ADVERSE EFFECTS OF SECOND HAND SMOKE EXPOSURE IN NON-SMOKING WOMEN: MATERNAL AND NEONATAL OUTCOMES

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Adverse Effects of Second Hand Smoke Exposure in Non-Smoking Women: Maternal and Neonatal Outcomes

By

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Précis

Exposure to second hand smoke in non-smoking pregnant women was found to significantly increase the risks of preterm birth less than 34 weeks of gestation and low birth weight < 2,500 g.

Abstract

Objective: To evaluate the effects of second hand smoke exposure in non-smoking pregnant women on perinatal outcomes.

Methods: This retrospective cohort study included all non-smoking pregnant women with singleton gestations delivering at the Health Sciences Centre, St. John's, Newfoundland and Labrador, from April 1, 2001 to March 31, 2007, who reported whether or not they had been exposed to second hand smoke during pregnancy. Data was drawn from the Newfoundland and Labrador Provincial Perinatal Program Database. The primary outcome was preterm birth less than 37 weeks of gestation. Secondary outcomes included preterm birth less than 34 weeks of gestation, type of labour (spontaneous or induced), and mode of delivery (Caesarean or vaginal delivery), as well as neonatal outcomes including birth weight (including birth weight less than 2,500 g) and admission to the neonatal intensive care unit (NICU). Other outcomes included Apgar scores at one and five minutes, respiratory complications, birth weight over 4,000 g, and use of tocolytics. Univariate analyses and multivariate logistic regression analyses (controlling for potential confounders) were performed and odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Results: A total of 10,002 women were included in the study – 1,051 with second hand smoke exposure and 8,951 without second hand smoke exposure. Although the rate of preterm birth less than 37 weeks of gestation was not significantly different between the two groups, second hand smoke exposure was independently associated with preterm birth less than 34 weeks of gestation (OR 1.84, 95% CI 1.23 – 2.77, $p = 0.003$) and low birth weight < 2,500 g (OR 1.75, 95% CI 1.15 - 2.67, $p = 0.009$). Second hand smoke exposure was also associated with trends towards higher rates of low one minute Apgar score (14.3% compared with 11.8%, $p = 0.023$), NICU admission (OR 1.24, 95% CI 1.00 - 1.54, $p = 0.046$), a lower mean birth weight (3,421 +/- 643g compared with 3,505 +/- 612g, $p = 0.036$), as well as an increased use of endotracheal intubation (3.4% compared with 2.9%, $p = 0.062$).

Conclusion: Exposure to second hand smoke during pregnancy can have serious adverse health effects for the pregnant woman and her fetus. Second hand smoke exposure is associated with preterm birth less than 34 weeks of gestation and low birth weight. Continued policy development and education are needed regarding the adverse effects of second hand smoke exposure.

Keywords

Second hand smoke exposure, preterm birth, low birth weight, NICU admission

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Don't let the fear of the time it will take to accomplish something stand in the way of your doing it. The time will pass anyway; we might just as well put that passing time to the best possible use.
~Earl Nightingale

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Chapter 1 - Introduction

1.1 The Problem

1.1.1 Preterm Birth

In today's society, women who are pregnant hope to have both a healthy pregnancy and a healthy infant. The level of care needed to facilitate a healthy pregnancy is often guided by a variety of people from the medical community. As such, pregnant women have come to rely on the medical community to provide them with the relevant information needed to make educated decisions. Without evidence-based research to support the information the medical community is at a disadvantage (Friedman & Sigman, 1981).

Major changes in lifestyle and in relationships often transpire when a pregnancy occurs. Thus, the pregnancy can be viewed as both a psychological and a biological growth period. As the pregnancy progresses through the different stages, issues and emotions evolve that form the context for the birth of the infant. This background development is incomplete when preterm birth occurs. Furthermore, preterm birth often causes a crisis for the people involved as there can be enormous emotional, financial, and physical strains (Friedman & Sigman, 1981; Goldberg & DiVitto, 1983; Sammons & Lewis, 1985).

Preterm birth is one of the central issues in perinatal health care. The international definition for preterm birth is an infant born prior to 37 weeks (less than 259 days) from the first day of the mother's last menstrual period (Yu & Wood, 1987). Preterm birth is a major cause of perinatal morbidity and mortality, and is estimated to account for 75% of neonatal mortality, excluding lethal malformations (Wang et al, 1997; Floyd et al, 1991; Clean Air Coalition of B.C., 2000; Jaakkola, 2002).

Preterm birth is the leading cause of newborn death, but survival is not the only outcome measure (UK Healthcare, n.d.). Infants born before 37 weeks are also vulnerable to many short- and long-term sequelae of premature birth. Even infants born only four to six weeks early can have effects from the preterm birth such as breathing difficulties, feeding problems, jaundice and effects on brain functions, as well as have long-term difficulties such as behavioral and social-emotional problems and learning difficulties (UK Healthcare, n.d.). In addition to the short-term complications of respiratory distress syndrome, intraventricular hemorrhage and necrotizing enterocolitis (Zwicker & Harris, 2008), preterm infants are at higher risk of being readmitted to hospital and death after they go home (UK Healthcare, n.d.). Infants born preterm can also suffer long-term effects such as central nervous system (CNS) complications (e.g., cerebral palsy), neurodevelopmental delay (Zwicker & Harris, 2008), respiratory complications (e.g., bronchopulmonary dysplasia), and visual and hearing impairments (UK Healthcare, n.d.). These complications have their highest incidence in births occurring at less than 28 weeks of gestation. The adverse sequelae of preterm birth are likely to have considerable long-term economic consequences for the health services, for society (Petrou, 2006) and the individual. In terms of the years of life lost, preterm birth is probably one of the most important diseases in all of medicine (Zwicker & Harris, 2008).

Despite improvements in perinatal care in the last 25 years that have allowed increased survival of preterm infants, the rate of preterm birth continues to rise. In Canada, the incidence of preterm birth has increased from 6.3% (1981 to 1983) to 7.8% (2005) (Joseph et al 1998; Canadian Perinatal Health Report, 2008).

1.1.1.1 Risk Factors for Preterm Birth

The causes of preterm birth can be divided into three main categories (Hollier, 2005; Preterm Birth, 2005, p. 855; Alexander, 2007, p. 604; Lockwood, 2009):

1. Preterm pre-labour rupture of membranes (PPROM) (30–40% of preterm births)
2. Spontaneous preterm labour with intact membranes (40–50% of preterm births)
3. Indicated preterm birth for maternal or fetal conditions (20–30% of preterm births)

Risk factors for spontaneous preterm labour and birth include (Caughey, 2009; Lockwood, 2009; Robinson & Norwitz, 2009):

→ Reproductive history:

- Previous spontaneous preterm birth
- Advanced reproductive technologies
- Ante partum bleeding (including second trimester bleeding)
- PPROM in current pregnancy
- Cervical/uterine factors
    - cervical insufficiency, uterine malformation and fibroids
    - excisional cervical treatment for cervical intraepithelial neoplasia
- Fetal/intrauterine factors
    - multifetal gestation
    - fetal anomaly
    - polyhydramnios

→ Infection

- chorioamnionitis
- bacteriuria
- periodontal disease
- current bacterial vaginosis with a prior preterm birth
- malaria (particularly in developing countries)

→ Demographic factors

- low socioeconomic status
- single women
- low level of education
- African-American race (US), First Nations race (Canada)
- maternal age < 18 and > 35 years

→ Lifestyle issues

- illicit drugs
- smoking
- stress
- physical abuse
- inadequate prenatal care
- low prepregnancy weight (weight < 55 kilograms)
- poor weight gain in pregnancy

1.1.2 Smoking and Preterm Birth

Research on the effects of lifestyle factors on birth outcomes has indicated that preterm birth is 20 percent more common, and very preterm delivery (less 33 weeks gestation) is 60 percent more common among pregnant women who smoke (Floyd et al, 1991; Makin et al, 1991; Ogawa et al, 1991; Wang et al, 1997; Jaakkola, 2002). Studies have shown a dose-response relationship with respect to the amount of cigarettes smoked and the effects on the rates of preterm birth. Women who smoke between 1 – 10 cigarettes per day during the pregnancy are 1.54 (OR, 95% CI 1.01 to 2.35) times more likely to have a preterm infant while women who smoke more than 10 cigarettes per day are 1.69 (OR, 95% CI 0.91 to 3.13) times more likely to have a preterm infant. Dose-response relationships have also been found between smoking and very preterm infants (< 35 weeks): 1.90 (OR, 95% CI 1.01 to 3.56) and 2.46 (OR, 95% CI 1.05 to 5.76) times for 1-10 and > 10 cigarettes/day, respectively (Fantuzzi et al, 2007).

1.1.3 Second hand Smoke Exposure

Second hand smoke exposure is a major preventable cause of death in many countries including Canada and as such, is becoming an increasing public health concern. Approximately two-thirds of the smoke from a cigarette is not inhaled by the smoker (Fuchs et al, 1993; Clean Air Coalition of BC, 2000). It enters the surrounding air, carrying with it more than 50 known carcinogens. Some of the toxins contained in second hand smoke are in greater concentrations than those inhaled by the smoker (Fuchs et al, 1993; Windham et al, 2000). Furthermore, second hand smoke contributes and causes a host of diseases including heart disease, cancer, and lung infections. For women who are pregnant, exposure to second hand smoke may increase the risk of having a low birth weight infant as well as the risk of delivering preterm (Fuchs et al, 1993; Clean Air Coalition of BC, 2000). However the majority of research regarding smoking exposure and pregnancy has focused on active smoking, with fewer studies evaluating second hand smoke exposure (also known as passive or environmental smoke exposure (ETS)).

Preterm birth can have a negative impact on both the developing fetus and on the pregnant woman. There is no single mechanism for the preterm activation of labour. That is, no predisposing factor is absolute in the sense that the presence of one of these factors necessarily leads to preterm birth (Fuchs et al, 1993). Thus, when a pregnant woman has some level of control over a predisposing factor such as exposure to second hand smoke, it is important to know and understand the adverse effects of second hand smoke on the pregnancy.

1.2 Purpose of the study

The purpose of this study was to investigate the effects of second hand smoke exposure in non-smoking pregnant women. The primary objective was to determine if the rate of preterm birth less than 37 weeks of gestation for non-smoking pregnant women who self-reported exposure to second hand smoke during the pregnancy is higher than for non-smoking pregnant women who self-reported no exposure to second hand smoke during the pregnancy. Secondary outcomes evaluated included gestational age by birth, preterm birth less than 34 weeks of gestation, the type of labour (spontaneous or induced), mode of delivery (Caesarean or vaginal delivery), birth weight (less than 2,500 g) and admission to the neonatal intensive care unit (NICU). Other outcomes evaluated were Apgar scores at one and five minutes, respiratory complications, birth weight greater than 4,000 g, and use of tocolytics.

1.3 Rationale

Each year, approximately 5,000 Canadians die as a result of second hand smoke exposure with countless more experiencing negative health effects (Floyd et al, 1991; Clean Air Coalition of BC, 2000). With over 4,000 chemicals, second hand smoke may be harmful to anyone exposed to it. People are exposed to second hand smoke through mainstream smoke (the smoke exhaled by the smoker), and/or side-stream smoke (the smoke emitted from the lit end of a cigarette) (Floyd et al, 1991; Clean Air Coalition of BC, 2000). While the fetus cannot be considered an active smoker, it can be considered a passive smoker as a result of the pregnant woman's active and/or passive smoking (Floyd et al, 1991).

Literature searches indicate that there is limited information on the effects of second hand smoke exposure in non-smoking pregnant woman on the pregnancy and the newborn infant. While smoking prevalence among women in the general population has been declining, approximately 25 percent of pregnant women continue to smoke (Floyd et al, 1991; Wang et al, 1997). It is believed that an even greater proportion of women are exposed passively to second hand smoke. The question of whether maternal exposure to second hand smoke also may be hazardous has not been thoroughly evaluated.

1.4 Definitions

The following terms are used frequently throughout this study.

Active smoking is the process of inhaling smoke emitted from the burning of tobacco leaves. The most common type of smoking is cigarette smoking.

Apgar score is a method for evaluating the condition of the newborn infant at one minute and five minutes after birth, and provides a standardized mechanism to record fetal to neonatal transition (Kattwinkel, 2006). This score is based on five criteria – colour, heart rate, reflex irritability, tone, and respiratory effort - and each assigned a value of 0 to 2. The scores for each criteria are then added together to yield an overall score out of 10. Nearly all newborns have Apgar scores of 7 to 10; however, some newborns have lower scores and may require additional care (Sielski, 2006).

Bag-and-mask is a hand-held device used to provide positive pressure ventilation to a newborn who is not breathing or who is breathing inadequately.

Caesarean section/Caesarean delivery is an abdominal surgical procedure to deliver one or more newborns.

Endotracheal tube is a tube that is placed into the newborn's trachea through the nose or mouth. It is usually placed if breathing remains depressed after using bag-and-mask.

Induced labour is when artificial means (such as use of medications) are used to start the labour process.

Low birth weight is a newborn whose birth weight is less than 2,500 grams. Newborns may have low birth weight if they are born preterm (before 37 weeks of pregnancy) and/or are small for their gestational age.

Intrauterine growth restriction (IUGR) is when the fetal weight is smaller than expected (less than the 10^{th} percentile) for the number of weeks of gestation (Divon & Ferber, 2009).

Neonatal intensive care unit (NICU) is a unit of a hospital specializing in the care of ill or premature newborn infants.

Newfoundland and Labrador Provincial Perinatal Program (NLPPP) is a program in Newfoundland and Labrador established in 1979 that is dedicated to optimizing pregnancy outcomes, and the provision of a follow-up clinic to infants at risk for developmental delay.

Nulliparous refers to a woman who has never given birth to a child or has had no previous deliveries ("nulliparous," Websters Medical Dictionary).

Provincial Perinatal Database (PPD) is a surveillance project of the NLPPP. This computerized database collects information on pregnancy outcomes for two health authorities of the province including the Eastern Avalon Region (served by the Women's Health Centre of Eastern Health).

Preterm birth is an infant born prior to 37 weeks (less than 259 days) from the first day of the mother's last menstrual period

Second hand smoke exposure is exposure to the smoke emitted from a burning cigarette, pipe or cigar, and/or the smoke exhaled by a smoker.

Small for gestational age is an infant whose weight is lower than the population norms. An infant is considered small-for-gestational age when the birth weight is below the 10^{th} percentile for gestational age or greater than 2 standard deviations below the mean.

Very preterm birth is defined as an infant born prior to 34 weeks.

Chapter 2 - Literature Review

2.1 Literature Searches

The searches were conducted at the Health Sciences Library, Memorial University of Newfoundland. The following databases were utilized: PubMed, Unicorn, UpToDate, and Cochrane. The search engine, Google, was also used. Searches were performed around two central themes: 1) the effects of passive smoking on pregnancy, and 2) the effects of active smoking on pregnancy. For searches regarding passive smoking and pregnancy the following terms were used: "Tobacco Smoke Pollution"[MESH] and "Pregnancy"; "Tobacco Smoke Pollution"[MESH] and "Infant, Newborn"[MESH] and "Pregnancy Complication"[MESH]; "Passive Smok*" and "Pregnancy"; Passive Smok*"[KW] and "Preterm Labour"[KW]; "Tobacco Smoke"[KW] and "Pregan*[KW]; "Tobacco Smoke"[KW] and "Preterm Labour"[KW]; "Tobacco Smoke"[KW] and "Preterm Birth"[KW]; "Tobacco Smoke"[KW] and "Ante-partum Bleeding"[KW]; "Tobacco Smoke"[KW] and "Pre-rupture of Membranes"[KW]; "Passive Smok*"[KW] and "Pregnancy"[KW]; "Passive Smoking"[KW] and "Ante-partum Bleeding"[KW]; "Passive Smoking"[KW] and "Pre-rupture of Membranes"[KW]; "Tobacco Smoke Pollution/Adverse Effects"[MESH] and "Ante-partum Bleeding"; "Tobacco Smoke Pollution/Adverse Effects"[MESH] and "Preterm Labour"; "Tobacco Smoke Pollution"[Mesh] AND "Apgar Score"[Mesh]; "Premature Birth"[Mesh] AND "Apgar Score"[Mesh]; "Intensive Care Units, Neonatal"[Mesh] AND "Premature Birth"[Mesh]; "Birth Weight"[Mesh] AND "Tobacco Smoke Pollution"[Mesh]; "Infant, Low Birth Weight"[Mesh] AND "Tobacco Smoke Pollution"[Mesh]; "Premature Birth"[Mesh] AND "Birth Weight"[Mesh]; "Premature

Birth"[Mesh] AND "Infant, Low Birth Weight"[Mesh]. For searches regarding active smoking and pregnancy the following terms were used: "Pregnancy Outcome"[MESH] and "Smoking"[MESH]; "Tobacco Smoke Pollution"[MESH] and "Pregnancy"; "Active Smok*" and "Pregnancy". Fewer search terms were used for searches regarding active smoking and pregnancy as the aforementioned terms yielded a large number of articles from which to choose.

Using the same databases listed above, searches were also conducted looking at the effects of second hand smoke exposure on birth weight, Apgar scores, admission to NICU, use of tocolytics, type of delivery, and type of labour.

Numerous key word searches were conducted. To ensure a representative sample was obtained, subsequent searches were conducted that expanded upon the keywords previously mentioned and cross-referenced with those already located, to establish if other pertinent papers could be located. Once all searches were performed, it was apparent that there was considerable overlap among the articles in each search. Some of the articles located discussed, among other things, the connection between smoking and outcomes of interest which were different from the current proposed study and interventions to deal with adverse pregnancy outcomes, while others dealt with the effects of smoking on non-human subjects. Such articles were excluded from the representative sample. Furthermore, given the overlap among the articles, final article selection was limited to articles that were written in the English language. The database PubMed was the primary database of choice. It contains over 15 million citations of the top periodical literature in health, medicine, nursing, pharmacy, biomedicine, and health administration dating from 1951 to June 2009. Other information sources such as books were also limited to those written in the last 20 years; however some books written beyond that time period were used.

2.2 Literature Review

2.2.1 Measurement of Active and Passive Smoking

The gold standard to confirm smoking exposure is biochemical as it is believed to be more objective and less susceptible to bias (Patrick et al, 1994). Cotinine, thiocynanate, and carbon monoxide are the most commonly used biochemical measures. But despite their proposed objectivity, biochemical measures do not provide a gold standard, nor are they perfect measures of accuracy. For example, carbon monoxide can be elevated in people who are not active smokers. Furthermore, repeated testing of biochemical specimens may generate results that are different even when the person's active smoking status has not changed (Patrick et al, 1994).

The biggest drawback to biochemical measures is the manner in which they are obtained. Biochemical measures are intrusive: blood, saliva, or breath samples need to be collected from the individual (Patrick et al, 1994; Marobia et al, 2001). This requires more contact with the individuals which can be difficult in studies with large sample sizes, or impossible in case control or retrospective cohort studies. Moreover, because of the short half-life for some of the biochemical measures, studies utilizing biochemical measures only validate the smoking status near the time of the specimen collection (Benowitz, 1983; Marobia et al, 2001).

To off-set these draw backs with biochemical measures, some studies rely on self-reported measures of smoking (Patrick et al, 1994). Self-reported smoking is assessed easily by either using self-administered questionnaires or by using interviewer-administered questionnaires. However, the validity of self-reported smoking is often questioned because of the widespread belief that smokers are inclined to underestimate the amount smoked or deny smoking all together (Patrick et al, 1994; Parazzine et al, 1996).

A study conducted by Patrick et al (1994) looked at whether or not biochemical measures of smoking produced higher or lower estimates of smoking than self-reports. They completed a review and meta-analysis of 26 reports containing 51 comparisons between biochemical measures and self-reported behaviour. Their results suggested that interview-administered questionnaires yielded higher estimates of sensitivity and specificity than did self-administered questionnaires. It is believed that in interview-administered situations, the respondent may be aware of sensory cues about smoking (ie. nicotine stains, smoke odour, etc) that would be obvious to an interviewer (Patrick et al, 1994).

Other studies have also found evidence of satisfactory validity of self-reported smoking habits in pregnancy. Parazzini et al (1996) examined the validity of self-reported cigarette smoking during the third trimester of pregnancy using saliva cotinine as a marker. A total of 109 pregnant women were enrolled. Data were collected by trained interviewers on variables such as demographic characteristics, smoking habits, etc. Women self-reporting current smoking or having quit smoking before the pregnancy were asked to provide saliva samples. The results from the study showed substantial agreement between biochemical and self-reported measures of smoking.

2.2.2 Adverse Effects of Active Smoking During Pregnancy

Smoking during the pregnancy can have serious negative health effects for both the pregnant woman and the fetus (Smoking and Reproductive Life, 2004). Numerous toxins such as carbon monoxide, cyanide, sulphide, nicotine, and carcinogenic hydrocarbons are emitted from cigarette smoke. Carbon monoxide is a highly toxic gas that binds tightly to haemoglobin and thus, prevents the transportation of oxygen (Smoking and Reproductive Life, 2004). Because fetal haemoglobin has a higher affinity for carbon monoxide than adult haemoglobin, unborn fetuses/infants are exposed to greater risks from this gas than pregnant women. Carbon monoxide also impairs enzymes participating in intracellular respiration. These pathologic changes can partially explain the impaired growth, prematurity, and intrauterine death observed among fetuses/infants of smokers more frequently than among those of non-smoking women (Koren, 1996; Smoking and Reproductive Life, 2004).

Since 1957, additional studies have been conducted which looked at the effects active smoking by a pregnant woman has on fetal development. The most consistent finding is a reduction in birth weight of 150 g to 300 g. Women who smoked more than one pack a day increased the risk of having a low birth weight infant by 130 percent over non-smokers. For women who smoked less than a pack a day, the risk increased by 53 percent. The risk of delivering a low-birth weight infant increases by 26% for each additional 5 cigarettes smoked per day by the mother (Kleinman & Madans, 1985).

The negative effects of smoking during the pregnancy are not limited to just intra-uterine growth restriction (IUGR) and low birth weight (Kallen, 2001). Epidemiological studies have also demonstrated the adverse effects of smoking on outcomes including Apgar scores, stillbirths, and neonatal deaths (Garn et al, 1981; Cnattingius et al, 1993; Horta et al, 1997; Kyrklund-Blomberg et al, 1998; Kolas et al, 2000; Kallen, 2001; Aliyu et al, 2007; Fantuzzi et al, 2007; Salihu et al, 2008).

2.2.2.1 Preterm Birth

The impact of active smoking during pregnancy on preterm birth has been mixed. Some studies have shown a relationship between active smoking during pregnancy and preterm/early preterm delivery (Cnattingius et al, 1993; Kyrklund-Blomberg et al, 1998; Kolas et al, 2000; Kallen, 2001; Fantuzzi et al, 2007) while others have found no association between smoking and preterm delivery (Horta et al, 1997).

The aforementioned studies which found an effect between active smoking and preterm birth were either prospective or retrospective cohort designs, and had fairly large sample sizes (ranging from 1,259 to1,413,811 women). Horta et al (1997) found no association between active smoking and preterm delivery. However, this study differed from the other studies in its choice to determine gestational age. The Horta et al (1997) study opted to use the Dubowitz method, a method which uses physiological and neuromuscular criteria of the infant to determine gestational age (McKee-Garrett, 2009). There are two disadvantages to using this system: 1) overestimation of gestational age, and 2) the large number of criteria required for evaluation often limit its effectiveness with sick or extremely premature infants (McKee-Garrett, 2009). It could be that the Horta study did not find an effect between active smoking and preterm delivery because gestational age of the infants may have been overestimated.

2.2.2.2 Apgar Score

Active smoking has been shown to have a negative impact on Apgar scores (Garn et al, 1981; Kallen, 2001). In the study, Garn et al categorized the participants based on the amount smoked per day, and found a dose-response relationship between amount smoked and resulting Apgar score – the more cigarettes smoked the lower the Apgar score. For pregnant women who smoked 41 to 60 cigarettes per day, there was a near quadrupling effect of infants with low one minute and five minute Apgar scores.

2.2.2.3 Intrauterine Growth Restriction (IUGR)

Horta et al (1997) found a direct dose-response association between the number of cigarettes smoked and the risk of IUGR. Given the use of the Dubowitz methods to assess gestational age, however, it is plausible that the effects of smoking on IUGR may have been under assessed in the study.

2.2.2.4 Fetal Death

Active smoking has also been shown to increase the risk for stillbirth and neonatal death. Aliyu et al (2007) found that pregnant women who smoked were 50% more likely to experience intrapartum fetal death as compared with non-smoking pregnant women. Salihu et al (2008) found that the risk of stillbirth was 34% greater among smokers than non-smokers. They also found a dose-response relationship. For each 10-unit increase in the number of cigarettes consumed per day prenatally, the likelihood of stillbirth rose by about 14%.

2.2.3 Incidence and Trends of Passive Smoking During Pregnancy

There are limited data on the prevalence of second hand smoke exposure among adults in Canada (Vozoris & Lougheed, 2008). In 2003, despite a steady decline in the prevalence of smoking in the general population, over one-third of non-smokers were regularly exposed to second hand smoke (Perez, 2004). At home and at work, the younger the non-smoker, the more likely they were to be exposed to second hand smoke, primarily because they have fewer options to avoid second hand smoke exposure (ie. may live in a household where a parent smokes, etc) (Perez, 2004).

With respect to pregnant women, there has been a decline in recent years in the rates of second hand smoke exposure. In 2001, 22.4% of women who gave birth reported exposure to second hand smoke; in 2005, that rate had decreased to 14.1% (Canadian Perinatal Health Report, 2008). Furthermore, much like the general population, the younger the pregnant women, the more likely she was to have been exposed to second hand smoke. In 2005, 41.9% of pregnant women under the age of 20 were exposed to second hand smoke while only 9.7% of pregnant women older than 40 years of age were exposed to second hand smoke (Canadian Perinatal Health Report, 2008).

2.2.4 Adverse Effects of Passive Smoking During Pregnancy

With the increasing awareness of the adverse effects of passive smoking on the health of the general public, recent research on pregnancy has begun to look at the effects of passive smoking on pregnancy. People exposed to second hand smoke also have high levels of toxins such as carbon monoxide, cyanide, sulphide, nicotine, and carcinogenic hydrocarbons (Smoking and Reproductive Life, 2004). Increases in the concentration of cotinine have been observed in the urine of non-smokers who live with smokers, and in the amniotic fluid of non-smoking pregnant women chronically exposed to second hand smoke (Floyd et al, 1991; Smoking and Reproductive Life, 2004).

Non-smoking women and their fetuses are exposed to risks when someone in close proximity to them smokes. The evidence of adverse perinatal effects of passive smoking is strongest for its effect on fetal growth and intrauterine growth restriction (Canadian Perinatal Health Report, 2008). The United States Surgeon General has concluded that there is a causal relationship between second hand smoke exposure in pregnancy and a reduction in birth weight. However, conflicting information has been found regarding the association of passive smoking and preterm birth, with some studies noting an association but others not. The Surgeon General in the United States feels that the evidence is suggestive, but not strong enough to conclude that there is a causal relationship (Canadian Perinatal Health Report, 2008).

During the past 30 years, extensive evidence on the effect of maternal smoking during pregnancy on fetal growth has been accumulating. To date, the majority of research which has investigated the effects of passive smoking during pregnancy has looked at outcomes such as birth weight, preterm birth, and small for gestational age (Martin et al, 1986; Mainous et al, 1994; Roquer et al, 1995; Misra et al, 1999; Hruba et al, 2000; Windham et al, 2000; Jaakkola et al 2002; Wilcox, 2001; Dejmek et al, 2002; Goel et al, 2004; Leonardi-Bee et al, 2008). The results from this research indicate that passive smoking has similar effects as active smoking, although to a lesser degree.

2.2.4.1 Birth Weight

Research on exposure to second hand smoke during pregnancy can be summarized as showing an approximate reduction of birth weight ranging from 33 g to 192 g (Martin et al, 1986; Mainous et al, 1994; Roquer et al, 1995; Misra et al, 1999; Hruba et al, 2000; Dejmek et al, 2002; Goel et al, 2004; Leonardi-Bee et al, 2008). In a pooled analysis of prospective studies, Leonardi-Bee et al (2008) found exposure to second hand smoke to be associated with an increased risk for birth weight below 2,500 grams (OR 1.32, 95% CI 1.07 to 1.63). A strong dose-effect has also been observed. An infant's birth weight can be up to 189 g lower in mothers heavily exposed to second hand smoke both at work and at home (Hruba et al, 2000).

A few studies have found slight, but not significant, reductions in birth weight (Windham et al, 2000; Jaakkola et al 2002). However, the study done by Jaakkola et al (2001) used 3,000 g as the cut off which is in contrast to the more widely accepted definition of low birth weight as less than 2,500 g (Wilcox, 2001), finding a higher incidence of birth weight < 3,000 g in women exposed to second hand smoke. Using a birth weight cut off higher than the standard definition may have reduced the true effect of second hand smoke exposure on birth weight. A study completed by Roquer et al (1995) found a large reduction in birth weight of 192 g, but the sample size was small (n = 129).

2.2.4.2 Preterm Birth

As previously mentioned, preterm birth is one of the central issues in perinatal health care, and there are a few recent studies which have investigated the effects of second hand smoke exposure on preterm birth. Windham et al (2000), Geol et al (2004), and Fantuzzi et al (2007) did not find any increase in risk for preterm birth less than 37 weeks (Windham: OR 1.6, 95% CI 0.65 to 1.31; Goel: OR 1.15, 95% CI 0.69 to 1.92; Fantuzzi: OR 0.92, 95% CI 0.65 to 1.31). In their meta-analysis, Leonardi-Bee et al (2008) found that second hand smoke exposure was not consistently significantly associated with an increased risk for preterm birth. In the retrospective cohort studies analysed, there was an increased risk for preterm birth (OR 1.18, 95% CI 1.03 to 1.35) but not with the case-control studies (OR 0.92, 95% CI 0.65 to 1.31). However, Fantuzzi et al (2007) did find that non-smoking women exposed to second hand smoke were at an increased risk for preterm birth < 35 weeks (OR 1.71, 95% CI 1.04 to 2.89). Windham et al (2000) found similar effects on preterm birth < 35 weeks (OR 2.4, 95% CI 1.0 to 5.3).

The risk of preterm birth has also been connected with level of exposure to second hand smoke and to age. Jaakkola et al (2002) found a dose-response relationship in that the risk of preterm delivery was higher when exposure to second hand smoke is moderate to high. Ahluwalia et al (1997) found that the risk for preterm delivery was elevated among older non-smokers exposed to ETS, but not in younger non-smokers exposed.

However, in Jaakkola et al (2002), Goel et al (2004), and Fantuzzi et al (2007) the sample sizes were small. In Ahluwalia et al (1997), the results may not be completely attributable to second hand smoke exposure. The subjects were low-income women, and while they were receiving health care services from publicly funded maternal and child health clinics, income status has been previously linked with poor overall health outcomes (Benzeval et al, 2001). Furthermore, the results could partially be attributed to the fact that older women in general are at a higher risk for preterm birth (Caughey, 2009).

2.2.4.3 Small for gestational age

Small for gestational age infants have a variety of associated clinical problems beginning at birth. Severely affected term newborns deprived of oxygen and nutrients may have a difficult cardiopulmonary transition with perinatal asphyxia, meconium aspiration, or persistent pulmonary hypertension (Mandy, 2009). Second hand smoke exposure during pregnancy has been shown to be associated with a higher risk for small for gestational age infants (Nafstad et al, 1997; Dejin-Karlsson et al, 1998; Goel et al 2004). Conversely, Chen and Petitti (1995) found that maternal exposure to passive smoking during pregnancy was not associated with an increased risk of term SGA.

These studies performed multiple logistic regression analyses to control for confounding variables but are limited because of their small sample sizes.

2.2.5 Gaps in the Literature

The majority of the literature investigating the effects of passive smoking on pregnancy outcomes focused much attention on its effects on the birth weight (Martin et al, 1986; Mainous et al, 1994; Roquer et al, 1995; Misra et al, 1999; Hruba et al, 2000; Dejmek et al, 2002; Goel et al, 2004; Canadian Perinatal Health Report, 2008; Leonardi-Bee et al, 2008). Fewer studies have investigated the effects of second hand smoke exposure in pregnant women on the outcomes of preterm birth, type of delivery and labour, as well as its effects on neonatal outcomes (Canadian Perinatal Health Report, 2008).

Chapter 3 - Methodology

3.1 Data Procurement

The most feasible design for this study was determined to be a retrospective cohort design utilizing self-reported measures of smoking. The data collected for this study was extracted from the prenatal records (documented antenatal by medical practitioners, midwives, regional nurses and nurse practitioners) and personal health records.

3.2 Sample

3.2.1 Inclusion/Exclusion Criteria

This retrospective cohort study included any woman with a singleton pregnancy who gave birth at the Health Science Centre (HSC), St. John's, NL, between April 1st, 2001, and March 31st, 2007. The majority of the women who give birth at the HSC reside within the Avalon Peninsula of NL. Furthermore, given the HSC is the only tertiary health care setting in the province, any pregnancy that is deemed "high risk" from elsewhere in the province would be more likely referred to the HSC for delivery. The data from "high risk" pregnancies is included in the database.

Criteria for inclusion were pregnant women who were not currently smoking, whose referring health authority was in the province of Newfoundland and Labrador, who gave birth to a singleton infant at the HSC, and who indicated if they had or had not been exposed to second hand smoke.

3.2.2 Sample Size

The data was analyzed in two groups: the exposed group (p_i) and non-exposed group (p_c). The primary objective was to determine if the rate of preterm birth less than 37 weeks of gestation was higher for non-smoking women exposed to second hand smoke, compared to non-smoking women who were not exposed to second hand smoke. Previous literature indicates that for the general Canadian population, the rate of preterm birth is approximately 8.0%; (Canadian Perinatal Health Report, 2008). Furthermore, preliminary review of the data indicates that the ratio of non-exposed to exposed is 7:1. Thus, by using the statistical package PEPI 3.01, 2000 (Computer Programs for Epidemiology, Stone Mountain, GA, USA), to detect a 1/3 increase in the preterm birth rate (from 8.0% to 10.7%), with a 2-tailed $\alpha = 0.05$ and $\beta = 0.20$, one requires 1,041 non-smokers exposed to second hand smoke and 7,287 non-smokers not exposed to second hand smoke. A 1/3 increase in the preterm birth rate was felt to be clinically important based on the opinion of clinical experts in this area. The database for the fiscal years April 1, 2001 to March 31, 2007 had adequate numbers for analysis.

3.3 Data management

The cohort for the study was identified using the Newfoundland and Labrador Provincial Perinatal Database (PPD). The PPD is a project of the Newfoundland and Labrador Provincial Perinatal Program (NLPPP). This computerized database collects information on pregnancy outcomes for two health authorities of the province including the Eastern Avalon Region (served by the Women's Health Centre of Eastern Health). Approximately 87% of women who give birth at the HSC reside within the Avalon, and approximately 55% of deliveries in the province occur at the HSC. The data is compiled in conjunction with Eastern Health (EH) in addition to the Discharge Abstract Database (DAD) required of all Canadian acute care institutions. Data is collected after delivery and upon the woman's discharge from the HSC, St. John's, NL. The NLPPP works with EH to obtain an additional 102 data elements (80 maternal and 22 neonatal). Data collected include demographic information, antenatal, intrapartum, and post partum events, and perinatal outcomes for deliveries of every pregnancy of at least 20 weeks gestation. The information for these additional variables is primarily extracted from the prenatal records (antenatal documentation by medical practitioners, midwives, regional nurses and nurse practitioners) and personal health records. The choice of variables for which data is collected was determined through consultation with other existing provincial perinatal programs from across Canada. There also exists a national committee to ensure consistency in the variables among the provincial perinatal programs.

As previously mentioned, the data is collected after delivery and upon the woman's discharge from the HSC. As such, the data set contains data pertaining to all pregnant women who gave birth at the HSC. Pregnant women who gave birth at the HSC but were from other regions of the province would have done so primarily because their pregnancy was deemed high risk and thus, referred to the HSC for delivery.

A subset of the PPD containing maternal and neonatal data was obtained for this study. The variables associated with the data set were primarily nominal and ratio/continuous. Nominal variables consist of named categories for which no order is implied (Norman & Streiner, 2000). Some of the nominal variables were: referring health board; mother's employment status; exposure to second hand smoke; etc. Ratio variables, on the other hand, have equal values between them and have a meaningful zero (Norman & Streiner, 2000). Ratio variables included, but were not limited to: maternal age; gestational age in weeks; birth weight; etc.

3.4 Data Analysis

The data were organized to facilitate the analysis of the primary outcome (preterm birth less than 37 weeks), secondary outcomes (preterm birth < 34 weeks, type of delivery, Apgar score, NICU admission, and birth weight), and other outcomes (type of labor, use of tocolytics and respiratory complications).

3.4.1 Analysis of the Pregnant Woman's Data

3.4.1.1 Analysis of Primary Outcome

Preterm Birth (Dependent Variable)

Whether or not a pregnancy was considered preterm was based on the gestational age of the pregnancy at delivery. In the original data set, the gestational age variable was a continuous variable and reported in completed weeks. For the analysis, two separate dichotomous variables were created: one where preterm birth was defined as delivery at less than 37 weeks of gestation (1 = less than 37 weeks, 2 = 37 weeks or longer) and one where very preterm birth was defined as delivery less than 34 weeks of gestation (1 = less than 34 weeks, 2 = 34 weeks or longer).

Second hand Smoke Exposure (Primary Independent Variable of Interest)

In the original data set obtained, the exposure to second hand smoke variable was coded as a yes/no string variable. There were pregnant women who indicated they were currently smoking and exposed to second hand smoke. Given the effects active smoking can have on a pregnancy have been well established, it was felt important to remove active smokers for the exposure to second hand smoke variable. The new variable created for this analysis contained only non-smoking women who were (coded as 1) or were not (coded as 2) exposed to second hand smoke while pregnant. There were 1,051 non-smoking pregnant women who indicated they had been exposed to second hand smoke while there were 8,951 non-smoking pregnant women who had not been exposed to second hand smoke.

Secondary Independent Variables of Interest

There are many risk factors for preterm birth (Ogawa et al, 1991; Zwicker & Harris, 2008). Based on the literature, consultation with experts practising in obstetrics, and the variables available in the data set, it was determined that covariates to include in the analysis would be:

→ Previous preterm birth

Prior preterm birth is one of the strongest risk factors for future preterm birth, although most women who have had a preterm birth will have subsequent pregnancies of normal duration (Bloom et al, 2001; Moore, 2008). If a woman has had one previous preterm birth, her risk of recurrence is 17.2%; with two previous preterm births it is 28%. If a woman had a prior term delivery, her risk of having a preterm delivery in her next pregnancy is only 4.4% (Bakketeig & Hoffman, 1981). The risk of preterm birth is highest when the previous preterm was in the penultimate pregnancy if there was a history of multiple preterm births (Wyly, 1995). Within the data set, this was a nominal variable with 1 indicating previous preterm birth and 0 indicating no prior preterm birth.

→ Nulliparity

Parity refers to the number of times a woman has delivered a pregnancy at least 20 weeks of gestation and is often divided into two groups: nulliparous (no previous deliveries) and parous (at least one previous delivery) (Bai et al, 2002). The influence of parity depends on the gestational age of delivery of prior pregnancies. If the woman has had prior term deliveries, being parous reduces her risk of preterm birth in the next pregnancy, compared with nulliparous women. If however she has had at least one prior preterm birth, being parous increases her risk of preterm birth, compared to nulliparous women (Smith et al, 2006). In the original data set, parity was a continuous variable. A new dichotomous variable based on parity was created for analysis. Parity of 0 (ie. nulliparous) was coded as 1 while parity of 1 or higher (ie. not nulliparous) was coded as 0.

→ Employment status

Employment status has been shown to have an impact on preterm birth. A study by Rodrigues and Barros (2008) showed that women who were unemployed when they became pregnant were at a significantly increased risk of spontaneous preterm delivery. In the original data set employment status was coded as not working, part-time, or full-time. This variable remained unchanged for the analysis.

→ Maternal age

The literature indicates that the woman's age can have an impact on preterm birth (Caughey, 2009). This variable was left as continuous in the analysis.

3.4.1.2 Analysis of Secondary/Other Maternal Outcomes

Type of Delivery

Caesarean delivery can impact the health of both mother and infant, in the short and long term (Udy, 2009). It is major abdominal surgery with potential maternal and neonatal complications (Levine et al, 2001).

Type of delivery was coded as vaginal/vaginal breech, Caesarean delivery, or stillbirth/stillbirth breech in the database. Frequency counts for stillbirth/stillbirth breech indicated that the numbers were insufficient (n = 34) to warrant being included in the analysis. Thus, the stillbirth/stillbirth breech option was excluded from the analysis. Women undergoing vaginal delivery were coded as 1 and those having a Caesarean delivery were coded as 2.

Type of Labour

Labour may be induced for a number of reasons, including maternal complications (such as pre-eclampsia, diabetes, chorioamnionitis,) and/or fetal complications (such as abnormal fetal surveillance) (Moleti, 2009). However, labour induction should only be undertaken for valid medical reasons because of the risks involved with induction of labour, including possible increased risks of Caesarean delivery, failure to achieve labour, chorioamnionitis, cord prolapse, and uterine rupture in certain circumstances (such as a scar on the uterus) (Moleti, 2009; Simpson & Thorman, 2009).

Type of labour was coded as spontaneous, induced, or no labour in the database. No labour included those women for whom a Caesarean delivery was performed prior to the onset of labour or induction and was excluded from the analysis for this specific outcome. Women who had their labour induced were coded as 1 and those who had spontaneous onset of labour were coded as 2.

Administration of Tocolytics

In some cases of preterm labour, medications called tocolytic agents are used to try to stop uterine contractions and delay delivery (Iams, 2002). In the database, this variable was coded 1 for yes and 2 for no.

3.4.2 Analysis of the Infant Data

3.4.2.1 Apgar Score

The Apgar score is a method for evaluating the condition of the newborn infant immediately after birth, and provides a standardized mechanism to record fetal to neonatal transition (Kattwinkel, 2006; see page 8 for full definition). A score of seven or higher indicates that the infant's condition is good to excellent (Casey et al, 2001). The Apgar score is determined at one and five minutes after delivery, and is therefore a rapid way to evaluate the physical condition of newborn infants (Finster, M, and Wood, M), and has been used to assess the condition and prognosis of newborn infants throughout the world for over 50 years (Casey et al, 2001).

In the original data set, the Apgar scores variable was a continuous variable. However, since a score of seven seems to be an indication of the infant's condition, a new dichotomous variable was created for both one minute and five minute Apgar scores. A score of less than seven was coded as 1 while a score of seven or higher was coded as 2.

3.4.2.2 Admission to the Neonatal Intensive Care Unit (NICU)

The NICU is a unit of a hospital specializing in the care of ill or premature newborn infants. Since the development of these units in the 1950's, technology has dramatically changed, increasing the chances of survival for the very low birth weight and premature infants (McGrath & Sullivan, 2002). While the NICU environment has facilitated better survival rates, they also present problems as the NICU environment can easily tax a premature infant (Ward et al, 2003). Consequently, infants who spend time in the NICU are at a higher risk for developing complications such as infection, (Ward et al, 2003) neurologic and ophthalmologic complications. The variable in the database was a dichotomous variable with yes coded as 1 and no coded as 2.

3.4.2.3 Respiratory Complications

Premature infants or those with an extremely low birth weight may need to be resuscitated, either by endotracheal intubation or manual inflation of the lungs (known as bag and mask) (Roberton, 1999; Finer et al, 2009; Rajani et al, 2009). Approximately 10% of newborns require some assistance to begin breathing, and 1% may require more intensive resuscitation methods (Wiswell, 2003; Kattwinkel, 2006). While death is the most severe complication, other complications such as brain injury and cardiovascular complications can occur (Wiswell, 2003).

There were three variables in the database that were indicative of respiratory issues: bag-and-mask, ventilation for at least 30 minutes, and insertion of endotracheal tube. For each variable, yes was coded as 1 and no was coded as 2.

3.4.2.4 Birth Weight

Birth weight is strongly associated with mortality risk during the first year of life (Wilcox & Skjoerven, 1992; Wilcox, 2001). Birth weight normally ranges between 2,500 and 4,000 g. Infants with a birth weight of less than 2,500 g are considered to be low birth weight (Wilcox, 2001). In the original data set, infant birth weight was a continuous variable. A new dichotomous variable was created with weights of less than 2,500 g being coded as 1 and weights of 2,500 g or higher being coded as 2. For high birth weight, the continuous variable was recoded into a dichotomous variable with a weight of less than 4,000 g being 1 and a weight of 4,000 g or more being 2.

3.5 Statistical Analysis

SPSS 16.0 (SPSS Inc, Chicago, IL, USA) was used as the statistical package for analysis of the data. Descriptive statistics were used to describe the demographics of the population. Student's *t* test was used to compare continuous outcomes, and categorical variables were compared with Chi-squared analysis. Multiple logistic regression was used to control for potential confounders to determine if exposure to second hand smoke in non-smokers independently increases the risks of adverse outcomes (that are categorical in nature). Potential confounders included in initial models were: previous preterm birth, maternal age, employment status, and parity (nulliparous). For the outcomes of type of delivery (Caesarean delivery), type of labour (labour induction) and NICU admission, gestational length and birth weight were also included in the models. For the outcome low birth weight, the logistic regression models were run both including and excluding gestational length, to determine if the gestational age explained the birth weight or were fetuses/infants truly a smaller birth weight by each gestational age week. The logistic model was created using the backwards stepwise selection method. This method starts with all explanatory variables included in the model and then removes the least significant explanatory variable at each step, until only variables with a p value ≤ 0.10 remain in the model. In this way, variables will be automatically removed until the optimum model is found. For the primary outcome, a p-value less than 0.05 was considered significant for the logistic regression models. For the secondary outcomes by logistic regression, a p-value of less than 0.01 was considered significant; and for other outcomes, a p-value of less than 0.001 was used. The reason for assigning different p-values was to avoid over interpretation of statistically significant findings given the number of comparisons. For the purpose of logistic regression models all dichotomous variables were recoded – 1 = yes and 0 = no.

3.6 Confidentiality and Ethics

Data obtained from the NLPPP database did not contain any identifying information pertaining to mother and/or child. Data was assimilated in aggregate form. Any data relevant to the proposed study was kept in a locked office. A password protected computer system and database were also utilized. Only the researchers affiliated with the study were able to have access to the information. Ethical approval for the study was obtained from the Human Investigation Committee of Memorial University.

Chapter 4 – Results

4.1 Sample

The time period for this study was from April 1, 2001 to March 31, 2007. Data on a total of 15,463 women were available. Women who indicated they were currently smoking (n=2,515) or for whom their current smoking status was unknown (n=155) were excluded. Women were also excluded if their health region status was unknown (n=27), they were from outside the province (n=153), or if they were pregnant with multiple gestations (n = 257). Lastly, women whose exposure to second hand smoke was unknown (n=2,354) were excluded. The resulting study size was 10,002 women, 1,051 non-smoking women exposed to second hand smoke and 8,951 non-smoking women not exposed to second hand smoke (Figure 1).

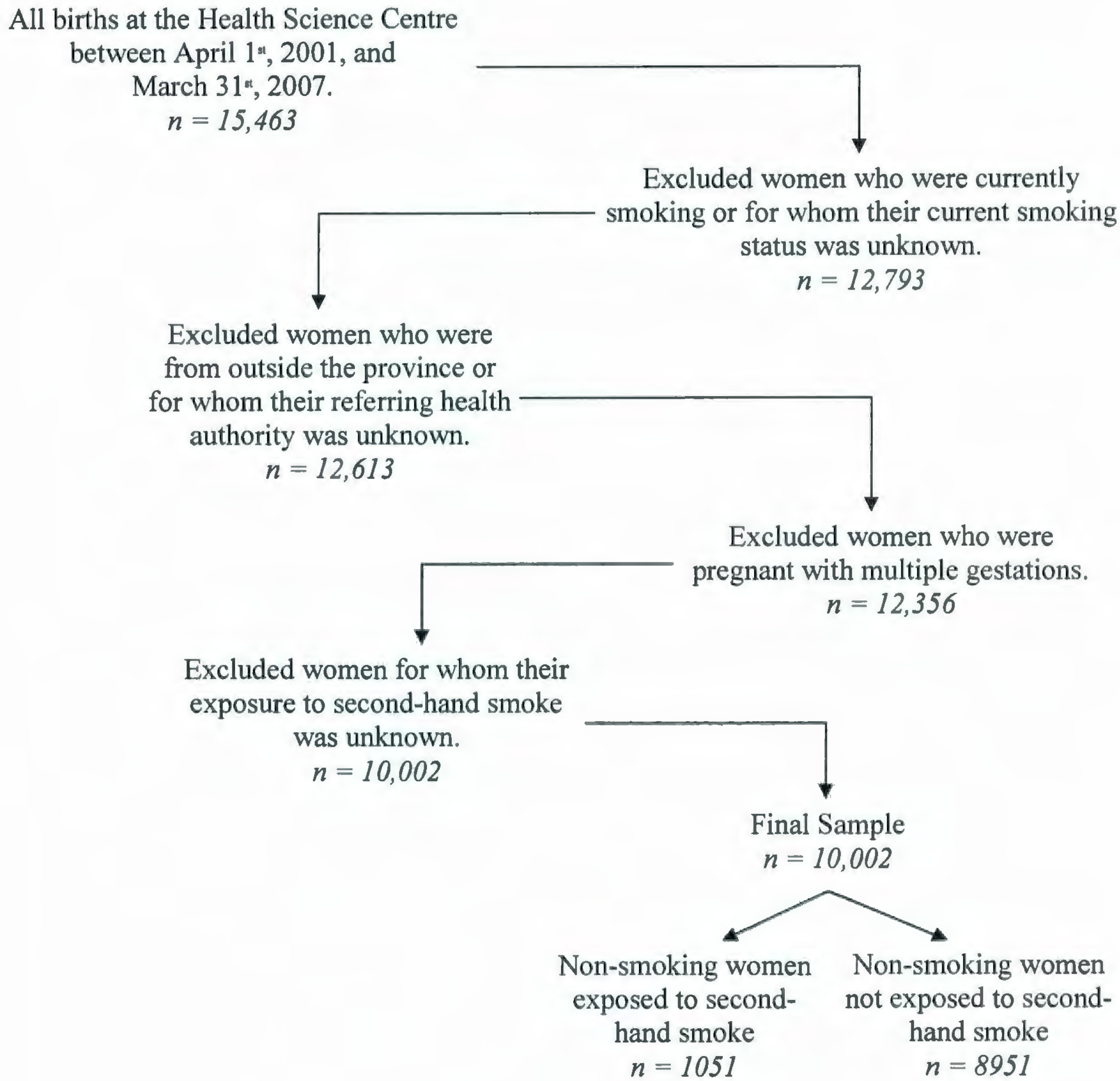

Figure 1. Exclusion Criteria.

4.2 Representativeness of the Sample

To ensure the representativeness of the sample between the study group and those for whom second hand smoke exposure was unknown and thus excluded from the study group, Pearson Chi-square analyses were performed on the following variables: nulliparous, age grouped less than 18 or greater than 35 and between 19 and 34, work status, and referring health authority. Student's *t* test was used to compare mean maternal age and mean gestational age. The results are summarized in Table 1.

There was no significant difference between the groups on the variables parity ($p = 0.566$), maternal age when grouped less than 18 or greater than 35 and between 19 and 34 ($p = 0.305$), and previous preterm birth ($p = 0.100$). Significant differences were found between the groups on group regarding mean maternal age ($p < 0.0001$), mean gestational age ($p < 0.0001$), working status ($p < 0.0001$), and referring health authority ($p < 0.0001$).

The biggest difference between the two groups was with respect to work status and to referring health authority. The missing group had a much higher percentage of women indicate they were not working (47.1%) when compared to the study group (21.4%). The missing group also had a much higher percentage from the Western Regional health authority (1.7%) than the study group (0.5%).

It is interesting to note that there was also a difference between the groups regarding overall rate of preterm birth (< 37 weeks). The mean gestational age between the groups, though statistically significantly different, was relatively close (and thus not likely clinically significant) – study group = 38.91 weeks, missing data group = 38.70. But the overall preterm birth rate for the missing data group was much higher at 12.1% than the study group preterm birth rate of 8.4% (n = 838/10,000).

Table 1: Representativeness of the Sample

	Study Sample n = 10,002		Sample for whom exposure to second hand smoke was unknown n = 2,354		p-value
Characteristic	n	(%)	n	(%)	
Parity					
Nulliparous	5,105	51.0	1,186	50.4	0.566
Para 1 or greater	4,897	49.0	1,168	49.6	
Maternal Age (years)					
<18 and > 35	1,896	19.0	468	19.9	0.305
Between 19 and 34	8,106	81.0	1,886	80.1	
Maternal Age (years)⅄	29.92 ± 4.99		29.45 ± 5.28		<0.0001
Gestational Length (weeks)⅄	38.91 ± 2.25		38.70 ± 3.91		<0.0001
Preterm Birth Rate	838	8.4%.	287	12.1%	
Previous Preterm Birth*					
Yes	356	3.6	100	4.3	0.100
No	9,636	96.4	2,239	95.7	
Maternal Work Status**					
Not working	1,542	21.4	297	47.1	<0.0001
Part-time	630	8.8	46	7.3	
Full-time	5,024	69.8	287	45.6	
Health Authority					
Eastern	9,681	96.8	2,241	95.2	<0.0001
Central	157	1.6	46	2.0	
Western	55	0.5	41	1.7	
Labrador/Grenfell	109	1.1	26	1.1	

⅄mean ± standard deviation
*n = 9992
**n = 7196

4.3 Characteristics

The characteristics of the 10,002 women are summarized in Table 2. Approximately half the women (51.0%) were nulliparous, 19.0% were less than 18 or older than 35 years of age, and 3.6% had had a previous preterm birth. The majority (96.8%) were from the Eastern Health Region, and over two-thirds (69.8%) were working full-time. The mean age was 29.92 (years) while mean gestation length was 38.91 (weeks). The overall preterm birth rate was 8.4% (n = 838/10,000).

Table 2: Characteristics of the Women in the Study

	Total Sample n = 10,002	
Characteristic	n	(%)
Parity		
Nulliparous	5,105	51.0
Para 1 or greater	4,897	49.0
Maternal Age (years)		
<18 and > 35	1,896	19.0
Between 19 and 34	8,106	81.0
Maternal Age (years)⅄	29.92 ± 4.99	
Gestation Length (weeks)⅄	38.91 ± 2.25	
Previous Preterm Birth*		
Yes	356	3.6
No	9,636	96.4
Maternal Work Status**		
Not working	1,542	21.4
Part-time	630	8.8
Full-time	5,024	69.8
Health Authority		
Eastern	9,681	96.8
Central	157	1.6
Western	55	0.5
Labrador/Grenfell	109	1.1

⅄ mean ± standard deviation
*n = 9992
**n = 7196

Table 3 summarizes the differences in maternal characteristics between those who were exposed to second hand smoke and those who were not. Significant differences were found between the two groups with respect to mean maternal age ($t = 120.696$, $\rho < 0.0001$), mean gestational age ($t = 5.060$, $\rho = 0.025$), previous preterm birth ($\chi^2 = 5.545$, $p = 0.019$, df

= 1), parity ($\chi^2 = 1.22$, $p < 0.0001$, df = 1), and work status ($\chi^2 = 1.23$, $p < 0.0001$, df = 2). The mean age for women exposed to second hand smoke was 27.11 years while for the women not exposed to second hand smoke the mean age was 30.24 years. Mean gestation length for women exposed to second hand smoke was 38.88 (weeks) and 38.91 (weeks) for women not exposed to second hand smoke. Only 2.3% of the women exposed to second hand smoke had had a previous preterm birth as compared to 3.7% of women not exposed to second hand smoke. Approximately two thirds (67.1%) of women exposed to second hand smoke had never given birth before while only 49.1% of women not exposed to second hand smoke had never given birth before. Slightly more than half (53.8%) of women exposed to second hand smoke were working full time as compared to 71.9% of women not exposed to second hand smoke.

Table 3: Characteristics of Women by Exposure to Second Hand Smoke

	Women Exposed to Second Hand Smoke n = 1,051		Women Not Exposed to Second Hand Smoke n = 8,951		P
Characteristic	n	(%)	n	(%)	
Maternal Age (years)⅄	27.11 ± 5.86		30.24 ± 4.77		<0.0001
Gestational Length (weeks)⅄	38.88 ± 2.17		38.91 ± 2.25		0.025
Previous Preterm Birth*					
Yes	24	2.3	332	3.7	0.019
No	1,025	97.7	8,611	96.3	
Parity					
Nulliparous	706	67.1	4,399	49.1	<0.0001
Para 1 or greater	345	32.8	4,552	50.8	
Maternal Work Status**					
Not working	293	35.1	1,246	19.7	<0.0001
Part-time	93	11.1	537	8.4	
Full-time	449	53.8	4,575	71.9	

⅄ = mean ± standard deviation
*n = 1049
**n = 835

4.4 Effects of Second hand Smoke Exposure on the Infant

Evaluating infants born to non-smoking women exposed to second hand smoke, 10.0% were born less than 37 weeks gestation, 3.4% less than 34 weeks gestation, 7.1% had a birth weight of less than 2,500g, 13.8% of the infants were admitted to the NICU, 14.3% had an Apgar score of less than seven at one minute, and 3.3% had an Apgar score of less than seven at five minutes. Table 4 shows the differences between the groups.

Table 4: Neonatal Outcomes by Exposure to Second Hand Smoke

	Women Exposed to Second Hand Smoke N = 1,051	Women Not Exposed to Second Hand Smoke n = 8,951	P
Characteristic	N (%)	N (%)	
Gestational Age - weeks ⅄	38.88 ± 2.18	38.91 ± 2.26	0.025
Gestation < 37 weeks	106 10.0%	732 8.2%	0.035
Gestation < 34 weeks	36 3.4%	199 2.2%	0.015
BW - grams ⅄	3,421 ± 643	3,505 ± 612	0.036
BW < 2,500 grams	81 7.1%	433 4.8%	<0.0001
BW > 4,000 grams	159 15.2%	1,566 17.5%	0.056
Apgar < seven, one minute	149 14.3%	1,055 11.8%	0.023
Apgar < seven, five minutes	35 3.3%	217 2.4%	0.076
NICU Admission	145 13.8%	938 10.5%	0.001
Respiratory Complications			
Use of bag-and-mask	93 8.9%	681 7.6%	0.155
Ventilation > 30 minutes	23 2.2%	129 1.4%	0.372
Endotracheal intubation	36 3.4%	262 2.9%	0.062

⅄ = mean ± standard deviation

Exposure to second hand smoke was associated with preterm birth less than 37 weeks of gestation ($\chi^2 = 4.450$, p = 0.035, df = 1), low birth weight ($\chi^2 = 15.930$, p < 0.0001, df = 1), and admission to NICU ($\chi^2 = 10.719$, ρ = 0.001, df = 1); and trends of preterm birth less than 34 weeks of gestation ($\chi^2 = 5.92$, p = 0.015, df = 1), and Apgar score at one minute ($\chi^2 =$

5.161, ρ = 0.023, df = 1). There was no significant difference between the groups with respect to high birth weight (χ^2 = 3.661, p = 0.056, df = 1) or the five minute Apgar score (χ^2 = 3.151, ρ = 0.076, df = 1). Three indicators for resuscitation were examined: bag-and-mask, requiring ventilation for more than 30 minutes, and placement of an endotracheal tube. None of the indicators were significant. However, the most invasive indicator, endotracheal intubation, had a p-value close to 0.05.

4.5 Effects of Second hand Smoke Exposure on the Woman

There was a significant difference between the groups regarding type of labour (χ^2=17.128, p <0.0001, df = 1). More women (40.9% compared with 34.1%) exposed to second hand smoke had their labour induced. Although fewer women (25.6% compare with 28.5%) exposed to second hand smoke had Caesarean delivery, this did not reach statistical significance by the preset p value for significance of < 0.01 for secondary outcomes. There was no significant difference regarding type of delivery (χ^2=4.118, p = 0.042, df = 1) or administration of tocolytics and exposure to second hand smoke (χ^2=0.044, p=.834, df = 1). The results are summarized in table 5.

Table 5: Maternal Outcomes by Exposure to Second Hand Smoke

	Women Exposed to Second Hand Smoke n = 1,051	Women Not Exposed to Second Hand Smoke n = 8,951	P
Characteristic	n (%)	n (%)	
Labour Induced*	387/946 40.9	2,622/7,686 34.1	<0.0001
Caesarean Delivery**	266/1,041 25.6	2545/8,916 28.5	0.042
Tocolytic Use	5/1,050 0.5	47/8,646 0.5	0.834

*Analysis only included those for whom labour was spontaneous or induced.
**Analysis only included those for whom delivery was vaginal or Caesarean delivery

4.6 Logistic Regression Evaluating Outcomes of Interest

4.6.1 Preterm Birth

Logistic regression analyses were done to examine the effects of second hand smoke exposure on preterm birth including the variables: second hand smoke exposure, previous preterm birth, maternal age (in years), employment status, and nulliparous. The results are summarized in Tables 6 and 7.

4.6.1.1 Preterm Birth Less than 37 Weeks

Significant differences were identified in previous preterm birth and nulliparity. Neither second hand smoke exposure, maternal age, nor work status yielded a significant difference. A non-smoking woman exposed to second hand smoke exposure was 1.24 times more likely to have a preterm birth of less than 37 weeks, but this did not reach statistical significance (p=0.106). Having had a previous preterm birth increased the risk for preterm birth of less than 37 weeks by a factor of 6.57, as did being nulliparous (odds ratio 2.26).

Table 6: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Preterm birth Less Than 37 Weeks

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	1.22	0.139	0.94	1.57
	Previous Preterm Birth	6.56	<0.0001	4.72	9.10
	Maternal Age (in years)	1.02	0.023	1.00	1.04
	Employment Status	0.93	0.225	0.83	1.04
	Nulliparous	2.30	<0.0001	1.87	2.84
Final Model	Previous Preterm Birth	6.57	<0.0001	4.74	9.14
	Maternal Age (in years)	1.02	0.085	1.00	1.03
	Nulliparous	2.26	<0.0001	1.85	2.77

4.6.1.2 Very Preterm Birth less than 34 Weeks

Much like with preterm birth at 37 weeks, significant differences were identified in previous preterm birth and nulliparity (Table 7). Having a previous preterm birth increased the risk for preterm birth less than 34 weeks by a factor of 8.78 as did being nulliparous (odds ratio 2.37). However, unlike preterm birth less than 37 weeks of gestation, second hand smoke exposure was found to have a significant independent impact on preterm birth less than 34 weeks of gestation. A woman exposed to second hand smoke was 1.84 times more likely to have a preterm birth less than 34 weeks (p=0.003).

Table 7: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Preterm birth Less Than 34 Weeks

All Variables	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
	Second Hand Smoke Exposure	1.87	0.003	1.23	2.84
	Previous Preterm Birth	8.71	<0.0001	5.03	15.08
	Maternal Age (in years)	1.01	0.448	0.98	1.05
	Employment Status	0.94	0.553	0.76	1.16
	Nulliparous	2.50	<0.0001	1.65	3.77
Final Model	Second Hand Smoke Exposure	1.84	.003	1.23	2.77
	Previous Preterm Birth	8.78	<.0001	5.07	15.20
	Nulliparous	2.37	<.0001	1.60	3.52

4.6.2 Birth Weight <2500g

Univariate analysis of the effects of second hand smoke exposure on birth weight indicated that second hand smoke exposure had a significant impact on low birth weight (less than 2,500g). Logistic regression analysis including the variables second hand smoke exposure, previous preterm birth, maternal age (in years), employment status, nulliparous, and gestational length was performed.

Second hand smoke exposure, maternal age, being nulliparous, and gestational age were all found to have a significant impact on birth weight (Table 8). If the woman had been exposed to second hand smoke, the newborn was 1.75 times more likely to be of low birth weight. This result indicates that in addition to increasing the risk for preterm birth, second hand smoke exposure increased the risk for small for gestational age infant, independent of gestational age.

Table 8: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Low Birth Weight

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	1.72	.013	1.12	2.63
	Previous Preterm Birth	0.82	.589	0.40	1.69
	Maternal Age (in years)	0.96	.017	0.93	0.99
	Employment Status	0.95	.588	0.77	1.16
	Nulliparious	2.08	<.0001	1.42	3.05
	Gestational Length (in weeks)	0.36	<.0001	0.33	0.39
Final Model	Second Hand Smoke Exposure	1.75	.009	1.15	2.67
	Maternal Age (in years)	0.96	.007	0.93	0.99
	Nulliparious	2.12	<.0001	1.49	3.00
	Gestational Length (in weeks)	0.36	<.0001	0.34	0.39

4.6.3 NICU Admission

Variables included in the logistic regression model for NICU admission were second hand smoke exposure, maternal age (in years), gestational length (in weeks), previous preterm birth, nulliparous, and birth weight (in grams). Results indicate that gestational length (in weeks) and being nulliparous were found to have a significant impact on admission to the NICU.

While second hand smoke exposure was not statistically significantly associated with NICU admission, by the preset significant p value of < 0.01, there was a trend to an increased risk of NICU admission (p= 0.046). If the woman had been exposed to second hand smoke, the newborn was 1.24 times more likely to be admitted to the NICU. A longer gestation length reduced the risk of the infant being admitted to the NICU, but being nulliparous increased this risk (see Table 9).

Table 9: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Admission to the Neonatal Intensive Care Unit (NICU)

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	1.25	.048	1.00	1.55
	Previous Preterm Birth	1.19	.332	0.83	1.68
	Maternal Age (in years)	1.00	.930	0.99	1.02
	Nulliparous	1.89	< .0001	1.61	2.21
	Gestation Length (in weeks)	0.62	< .0001	0.59	0.64
	Birth Weight (in grams)	1.00	.971	1.00	1.00
Final Model	Second Hand Smoke Exposure	1.24	.046	1.00	1.54
	Nulliparous	1.85	< .0001	1.60	2.14
	Gestation Length (in weeks)	0.61	< .0001	0.59	0.63

4.6.4 Type of Delivery

The following variables were included in the logistic regression model for type of delivery: previous preterm birth, nulliparous, employment status, second hand smoke exposure, maternal age (in years), gestational length (in weeks), and birth weight (in kilograms). Maternal age, gestational length, and birth weight were continuous variables. The results are summarized in Table 10.

Being nulliparous, maternal age, gestational length, and birth weight were found to have a significant impact on type of delivery. The longer the gestational length, the lower the risk of Caesarean delivery. However, parity, maternal age, and birth weight increased the risk of Caesarean delivery. For each year older in age, there was a 7% increase for

Caesarean delivery, and for each kilogram increase there was an 86% increase for Caesarean delivery. Second hand smoke exposure was not independently associated with Caesarean delivery, suggesting that its significance in the univariate analysis is mediated through other confounders including birth weight and parity.

Table 10: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Type of Delivery (Caesarean Delivery)

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	1.04	.644	0.88	1.24
	Previous Preterm Birth	1.10	.507	0.83	1.47
	Maternal Age (in years)	1.08	<.0001	1.06	1.09
	Employment Status	0.96	.231	0.89	1.03
	Nulliparous	1.52	<.0001	1.35	1.71
	Gestation Length (in weeks)	0.81	<.0001	0.79	0.84
	Birth Weight (in kilograms)	1.87	<.0001	1.67	2.10
Final Model	Maternal Age (in years)	1.07	<.0001	1.06	1.09
	Nulliparous	1.49	<.0001	1.33	1.67
	Gestation Length (in weeks)	0.81	<.0001	0.79	0.84
	Birth Weight (in kilograms)	1.86	<.0001	1.66	2.10

4.6.5 Type of Labour

The results for the logistic regression regarding type of labour are summarized in Table 11. Previous preterm birth, nulliparous, employment status, second hand smoke exposure, maternal age (in years), gestational length (in weeks), and birth weight (in kilograms) were the variables included. Maternal age, gestational length, and birth weight were continuous variables.

Second hand smoke exposure and being nulliparous increased the risk of being induced as did increasing maternal age and gestational age Women exposed to second hand smoke were 1.31 times more likely to be induced, and were 2.02 times more likely to be induced if nulliparous. For each year older in age there was a 2% increase in induction, and for each week further in gestation, there was a 23.4% increase in induction.

Table 11: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Type of labour (Labour Induction)

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	1.31	.001	1.11	1.54
	Previous Preterm Birth	1.11	.546	0.79	1.56
	Maternal Age (in years)	1.02	.001	1.01	1.03
	Employment Status	1.00	.979	0.93	1.07
	Nulliparous	2.04	<.0001	1.81	2.30
	Gestation Length (in weeks)	1.24	<.0001	1.19	1.29
	Birth Weight (in kilograms)	0.86	.012	0.77	0.97
Final Model	Second Hand Smoke Exposure	1.31	.001	1.11	1.54
	Maternal Age (in years)	1.02	.001	1.01	1.03
	Nulliparous	2.02	<.0001	1.80	2.27
	Gestation Length (in weeks)	1.23	<.0001	1.19	1.28
	Birth Weight (in kilograms)	0.86	.012	0.77	0.97

4.6.5.1 Additional Analysis of Spontaneous Preterm Birth Less Than 34 Weeks of Gestation

Initial analysis evaluating the effects of second hand smoke exposure on labour induction and on preterm birth less than 34 weeks included all spontaneous and indicated births. In light of these findings, an additional analysis was performed to investigate whether spontaneous preterm birth less than 34 weeks was more likely in women exposed to second hand smoke. To answer this question, a new variable was created where preterm birth less than 34 weeks and spontaneous labour was coded as 1, while preterm birth less than 34 weeks with induction or Caesarean delivery, or women with delivery at 34 weeks or greater was coded as 0.

The results from the logistic regression are summarized in Table 12. Exposure to second hand smoke, previous preterm birth, and being nulliparous were found to have a significant impact on spontaneous preterm birth less than 34 weeks. Non-smoking women exposed to second hand smoke were 2.1 times more likely to have spontaneous preterm birth less than 34 weeks.

Table 12: Logistic Regression Analysis Comparing Exposure and No Exposure to Second Hand Smoke in Non-smoking Women on Spontaneous Preterm Birth Less than 34 Weeks

	Outcome	Adjusted OR	P	95% CI	
				Lower	Upper
All Variables	Second Hand Smoke Exposure	2.04	.011	1.18	3.52
	Previous Preterm Birth	12.62	<.0001	6.32	25.21
	Maternal Age (in years)	1.06	.015	1.01	1.10
	Employment Status	0.88	.368	0.68	1.16
	Nulliparous	2.88	<.0001	1.64	5.07
Final Model	Second Hand Smoke Exposure	2.10	.007	1.22	3.62
	Previous Preterm Birth	12.68	<.0001	6.35	25.33
	Maternal Age (in years)	1.05	.025	1.01	1.10
	Nulliparous	2.76	<.0001	1.58	4.81

Chapter 5 - Discussion

Second hand smoke has been classified as a Class A cancer-causing substance (Floyd et al, 1991; Clean Air Coalition of BC, 2000). Scientific evidence indicates that there is no risk-free level of exposure to second hand smoke (Changing Fertility Patterns, 2005). In Canada, tobacco use – and by extension second hand smoke - is a very preventable cause of death and disease (Greaves & Barr, 2007).

Rates of preterm birth in Canada as well as many other countries have been increasing over the last 25 years (Joseph et al, 1998). This is an important health issue as, together with low birth weight, it is now the leading cause of infant mortality in the United States (Blackmore et al, 1994).

Research to date has shown that pregnant women exposed to second hand smoke are at increased risks for adverse outcomes. This is a particularly important fact given that recent fertility trends occurring in Canada and other industrialized nations show that women are having children at a more advanced age (Changing Fertility Patterns, 2005). This, in itself, places these women at greater health risks.

5.1 Study Outcomes

5.1.1 Perinatal Outcomes and Second Hand Smoke Exposure

5.1.1.1 Preterm Birth

The primary objective was to determine if the rate of preterm birth less than 37 weeks of gestation for non-smoking pregnant women who self-reported exposure to second hand smoke during the pregnancy was higher than for non-smoking pregnant women who self-reported no exposure to second hand smoke during the pregnancy. After controlling for potential confounders, the results indicated that exposure to second hand smoke did not have a significant impact on preterm birth less than 37 weeks. This finding is consistent with the current findings in the literature. Studies done by Windham et al (2000), Geol et al (2004), and Fantuzzi et al (2007) found no increase for preterm birth < 37 weeks with second hand smoke exposure. However, unlike Goel et al (2004) and Fantuzzi et al (2007), who had small sample sizes, this study had a larger sample size. The large sample size of the current study reduced the risk for Type II error. The current study had an 80% power to see a 1/3 increase in preterm birth less than 37 weeks of gestation, had it existed. There was not however, adequate power to see a smaller difference in preterm birth less than 37 weeks.

More importantly, though, analysis of the data did show that second hand smoke exposure had a significant impact on preterm birth less than 34 weeks of gestation. Finding that second hand smoke exposure, even when controlling for other variables, increased the risk for preterm birth less than 34 weeks is a very important clinical finding as infants born at less than 34 weeks have higher rates of morbidity and mortality than those born at 34 to 37 weeks. Preterm birth is one of the central issues in perinatal health care. Preterm infants are at higher risk of being readmitted to the hospital, (UK Healthcare, n.d.), can suffer long-term effects such as central nervous system (CNS) complications, neurodevelopmental delay (Zwicker et al, 2008), respiratory complications, and visual and hearing impairments (UK Healthcare, n.d.). While Windham et al (2000) and Fantuzzi et al (2007) did find an increased risk for very preterm birth, their cut-off for very preterm birth was 35 weeks. The current study used the definition of very preterm birth of 34 weeks as the cut-off and found a higher rate of preterm birth less than 34 weeks with second hand smoke exposure. From the studies identified in the literature review, this is the first study to find such effects at preterm birth less than 34 weeks.

5.1.1.2 Birth weight and low birth weight

Birth weight is strongly associated with mortality risk during the first year of life (Wilcox et al, 1992; Wilcox, 2001). While the majority of children born with a birth weight less than 2,500 g do not experience long term negative effects, they are at a higher risk for health and developmental challenges than are normal birth weight infants (Hack, 2007). Infants with a birth weight of less than 2,500 g experience combinations of various neurosensory, developmental, and health problems which compound the clinical and educational outcomes (Hack et al, 1995). In the current study, the mean birth weight of infants born to non-smoking women exposed to second hand smoke was lower than infants born to non-smoking women not exposed to second hand smoke, and the rate of low birth weight <2,500 g was significantly higher in those exposed to second hand smoke.

This finding is in agreement with the current literature. As previously mentioned, exposure to second hand smoke during pregnancy has an approximate reduction of birth weight ranging from 33 g to 192 g (Martin et al, 1986; Mainous et al, 1994; Roquer et al, 1995; Misra et al, 1999; Hruba et al, 2000; Dejmek et al, 2002; Goel et al, 2004; Leonardi-Bee et al, 2008). This study found a decrease in mean birth weight of 84 g. In addition to the negative health effects, low birth weight has substantial financial implications as well. It is estimated that the lifetime costs for each preterm, low birth weight baby is about $675,000 (1995 data). This translates to a tremendous financial burden on the Canadian health care system (Ottawa Coalition for the Prevention of Low Birth Weight, n.d.). The financial impact of low birth weight infants is not limited to the infant themselves. Over 5 billion dollars in workplace productivity is lost annually in the time away from work for parents of low birth weight infants (Ottawa Coalition for the Prevention of Low Birth Weight, n.d.).

5.1.1.3 NICU Admission

Significant results were not found when comparing NICU admissions and exposure to second hand smoke. However, there was a trend towards a higher rate of NICU admission in this group, and this may be clinically important. Admission to the NICU can be considered a surrogate marker of perinatal morbidity (McGrath & Sullivan, 2002; Kirkby et al, 2007). Infants are only admitted to the NICU when they have clinical concerns.

The NICU environment can easily tax a premature infant due to the excessive stimulation that is typical for the care evident in the units (Wyly, 2001; Ward et al, 2003). Infants in the NICU are exposed to numerous sounds and lights, and must try to adapt to this environment. Responding to this environment may result in changes in the infant's colour, increased or decreased respiration rates, and interruptions in the sleep-wake pattern (Wyly, 2001).

Infants who spend time in the NICU are at a higher risk for developing complications such as infection, (Ward et al, 2003), ophthalmologic or neurologic complications, including hearing loss (Wyly, 2001). Furthermore, these infants are at increased risk for re-hospitalization, spending on average 2.1 days in hospital by their first birthday, are at an increased risk of dying before their first birthday (Niven et al, 1995), and are more likely to have developmental problems (Darlow et al, 2009). Additionally, parental separation when babies are in NICU is a major stressor to parents, even when the baby is not seriously ill (Nystrom & Axelsson, 2002). Parent-infant interaction is adversely altered when infants are in the NICU (Wyly, 2001). Finally, NICU care is costly ($1,180 to $1,702 per day) (Lee &

Anderson, 2004), even in the absence of morbidities without long-term consequences (Kirkby et al, 2007).

5.1.1.4 Apgar Score

The Apgar score is a way to evaluate the physical condition of newborn infants (Finster et al, 2005; Kattwinkel, 2006). A trend was found at the one minute testing, and this may indicate that infants born to women exposed to second hand smoke are in greater distress at birth than those infants born to women not exposed to second hand smoke. A low one minute Apgar score is beneficial in helping to identify the newborn that requires special attention; however, the one minute Apgar score does not correlate with any particular future outcome (Letko, 1994).

While there was no statistically significant difference in the five minute score, the p-value was close to 0.05 which would indicate a trend for infants born to women exposed to second hand smoke to have a lower five minute Apgar score. A low Apgar score at five minutes can often be an indicator for complications, namely that the newborn infant has not transitioned to extra-uterine life (Thorngren-Jerneck et al, 2001). Furthermore, an association between an Apgar score of less than seven at five minutes and low cognitive function in early childhood has been shown (Odd et al, 2008; Ehrenstein et al, 2009). This could be taken to indicate that the effects of second hand smoke exposure extend well beyond birth, and could have long lasting effects.

5.1.1.5 Respiratory complications

While no significant results were found between second hand smoke exposure and the respiratory issues of bag-and-mask, ventilation for at least 30 minutes, and insertion of endotracheal tube, the p-value for insertion of the endotracheal tube was close to significance. This would indicate that there is a trend for infants born to non-smoking mothers exposed to second hand smoke to require an endotracheal tube. Insertion of an endotracheal tube is an invasive procedure which can result in complications such as hypoxia, bradycardia, lacerations of the tongue, gums, or airway, and infection (Kattwinkel, 2006).

In addition to the problems facing placement of the endotracheal tube, there are other complications that arise when an infant requires resuscitation. Infants, especially preterm infants, are vulnerable to ophthalmic and neurologic injury from excess oxygen (Kattwinkel, 2006). They are also more susceptible to having their lungs injured (Kattwinkel, 2006).

5.1.2 Maternal Outcomes and Second hand Smoke Exposure

5.1.2.1 Caesarean delivery

A trend was noted when type of delivery was examined by univariate analysis. Initially, the finding that more women exposed to second hand smoke had vaginal delivery was surprising. However, evaluation of this finding in the context of the entire analysis would indicate that this makes sense. Since infants born to mothers exposed to second hand smoke are of a smaller birth weight and an earlier gestation, it is plausible that more of these infants were born vaginally. When logistic regression controlled for potential confounders, exposure to second hand smoke was not independently associated with type of delivery, suggesting that the mechanism for the trend seen by univariate analysis is possibly through other independent variables, such as maternal age, parity, gestational age and birth weight.

5.1.2.2 Labour Induction

Owing to the negative effects of second hand smoke exposure as described in the literature, it was plausible to expect second hand smoke exposure to also increase the risk for induction of labour. Labour is induced when either the health of the pregnant woman and/or the fetus is at risk, such as placental insufficiency. Thus, it could be inferred that the fetuses of women who are exposed to second hand smoke are at a greater risk for adverse effects, such as placental insufficiency and growth restriction, and consequently labour may need to be induced.

This was found to be so as there was a significant increase in the risk of being induced with respect to having second hand smoke exposure. It is interesting to note that in addition to being at a greater risk for spontaneous preterm birth less than 34 weeks of gestation (OR = 2.10), they are also more likely to need induction of labour at some point in pregnancy (OR = 1.31). This could be taken as indication that second hand smoke exposure causes other more far-reaching complications on both the woman and the fetus.

5.1.2.3 Impact of Nulliparity on Outcomes of Interest

An interesting secondary finding was the impact of nulliparity on the outcomes of interest, including preterm birth less than 37 weeks, preterm birth less than 34 weeks, spontaneous preterm birth less than 34 weeks, low birth weight, NICU admission, Caesarean delivery, and induction.

The relationship of parity, past obstetric history, and risk of preterm birth has been previously described. Bakketeig and Hoffman (1981) noted that if a woman has had a previous term delivery, her risk of preterm birth in the next pregnancy is reduced by 4.4%. But if she had a preterm birth, her recurrence risk is 17.2%. As most women in the general obstetric population have term pregnancies (and thus lower their risk of preterm birth in the next pregnancy), it is not surprising that nulliparous women have a higher risk of preterm birth than parous women overall. As they have a higher rate of preterm birth, it is not surprising that other neonatal outcomes that are increased, including low birth weight and NICU admissions are not surprising.

5.2 Limitations

While much effort was taken to ensure the project adhered to rigorous research methodology practices, certain limitations existed within the study.

5.2.1 Exclusion of variables

The data for this project were obtained from the NLPPP for which data is collected after delivery and upon the woman's discharge from the HSC. As such, data collection is contingent on a combination of factors: accurate self reporting by the patient, thorough documentation by the health care provider, and accurate extraction by the coder. For certain variables, namely Body Mass Index (BMI) and alcohol consumption, there was not sufficient data to include them in the analysis.

BMI has been significantly associated with adverse outcomes such as an increased risk of Caesarean delivery and preterm delivery (Driul et al, 2008). In order to calculate the BMI both the height and weight of the individual must be known. In the current study, the height was missing for over 32% of the women in the database. This number was deemed too high to warrant calculating the BMI and thus, BMI was not included in the covariates for preterm birth.

Alcohol consumption by pregnant women is often underreported and sensitive to response bias (Alvik et al, 2006). The adverse effects of alcohol consumption during pregnancy have been well established. As such, it is not socially acceptable for a pregnant woman to consume alcohol while pregnant and is subject to being underreported (Durant et al, 2002). As approximately 98% of the women in the sample reported no alcohol consumption during the pregnancy, possibly owing to the inclination to under report alcohol consumption, it was determined that this variable would not be included in the analysis.

5.2.2 Measuring Second Hand Smoke Exposure

For this study, the determination of exposure to second hand smoke was based on a yes/no question. This format precluded the ability 1) to quantify the amount exposure, and 2) to assess the impact of the environment in which the exposure was had. Active smoking during the pregnancy can be quantified in terms of the actual number of cigarettes smoked, and as such studies have looked at adverse effects on the pregnancy in relation to the amount of cigarettes smoked. The more cigarettes smoked, the more adverse the effects on the pregnancy. Owing to the fact that the adverse effects of second hand smoke exposure during the pregnancy have been similar to the adverse effects of active smoking during the pregnancy, it stands to reason that there would be a similar gradient scale with respect to the adverse effects of second hand smoke exposure. That is, the greater the second hand smoke exposure, the greater the adverse effects. Furthermore, the impact of the environment in which the second hand smoke exposure occurred was not assessed. It was unknown whether the second hand smoke exposure occurred in an enclosed room with poor ventilation or in an outdoor environment.

5.2.3 Second hand Smoke Exposure Status Unknown

Even though Patrick et al (1994) demonstrated that self-reports of smoking are accurate, it is possible that some women may not acknowledge they were exposed to second hand smoke. Smoking and exposure to second hand smoke are continually becoming less socially desirable behaviours in today's society, especially for a pregnant woman, although exposure to second hand smoke at the work place may have been unavoidable for some women in the past. Thus, when asked if exposed to second hand smoke, the pregnant woman may be more inclined to deny exposure to second hand smoke. It is also possible that women may not have been asked by their health care provider about their second hand smoke exposure. In the database for the current study, exposure to second hand smoke was unknown for approximately 19% of women.

5.2.4 Inclusion of High Risk Pregnancies

As previously mentioned, the HSC is the primary tertiary hospital in the province of Newfoundland and Labrador. As such, it is the facility to where pregnancies deemed high risk, from other regional health authorities within the province, are referred. However, even though it was possible to determine the referring regional health authority within the database, it was not possible to determine which pregnancies were high risk. The assumption could have been made that many of the pregnancies from health authorities outside of Eastern Health were at an increased risk and thus, all those pregnancies excluded from the analysis. However, it was not possible to determine which pregnancies from EH were at an increased risk, especially as there was not a single definition of a "high risk" pregnancy. To exclude all the pregnancies from outside Eastern Health would not have resolved the determination of which pregnancies were high risk, and thus, it was decided to exclude only those pregnancies for which the referring health authority was unknown or were from outside the province.

5.2.5 Analysis of Rare Events

The sample size for this study was large and met the sample size calculation. However, for certain rare events such as perinatal mortality, the sample size was too small to warrant analysis of such events. Also the sample size was not large enough to see a smaller difference in the primary outcome of preterm birth less than 37 weeks of gestation had it existed. Other neonatal outcomes (such as head circumference, overall length, etc) or longer term outcomes were not evaluated in the current study. Future studies may investigate these outcomes.

5.3 Dissemination

On a community level, contact has been established with members of the Newfoundland and Labrador Alliance for the Control of Tobacco (ACT). The mandate of this organization, which officially formed in 1999, is to develop and implement a comprehensive provincial tobacco reduction strategy. Recent campaigns have focused on educating the public of the effects of second hand smoke. The 2003 campaign, in particular, publicized some of the effects of second hand smoke during pregnancy. In speaking with members of ACT, an interest has been expressed in the proposed research project with the hopes of possibly using the results in future campaigns.

Continuing on a community level, the Women's Health Program of EH, as well as Community Health Nurses in the province, regularly offers prenatal classes to pregnant women to provide them with information on the importance of, and how to achieve, a healthy pregnancy. The assimilation of knowledge is crucial to educating pregnant women of potential health risks. With the help of professionals from the Women's Health Centre, it is hoped the findings will help tailor future education programs offered at the centre.

Finally, publication in a peer-reviewed journal is important in the circulation of evidence-based research. It is intended that an article be written and submitted to a peer-reviewed journal for publication. Furthermore, presentations at regional, provincial, and national meetings of obstetrics, gynaecology, paediatrics, and perinatal epidemiology are planned.

5.4 Conclusion

Second hand smoke exposure is the leading cause of preventable illness and death (Second-hand Smoke Resource Document, 2000). As such, research has begun investigating the adverse effects of second hand smoke exposure on health.

Using the database from the NLPPP, this study found that exposure to second hand smoke while pregnant can have very serious adverse outcomes. This study is one of the first to demonstrate the effects of second hand smoke exposure on preterm birth less than 34 weeks of gestation. Second hand smoke exposure was also shown to be independently associated with low birth weight.

Not only were many of the results statistically significant, they were also clinically significant – i.e. the research results "matter" in the real world. There is no predisposing factor that is absolute in the sense that the presence of one particular factor necessarily leads to an adverse outcome in pregnancy. However, exposure to second hand smoke is one variable that can be controlled. Limiting exposure to second hand smoke is one way to reduce the risk for adverse pregnancy outcomes.

The findings from this study lay credence to the continued need for increased public policy on prevention of exposure to second hand smoke.

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