 years of age or older in our study; an age by which most women are physically mature enough to deliver healthy babies (5,9).

The greater complexity of the Prem<35 compared with the Prem≥35 model suggests that Prem<35 may represent a more complex array of outcomes than Prem≥35; this supports previous research which has postulated that the different levels of prematurity have different etiologies and should be broken into more sub-facets (e.g. stages of gestational age) in order to be more parsimoniously and effectively modeled (15,16).

Differences in complexity between provincial and local area models may have been due at least in part to provincial models explaining a larger population spread over a much larger and diverse geographic area. Hotspot group models were striking for their simplicity, possibly because they were explaining more homogeneous subpopulations.

Local area models for Prem<35 outcomes were markedly different. While the finding of the importance of ecologic level risk factors was consistent with previous research (9,16-18) the character of the interaction effects found in the current study contradict many earlier findings.

This was an observational cross-sectional study that as such was subject to possible selection bias. The BORN Ontario Niday database represented about 90% of all births in Ontario during the 2004–2009 periods; small numbers may have led to over representation of hotspots in northern areas but this concern was not verified by identified hotspots. The number of risk factors included was limited to those available from the BORN database and the Statistics Canada 2006 census. While those included have been found to be significant in past research, a number that have also been found to be important were not included.

The strong role of ecologic-level risk factors in hotspot group models supports the suggestion that ecologic-level variables play an important role in explaining hotspot patterning. Individual-level variables explain individual outcomes but ecologic-level variables explain broader patterns. Ecologic level risk factors played an important role in understanding adverse birth outcomes in local group models. All individual level risk factors *Olderage*, *Smoked* and *HlthProb* were modified and amplified by ecologic level risk factors, sometimes paradoxical inconsistencies in effects in the different local models.

Distinct, substantive differences in full-province and local models for both outcomes suggest that there may be different etiologies the two different scales; the combinations of risk factors and interactions that are sufficient to explain a hotspot for Prem<35 are insufficient to explain hotspots for Prem≥35. It also suggests that models developed using large scale data, such as for the full province, may not accurately represent any given local area. A more effective understanding of adverse outcomes may require separate analysis for different local areas.

While education and median income have often been grouped together as indicators of socioeconomic status, our findings suggest that education may be a more consistently influential risk factor. It seems clear that the two factors act differently in influencing birth outcomes.

The effect of individual risk factors are better understood when one considers their interactive relationships with the surrounding social and physical environment. Identifying these significant interactions may assist in the development of community-based health interventions.

References

(1) Canadian Institute for Health Information. Giving Birth in Canada: Regional Trends from 2001-2002 to 2005-2006. CIHI 2007 25 July, 2007:1-42.
(2) Canadian Institute for Health Information. Highlights of 2010–2011 Selected Indicators Describing the Birthing Process in Canada. 2012; Available at: https://secure.cihi.ca/free_products/Childbirth_Highlights_2010-11_EN.pdf. Accessed 9/14, 2012.
(3) Canadian Institute for Health Information. Highlights of 2011-2012 Selected Indicators Describing the Birthing Process in Canada. 2013; Available at: https://secure.cihi.ca/free_products/Childbirth_Highlights_2010-11_EN.pdf. Accessed 07/20, 2013.
(4) Canadian Institute for Health Information. Highlights of 2009-2010 Selected Indicators Describing the Birthing Process in Canada. 2011; Available at: https://secure.cihi.ca/free.../quickstats_childbirth_2009_10_highlight_en.pdf. Accessed 07/20, 2013.
(5) Bierman AS editor. Project for an Ontario Women's Health Evidence-Based Report: Volume 2: First ed. Toronto: Ministry of Health and Long Term Care; 2011.
(6) Canadian Institute for Health Information. Childbirth Indicator Results by Province/Territory of Residence in Canada. 2009; Available at: http://qstat.cihi.ca. Accessed 08/05, 2009.
(7) Joseph KS, Allen AC, Dodds L, Turner LA, Scott H, Liston R. The perinatal effects of delayed childbearing. Obstet Gynecol 2005 Jun;105(6):1410-1418.
(8) Kramer S, et al. Secular Trends in Preterm Birth, a Hospital-Based Cohort Study. JAMA 1998 December 2, 1998(280):21.
(9) Canadian Institute of Health Information. Too Early, Too Small: A profile of Small Babies Across Canada. 2009;ISBN 978-1-55465-480-2:8,28,11,viii,12,15,14,10,11,2,57,59,20,21,27,268,27,39,31,30,39,30,38,14,18.
(10) McDowell I. Thesis: From risk factors to explanation in public health. Journal of Public Health 2008 July 11;30(3):219.
(11) BORN Ontario. Better Outcomes Registry and Network. 2013; Available at: http://www.bornontario.ca/. Accessed 07/22, 2013.
(12) Statistics Canada. Statistics Canada Community Profiles Census Division. 2008; Available at: www12.statcan.ca/english/census06/data/profiles. Accessed April 5, 2008.
(13) SAS Institute Inc. SAS/STAT(r) 9.2 User's Guide: The GLIMMIX Procedure (Book Excerpt). Second ed. Cary, NC; 2008.
(14) Resnik R. Intrauterine Growth Restriction. Obstet Gynecol 2002 March 2002;99(3):2002.
(15) Behrman RE, Butler AS editors. Preterm Birth: Causes, Consequences, and Prevention. first ed. Washington (DC): National Academies Press; 2007.
(16) Diez Roux AV, Schwartz S, Susser E. 6.2 Ecological variables, ecological studies, and multilevel studies in public health research. 2012; Available at: http://medtextfree.wordpress.com/2011/04/25/6-2-ecological-variables-ecological-studies-and-multilevel-studies-in-public-health-research/. Accessed 02/11, 2011.
(17) O'Campo P, Xue X, Wang M, Caughy M. Neighborhood Risk Factors for Low Birthweight in Baltimore: A Multilevel Analysis. American Journal of Public Health 1997 July 1997;87(7):1113.
(18) McCowan L, Dekker G, Chan E, Steward A, Chappell L, Hunter M, et al. Spontaneous preterm birth and small for gestational age infants in women who stop smoking early in pregnancy: prospective cohort study. BMJ 2099;338:b1091.

(19) Holzman C, et al. Maternal Weathering and Risk of Preterm Delivery. American Journal of Public Health 2009 October 2009;99 (10):1964.
(20) Public Health Agency of Canada (Maternal and Infant Health Section). Canadian Perinatal Health Report 2008 Edition. 2008 2008;2008 edition:131,131,130,137,306,141,306,139,43,62,299,302,300,155,155,40,43,304.
(21) Joseph K, Liston R, Dodd's L, Dahlgren L, Allen A. Socioeconomic Status and Perinatal Outcomes in a Setting with Universal Access to Health Care Services. CMAJ 2007 September 11, 2007;177(6):583-587.
(22) Canadian Institute of Child Health. The Health of Canada's Children. 2001.
(23) Kramer M, Seguin L, Lydon J, Goulet L. Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? Paediatric and Perinatal Epidemiology 2000;14:194.
(24) Luo Z, Kierans W, Wilkins R, Liston R, Mohamed J, Kramer M. Disparities in Birth Outcomes by Neighborhood Income: Temporal Trends in Rural and Urban Areas, British Columbia. Epidemiology 2004 November 2004;15(6):679.