THE ASSOCIATION OF ACUTE AND CHRONIC POSTPARTUM PAIN WITH POSTPARTUM DEPRESSION IN A NATIONALLY REPRESENTATIVE SAMPLE OF CANADIAN WOMEN

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Abstract

The association between pain and depression is well documented across various populations, but not in puerperal women. This study examined the association of childbirth pain with postpartum depression (PPD) in a nationally representative sample of Canadian women. Data from the Canadian Maternity Experiences Survey (n=6421) was used. Multivariate logistic regressions and partial proportional odds models were fitted and included socio-demographic, obstetric, health, psychological, and psychosocial factors. Chronic pain sufferers at mean 7.3 months postpartum had adjusted odds of PPD of 2.4 (95% CI: 1.6, 3.6) compared to women without pain. Adjusted odds of PPD increased with the number of areas of chronic pain, reaching 4.2 (95% CI: 0.7, 25.0) for 3 or more areas. Immigration, obesity, cesarean section and social support increased the strength of the association while smoking and the use of pain relief were protective effect modifiers. Persistent postpartum pain is a major risk factor for PPD.

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List of abbreviations and acronyms

ALPHA	Antenatal Psychosocial Health Assessment
AP	Attributable proportion due to interaction
BDI	Beck Depression Inventory
BMI	Body Mass Index
BRR	Balanced Repeated Replication
CBT	Cognitive Behavioural Therapy
CI	Confidence intervals
COOL RDC	Carleton Ottawa Outaouais Local Research Data Centre
CPSS	Canadian Perinatal Surveillance System
CV	Coefficient of variation
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition, Text Revision
ECT	Electro-Convulsive Therapy
EPDS	Edinburgh Postnatal Depression Scale
GABA	Gamma-aminobutyric acid
IASP	International Association for the Study of Pain
IFSACP	Inventory of Functional Status After Childbirth
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th Revision
IPT	Interpersonal Therapy
MES	Canadian Maternity Experiences Survey
MI	Multiple imputations
MINI	Mini-International Neuropsychiatric Interview
OR	Odds ratio
PDSS	Postpartum Depression Screening Scale
PHAC	Public Health Agency of Canada
PPD	Postpartum Depression
RERI	Relative excess risk due to interaction
S index	Synergy index
SAD	Scale for Anxiety and Depression
SCID	Structured Clinical Interview for DSM-IV
SES	Socioeconomic status

The present research and analyses are based on data from Statistics Canada, and the opinions expressed do not represent the views of Statistics Canada.

1.0 INTRODUCTION

This thesis aimed to examine the association between postpartum pain and postpartum depression (PPD) in Canadian women. Postpartum pain and PPD are two complex health concepts. To facilitate the comprehension of this project, a thorough review of both these concepts was warranted. The first part of the literature review focuses on PPD. It includes its epidemiology, public health impact, diagnosis, etiology, risk factors, screening, and treatment. The second part of the literature review gives the definition of pain, its measurement, and its presence in childbirth. The main focus of this thesis is the exploration of the association between childbirth pain and PPD. Three different associations related to childbirth pain and PPD were explored in this thesis:

1) The association between the presence of problematic pain caused by childbirth and PPD
2) The association between the duration of pain caused by childbirth and PPD
3) The association between the number of chronic postpartum pains caused by childbirth and PPD.

The analytical strategies used in this thesis include:

1) Descriptive statistics
2) Confounding analyses
3) Effect modification and additive interaction analyses
4) Multivariate logistic regression modeling using SAS and Statistics Canada`s BOOTVAR program to obtain bootstrapped confidence intervals
5) Brant test for the proportional odds assumption for ordered logistic regression modeling
6) Multivariate ordered logistic regression modeling using STATA's OLOGIT and GEOLOGIT2 programs with the balanced repeated replication (BRR) variance estimation method
7) Model fit analyses and statistics (Likelihood ratio tests, Hosmer-Lemeshow tests, c statistic)
8) The creation of a multiply imputed dataset with the IVEware software.
9) Sensitivity analyses with the multiply imputed dataset and a sample restricted to never previously depressed mothers.

This thesis ends with a discussion of the results, and presents a detailed description of the various threats to the validity of the results of this thesis. Finally, issues that need to be addressed in PPD research are highlighted.

This thesis satisfies the requirements of a category 2 thesis, and is presented as part of partial fulfillment of the requirements to obtain the M.Sc. degree in Epidemiology at the University of Ottawa.

2.0 LITERATURE REVIEW

2.1 The epidemiology of postpartum depression

Depression is the leading cause of disability worldwide, and a major contributor to the global burden of disease, surpassing ischemic heart disease and cerebrovascular disease in middle to high income countries.(1) Throughout the world, women have a 50% higher prevalence and burden of depression compared to men.(1,2) In 2003, 7% of Canadian women experienced mood disorders and resulting disability compared to 4% of men.(3) Mood disorders occur at a higher rate during the reproductive years.(4) PPD, a disorder that occurs in the puerperal period, affects 12% to 20% of women although 13% is more commonly reported.(5) The results of the Maternity Experience Survey (MES) indicate a 7.5% prevalence of PPD in Canadian women.(6)

2.2 Postpartum depression as an important public health problem

PPD is an important public health problem for many reasons. It is often missed by clinicians and remains undiagnosed and untreated in many women.(7) Clinicians may confuse the symptoms of depression with the stress of being a new mother.(7) When depression is diagnosed, depressed mothers are treated with less intensity than what is required.(7) Lack of energy and fear may prevent depressed mothers from seeking medical help for their depression, making the

diagnosis and treatment of depression even less likely.(8, 9) Depressed mothers who are offered treatment may also refuse to be treated. Murray et al.(10) found that these mothers tended to be younger and less educated. Choi et al.(10) emphasize the need for better referrals for women who suffer from this pervasive disorder.

PPD affects the daily life of women who suffer from this debilitating disease. Posmontier et al.(9) examined the functional level of women from 6 to 26 weeks postpartum with the Inventory of Functional Status After Childbirth (IFSACP).(9) PPD was associated with lower household, social, personal, and overall function.(9) Results also showed that the level of function decreased according to the severity of symptoms.(9) Depressed women were less likely to return to their pre-pregnancy level of function compared to their non-depressed counterparts.(9) Even if PPD was not associated with decreased infant care in the study by Posmontier el al.(9), other studies reveal that depressed mothers may offer less physical and psychological care to their infant, and their infants have poorer health outcomes.(4, 9)

PPD has pervasive and long lasting consequences for the new mother and those close to her; it can negatively affect the marital relationship resulting in family dysfunction; the fathers are more likely to have difficulties adjusting; and

their children are also at increased risk of suffering cognitive, psychosocial and behavioral issues. (11, 12)

Prevention is always the key. However, for preventive measures to work, women who are at increased risk for PPD need to be identified and targeted. There lies the problem. Women who are already depressed during pregnancy, and are therefore at risk for PPD, are more likely to opt-out of prenatal care then their non-depressed counterparts.(4) When they do seek care, depressed pregnant women may have issues following medical recommendations.(4) Untreated depression during pregnancy not only puts the woman at risk for PPD, but the physiological changes associated with depression can affect the fetus and cause prematurity and low birth weight.(4, 7)

2.3 Diagnostic criteria of postpartum depression

PPD is part of the group of mood disorders.(13) There are three postpartum mood disorders:

1) The postpartum blues
2) Non psychotic postpartum depression (PPD)
3) Puerperal psychosis (7)

2.3.1The postpartum blues

The postpartum blues is the most common and the least severe form of these disorders, affecting up to 70% of new mothers.(7, 13) It does not usually extend beyond 10 days postpartum.(7, 13)

2.3.2 Non psychotic postpartum depression

PPD is less common, but more debilitating. Its signs and symptoms are the same as those associated with major depression.(7) In a study of the onset of PPD, researchers found that although most women reported early postpartum onset for PPD (66.5%), there were still a significant number of women who reported pregnancy onset of PPD (11.5%) and late postpartum onset of PPD (13.3%).(14)

2.3.3 Postpartum psychosis

Postpartum psychosis is rare. It affects 0.1% to 0.2% of new mothers, mostly first time mothers who previously lived through a psychiatric episode.(7, 15) Its onset can range from 48 hours postpartum to 2 weeks postpartum.(7)

2.3.4 DSM-IV-TR and ICD 10 criteria for postpartum depression

To diagnose PPD, the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for major depression with the addition of the postpartum onset specifier is used if the symptoms occur within one month of delivery.(13) Symptoms must have been present for at least two weeks. Physical symptoms

associated with PPD include changes in appetite, disturbed sleeping patterns, fatigue and lack of energy, as well as psycho motor changes.(13) Affective symptoms are abnormal depressed mood, loss of interest and pleasure, and irritability while cognitive symptoms include guilt, difficulty concentrating, indecisiveness, and abnormal thoughts of death and self-harm.(13) The most commonly reported symptoms include "fluctuations in mood, mood lability, and preoccupation with infant wellbeing".(13)

The International Statistical Classification of Diseases and Related Health Problems (ICD-10) may also be used. It classifies PPD using the "mental and behavioural disorders associated with the puerperim, not elsewhere classified" category (F53).(16) The ICD-10 allows a 6 weeks period for the diagnosis of PPD, which is longer than what the DSM-IV-TR allows.(13,16) However, as Stowe(14) demonstrated, the onset of PPD can be much later than what both criteria allow. This is a major issue in PPD research. There is a disconnect between what information is used in clinical practice to diagnose PPD and what research is uncovering. As more research is carried out, and the exact mechanisms underlying PPD are discovered, it is very probable that the clinical definition of PPD will evolve and become more precise. But for the moment, there is a lack of homogeneity in case definition of PPD both in a clinical and research settings.

2.4 Causes of postpartum depression

The aetiology of PPD is complex and is believed to involve hormonal, psychosocial, and biologic vulnerability.(7) Research has not demonstrated a clear causative or predictive factor for the postpartum blues which is a precursor to PPD.(17) Potential factors on the PPD causal pathway include estrogen and progesterone fluctuations, cytokines, hypothalamic-pituitary-adrenal axis hormones, fatty acids, oxytocin, arginine vasopressin, the serotonin system, sleep deprivation, and hypothyroidism.(8, 17-20) The complex aetiology of PPD can be appreciated in the number of risk factors that have been associated with this condition.

2.5 Postpartum depression risk factors

Many psychosocial, psychological, socioeconomic, and obstetric and health risk factors have been associated with PPD. These risk factors include: anxiety during pregnancy, history of depression, history of psychiatric disorders, previous use of antidepressants or psychotherapy, mental health hospitalization, the postpartum blues, stressful life events, perceived stress, lack of social support, maternal personality characteristics, marital problems, obstetric factors, multiple births, assisted reproductive technology, smoking, body mass index, low socioeconomic status, age, the use of drugs and alcohol, smoking, infant sleep pattern, refugee, immigrant, or asylum seeker status.(8-10, 21-24) But surely, all these risk factors cannot be equally associated with PPD. Major systematic

reviews and meta-analyses on PPD risk factors are indicating that psychological and psychosocial factors are the most significant risk factors for PPD.(22, 25)

It appears that PPD may have fallen victim to hot topic bias, which is a subtype of publication bias.(26) There are many publications describing variables that are associated with PPD. However, these studies do not always corroborate each other. For example, there has been a lot of research into the association of caesarean section with psychological consequences such as PPD over the last 40 years, without any clear conclusions.(27) Part of the objectives of this study, as will be discussed later, was to determine which risk factors are independent predictors of PPD.

2.6 Screening for postpartum depression

There have been many efforts to develop PPD screening programs to identify women at risk for PPD and prevent the development of this debilitating disease. These efforts have resulted in screening programs both during pregnancy and after birth.

PPD screening programs during pregnancy include the use of the Antenatal Psychosocial Health Assessment (ALPHA) tool. The ALPHA was recently developed in Ontario to be used as a screening tool for psychosocial risk factors

in pregnancy, over concerns that pregnant women were not properly assessed by their healthcare provider.(28) The 2000 revision of the Ontario Antenatal Record includes a section for data obtained from the ALPHA.(28) Stewart(4) warns that the abbreviated version, incorporated in the Ontario Antenatal Record, needs to be evaluated. The ALPHA has been endorsed by major medical bodies and relevant stakeholders in Canada such as the Canadian Pediatric Society, the College of Family Physicians of Canada, the College of Physicians and Surgeons of Canada, the Society of Obstetricians and Gynecologists of Canada, and many others.(28)

There are many screening tools used to screen for PPD in the postpartum period. The Edinburgh Postnatal Depression Scale (EPDS), developed by Cox et al.(28) is probably the most well-known as well as being the most used worldwide.(29, 30) The EPDS is an essential part of this thesis, as this is the tool used as the outcome measure. It is used to classify respondents according to PPD status. The EPDS is also the most often used in clinical trials to evaluate PPD.(31) See Appendix A for a copy of the EPDS. This tool was developed specifically for a puerperal population after reported validity issues regarding the postpartum use of the Anxiety and Depression Scale (SAD), the General Health Questionnaire, the Beck Depression Inventory (BDI), and the Zung Depression Scale.(32-35)

The EPDS is a 10 item questionnaire that has been validated for research and for use in the community to screen for PPD.(29) The recommended threshold to identify women with Major Depressive Illness is a score of 12/13 (13 or more), and a score of 9/10 (10 or more) can be used to identify probable cases.(30) The EPDS has a sensitivity of 86% and a specificity of 78%, as well as a positive predictive value of 73%.(29) A major strength of the EPDS is that is "sensitive to change in the severity of depression over time".(29) It is recommended that women complete the EPDS alone, as the presence of another member of the family may decrease the sensitivity and specificity of the tool.(29) Since the EPDS is a screening tool, there is still a need to confirm PPD by a diagnostic interview like the Structured Clinical Interview for DSM-IV (SCID).(29, 36) This interview is useful to distinguish PPD from other type of conditions such as post-traumatic stress disorders and obsessive-compulsive disorders.(32) There are many other tools used as to screen for PPD: the Centre for Epidemiologic Studies Depression Scale, the Beck Depression Inventory (BDI), the Mini-International Neuropsychiatric Interview (M.I.N.I.), and the Postpartum Depression Screening Scale (PDSS).(34,37-39) The EPDS has a clear advantage over these other screening tools as it is the most consistently used validated tool in PPD research internationally.(30) The EPDS was the tool chosen to be used in the MES to assess PPD in the respondents to this national survey.(6)

Screening in the postpartum period is probably more efficient than screening in the antenatal period. A review conducted by Austin et al.(40) examined the available screening tools for PPD to be used in the antenatal period, including the ALPHA.(40) In general, the studies used their own home-made study screening tool, some used the EPDS. They were generally of poor quality. Although Austin et al.(40) express that "although the use of antenatal psychosocial assessment may increase the clinician's awareness of psychosocial risk, these tools have not been associated with improved perinatal health outcomes".(40) No current screening tools meet the criteria to be used as part of routine screening efforts during pregnancy.(40) Cox (32) believes that a screening program in early postpartum period rather than during pregnancy would prove to be more cost-effective and feasible. It should aim at the early identification of onset of PPD, such as severe cases of postpartum blues, as they may share common physiological pathways.(32)

2.7 Treating postpartum depression

The postpartum blues are a precursor to PPD and should be treated with the use of support, reassurance, and patient education.(7) New mothers with severe blues should be closely monitored to prevent the blues from developing into PPD. Antidepressants are also used in early postpartum to prevent PPD. A Cochrane group reviewed their use as preventive measures.(41) Only two trials were included in the meta-analysis with a combined 73 participants, and only two

types of antidepressants were analysed: Nortriptyline and Sertraline.(41) The review was not conclusive, and it remains unknown whether antidepressants are effective in preventing PPD, when taken in early postpartum.(41)

When PPD does develop, the recommended treatment depends on the severity of the symptoms and the loss of function.(7,8) Nonacs et al.(7) argue that women suffering from PPD should follow the same course of treatment as non-puerperal women. Treatment for PPD includes both pharmacological and non-pharmacological interventions such as psychotherapy, pharmacotherapy, as well as support.(8) In the case of severe depression, when antidepressants do not work or are not wanted due to breastfeeding, treatment can include electro-convulsive therapy (ECT).(8)

Hoffbrand et al.(42) reviewed the use of antidepressants for the treatment of PPD. Surprisingly, only one trial made the criteria for inclusion. The researchers conclude that there is a need for bigger trials, with longer follow-ups, and are concerned that "treatment of PPD is an area that has been neglected despite the large public health impact".(42) This is a concern that many researchers share regarding pharmacological treatment of PPD.(7,8) However, there is strong evidence supporting the use of non-pharmacological treatment options for treatment of PPD. Dennis et al.(31) examined the evidence for non-pharmacological treatment options for PPD such as Cognitive Behavioural

Therapy (CBT), Interpersonal Therapy (IPT), Psychodynamic therapy, non-directive counselling, peer support etc.(31) These types of treatment are effective and valid options to treat PPD.(31) Results of the meta-analysis showed that the relative risk of PPD for women receiving any type of psychosocial or psychological intervention, at any time postpartum, compared to those receiving usual postpartum care was 0.70 (95% CI: 0.60 to 0.81).(31)

2.8 The definition of pain

Pain can be a difficult concept to understand although everyone has felt pain at some point in their lives. The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".(43) Because of the inherent subjectivity and multi-dimensionality of pain, as noted in the IASP definition, "pain cannot be measured by an observer".(44) The experience of pain varies from person to person in its intensity, quality, time course, impact, and personal meaning.(44)

Pain comes in different forms and it is easy to become lost in terminology. Pain can be associated with illnesses such as AIDS and cancer, or it can have no underlying disease.(44) There are two main factors that are used to define pain: duration and underlying pathology.(44) Interestingly, these factors are the ones that are the most objective and measurable.

Acute pain is "short in duration and has high evidence of physical pathology" (such as inflammation, or infection).(44) Acute pain is associated with an injury, and the pain resolves quickly, within days or weeks.(45-47) Chronic pain, on the other hand, persists even when the initial cause of pain has healed and is often defined as "a pain that persists for at least 3-6 months".(45-47) The correct definition of Chronic pain is given by the IASP: "a persistent pain that is not amenable, as a rule, to treatments based upon specific remedies, or to routine methods of pain control such as non-narcotic analgesic".(43)

There is an intimate relationship between acute pain and chronic pain. Acute pain can develop into chronic pain under certain conditions that alter the perception of pain such as stress, environmental, affective, and physical factors.(48) Under these circumstances, the body is "unable to return to a normal state"(48), and pain persists even when there are no longer any physical or physiological explanations for the pain (ex: wound has completely healed).(48) The development of chronic pain, and how it can lead to psychological issues such as depression, can be better understood by considering Gatchel's model of transition from acute to chronic pain.(49) In this model, the suffering associated with the experience of pain causes both significant physical and mental deconditioning.(49)

Following Gatchel's model of transition from acute to chronic pain, a new mother who feels considerable amount of pain such as back pain or migraines following birth may neglect to follow medical recommendations because she is too busy attending to the needs of her newborn and adjusting to her new role. The pain may worsen and her sleep may become even more affected. She may not be able to recover properly. As a result, she may become less active, take excessive amounts of pain medication or none at all, or worse, start self-medicating with alcohol and other substances. She may become fearful and feel anxious and guilty regarding her pain as well as her ability to take care of her newborn. The relationship with her partner and others may become strained. The lack of ability to cope with this situation could result in a downward spiral of psychological and behavioral issues, such as PPD.(49) In this case, the development of chronic pain and PPD would depend on the individual's psychological/personality characteristic, as well as socioeconomic and environmental conditions.(49) Gatchel (48) explains that "one of the consequences of dealing with chronic pain is the development of emotional reactions such as anxiety and dysphoria produced by the long term "wearing down" effects and drain of psychological resources".(49)

2.9 Measuring pain

Three types of measures are used to assess pain. These measures are "self-reports, observational measures, and physiological measures".(50) Strong et

al.(50) explain that "self-reports are the gold standard in pain measurement because it is consistent with the definition of pain".(50)

2.10 Pain and childbirth

Pain following childbirth is the key exposure under study in this thesis. The development of chronic pain after childbirth has been well documented. Acute pain caused by cesarean and vaginal deliveries can persist and become chronic pain. The prevalence of pain at eight weeks after vaginal and cesarean deliveries were 10% and 9.2% in a study by Eisenach et al.(51) A study by Nikolajsen et al.(52) reports a 18.6% prevalence of pain at more than three months post cesarean, and the pain persisted in 12.3% of cases at mean 10.2 months post cesarean section (range: 6 to 18 months postpartum).(52) The sample included women who had undergone planned as well as unplanned cesarean sections and received general anaesthesia or spinal anaesthesia.(52) Another study by Kainu et al.(53) reports a persistent pain prevalence of 18% in cesarean and 10% in vaginal birth at a standardized one year after delivery.(53) Again, the sample included planned as well as unplanned cesarean section, non-operative and operative vaginal deliveries aided with vacuum, and various surgical anaesthetic methods such as general anaesthesia, combined spinal-epidural or spinal anaesthesia, as well as epidural anaesthesia.(53) In a third study, Sng et al.(54) found that the prevalence of persistent pain after elective cesarean section under spinal anaesthesia was 9.2% at three months postpartum.(54)

Different surgical procedures as well as anaesthetic method may account for the variation in persistent pain (chronic pain) prevalences.

In this thesis, postpartum pain in five key body areas (vagina, site of cesarean incision, breast, back, and migraine) is measured by self reports. During the interview, mothers were asked if pain in any of these areas had been problematic in the first three months after giving birth (period that would be considered acute pain period). If a mother said yes, she was then asked if the pain was still present at the time of interview. Pain at the time of interview was considered chronic pain. It must be emphasized that a major assumption of this thesis is that the pain was a direct consequence of birth and immediately followed birth, while PPD developed much later. We assume that PPD developed at two weeks postpartum at the earliest, to be consistent with PPD diagnostic criteria and to rule out the blues which is highly prevalent, but usually resolves quickly.

2.11 Causal association between pain and depression

Ever since Melzack and Wall's famous gate control theory in 1965, numerous disciplines have added to the understanding of the association between pain and depression by proposing various theories and hypotheses.(49) A systematic review by Fishbain et al.(55) has unveiled three major causal hypothesis between pain and depression:

1) The "Antecedent" hypothesis: Depression causes pain
2) The "Consequence" hypothesis: Pain causes depression
3) The "Scar" hypothesis: "Episodes of depression occurring before the onset of pain predispose to a depressive episode after pain onset"(55)

Fishbain (55) reports that "the consistency of the results across various diagnostic categories would indicate that the pain depression relationship may be a universal phenomenon".(55) It would therefore be logical to expect the same type of results in a puerperal population. There is limited research on pain and PPD in a puerperal population. Many studies only examine pain and PPD only as co-morbidities.(56, 57)

In this thesis, the association between pain caused by birth and PPD is thoroughly examined through complex statistical analyses such as multivariate logistic regression, multivariate ordered logistic regression, and multiple imputation through regression analysis. Although causality cannot be demonstrated, the direction of the hypothetical causal association between postpartum pain and PPD was explored with sensitivity analyses using the sample restricted to respondents who have never previously been depressed (to rule out the Scar hypothesis).

2.12 The association between postpartum pain and postpartum depression

One study demonstrates an association between acute pain at 36h postpartum and both persistent pain and PPD at eight weeks after giving birth.(51) In a small French study by Boudou et al.(58) of 43 women who had a vaginal delivery, there was a statistically significant relationship between the intensity of pain in childbirth and mood in the three days following childbirth (affective dimension of pain; r=0.48, sensory dimension: r=0.32).(58) In another small cohort study (n=267) by Gutke et al.(59), women with lumbopelvic pain were three times more likely to have PPD than women without lumbopelvic pain at three months postpartum.(59) Finally, in a population-based study in Australia, back pain at 6 months postpartum was associated with PPD (OR: 2.2).(56) However heterogeneous these studies may seem at first glance, these studies do have something in common. They suggest that there is indeed an association between pain and mood disorders in a puerperal population.

If there is a causal relationship between postpartum pain and PPD, results would indicate that there is an association between the presence and/or intensity of PPD and:

1) The presence of pain
2) The duration of pain
3) The severity of perceived pain
4) The number of painful sites

5) The frequency of pain/pain intrusion/pain breakthrough

6) The percentage of body affected by pain.(55)

This thesis aimed to address points 1), 2), and 4), without aiming to prove a causal relationship.

This thesis has the potential to provide evidence that will advance the state of knowledge regarding the association between various types of postpartum pain and PPD. The analyses in this research were performed on a high quality dataset containing a large population based sample of new Canadian mothers. The dataset also contained information on most of the known risk factor for PPD, and many risk factors for chronic pain. This proved to be useful when exploring and adjusting for confounding factors. The exposures under study follow a set timeline (1.birth → 2.pain → 3.PPD). It was therefore possible to explore the causal relationship between pain and PPD. This exploration might prove to be an be an important building block for future research aimed at confirming or disproving a causal association between pain caused by birth and PPD.

3.0 AIMS AND OBJECTIVES OF THE STUDY

3.1 Aim of the study

The aim of this study was to generate new knowledge regarding postpartum pain and PPD in Canadian women through a secondary data analysis of the MES.

3.2 Study objectives

3.2.1 Objective 1

The first objective was to describe the nature of the association between postpartum pain and PPD in a nationally representative sample of postpartum women, and to estimate whether pain is a significant independent risk factor for PPD using multivariate logistic regression modeling techniques.

3.2.2 Objective 2

The second objective was to explore the use of ordered logistic regression as a valid method to study the association between postpartum pain and PPD, and to examine what subtype of ordered logistic regression is best suited for this type of research (ex: proportional odd modeling) when the outcome is divided into three PPD categories:

1. No PPD (EPDS scores of 0-9)
2. At risk for PPD (EPDS scores of 10-12)

3. PPD (EPDS scores of 13 and +)

4.0 GENERAL METHODOLOGY

The following section contains the general methodology for this thesis. Specific methods pertaining to the two objectives are presented in sections 5.0 and 6.0. The present study is a secondary data analysis performed on the MES dataset, which is describe in detail in the paragraphs that follow. This study was approved by the Ottawa Hospital Research Ethics Boards.

4.1 Literature search strategy

The literature search strategy for this thesis was developed with the help of Lee-Anne Ufholz, Health Sciences Research Liaison Librarian at the University of Ottawa. For the literature review of the association between postpartum pain and PPD, the main database that was used was Psychinfo. The search strategy developed in Psychinfo was then replicated in Medline, Embase, and CINHAL to ensure all the relevant studies were identified. For the details of the search strategies used with the different databases, please see Appendix B. The search was initially done in October 2009 and then redone regularly to ensure new studies would be included. Key words were also included in the literature search strategy to ensure new not yet indexed studies would be detected. The references sections of key papers were hand searched, and grey literature was

also consulted, primarily found using expert consultation and internet search engines such as Google.

4.2 The Maternity Experiences Survey

This study is a secondary data analysis of the Canadian MES. The MES is a survey conducted by Statistics Canada for the Public Health Agency of Canada's (PHAC) Canadian Perinatal Surveillance System (CPSS).(6) The aim of the survey was to capture aspects of Canadian women's experiences of maternity, such as perceptions and behaviors that were not available in the data sources that are used to create the usual CPSS reports on determinants and outcomes of maternal-fetal health in Canada.(6) It was crucial for policy and practical purposes to address this gap in knowledge.(6)

4.2.1 The Maternity Experiences Survey data gathering

The survey questionnaire contains over 300 questions regarding pregnancy, birth, and postpartum, and was created following an extensive process.(6) The Statistics Canada interviewers went through an extensive training program in order to ensure consistency and quality of the data gathering process.(6)

4.2.2 The Maternity Experiences Survey inclusion and exclusion criteria

The MES population included 6421 Canadian women.(6) The following Canadian women were eligible for inclusion in the survey: "birth mothers 15 years and older who had a singleton live birth in Canada, between February 15, 2006 and May 15, 2006 in the provinces or between November 1, 2005 and February 1, 2006 in the territories and who lived with their infants at the time of data collection".(6) Women who were excluded from the survey were "under 15 years of age at the time of giving birth and mothers living on First Nations reserves or living in institutions at the time of the survey".(6)

4.2.3 The Maternity Experiences Survey sampling frame

The sampling frame for the MES was created from the 2006 Canadian Census and contained 58 972 mother-baby pairs.(60) From the mother-baby pairs, "a stratified random sample of 8542 women was selected".(6) Stratification variables were province or territory of residence, maternal age, parity, area of residence, and the presence of other children in the household, while post stratification variables were mother`s first language and aboriginal status.(6) A total of 6421 mothers were included in the final analyses.(6) The authors of the MES explain that "the sample size was calculated to produce reliable estimates at provincial and territorial levels, based on an expected response rate of 75% in the provinces and 70% in the territories".(6) The actual response rate was higher

than expected with a 78% response rate.(60) Dzakpasu and colleagues(60) report a cooperation rate of 92%, a contact rate of 85% and a refusal rate of 1%. Non-respondents tended to be younger and of disadvantaged groups.(60)

4.2.4 The Maternity Experiences Survey sampling weight

There are two main reasons why it is imperative to use the population weights in the analyses. First of all, each respondent was given a specific sampling weight in order to adjust for the complex sample design and non-response.(6) This was calculated with regards to the strata that were used in the sampling as well as post-strata.(6) For example, respondents with aboriginal status were given a bigger weight than women without aboriginal status.(6) The second reason to use the population weight is to be able to make valid inferences about the total population, not just the specific survey sample. A single survey respondent may represent more than one person depending on her characteristics.(61) Indeed, The final 6421 respondents represent a total of 76 508 puerperal Canadian women.(6) Analyzing the MES data without using the weights would give inaccurate results.

In all, researchers report that non-respondents to the MES were "younger, reporting a first language other than English or French, more likely to be living in Toronto, and to be single".(6) However, when weighted, the MES respondents were deemed to be representative of the sampling frame population.(6)

4.3 Variable selection

4.3.1 Outcome variable

The outcome of interest was PPD. The PPD indicator variable was derived from the summary score to the 10 EPDS questions that were included in the MES survey questionnaire. For more information, please refer to the EPDS tool in appendix A. The EPDS asks about feelings such as anxiety and fear for the past seven days.(29) Scores of 13 or higher are defined as PPD.(29) Also, a cut off of 9/10 (10 or more) can be used to identify those at increased risk for PPD.(29) The EPDS scores are continuous; however, they were transformed into a binary variable, as well as a three level indicator variable for PPD.

Cut offs used for postpartum depression for objective 1 (Logistic Regression)	
EPDS score	PPD Category
0 to 12	Not depressed
13 and +	PPD

Cut offs used for postpartum depression for objective 2 (Ordered Logistic Regression)	
EPDS score	PPD Category
0 to 9	Not depressed
10 to 12	At risk/possible depression
13 and +	PPD

4.3.2 Main exposures of interest

Self-rating of pain is considered the gold standard in pain measurement.(50) Fortunately, the MES gathered data about self perceived postpartum pain for the five following body areas:

1) Vagina
2) Cesarean incision
3) Breasts
4) Back
5) Head (Migraine pain)

The presence of problematic postpartum pain

The first exposure of interest is the presence of problematic postpartum pain. Participants to the MES were asked about their postpartum experience of pain. For each of the five possible sites of postpartum pain, they were asked:

"During the first three months after the birth of your baby, how much of a problem was pain (in this body area)?" (62)

The choices of response were:

1) Not a problem
2) Somewhat of a problem
3) A great deal of a problem (62)

For the present study, a binary indicator variable for problematic pain was created with the answers to these questions. The categories "Somewhat of a problem" and "a great deal of a problem" were collapsed into a single overall problematic pain indicator. Therefore, if for any body area a survey respondent answered that she had pain that was either "somewhat of a problem" or "a great deal of a problem", she was deemed to have problematic postpartum pain. Women who responded as not having pain that was either "somewhat of a problem" or "a great deal of a problem" were deemed to be pain-free. It was assumed that pain was childbirth onset, a direct consequence of having given birth.

The duration of pain

Respondents who answered having pain that was either "somewhat of a problem" or "a great deal of a problem" in the first three months after delivery were then asked:

"Do you still have (pain in this area)?"(62)

If a respondent answered yes to this question, she was deemed to have chronic pain in this particular area. This question asked about pain at the time of interview at mean 7.3 months postpartum (interview time range: 6 to 14 months postpartum), and satisfies the chronic pain criteria.(46,47) If the respondent

answered she no longer felt pain, she was deemed to have had acute pain that did not become chronic. Respondents who were not asked this question since they did not report any problematic pain were simply coded as no pain. Again, it was assumed that the pain was childbirth onset and that the same pain persisted until the time of interview. The three levels of the duration of pain variable are:

1) No pain
2) Acute pain only
3) Chronic pain

The number of sites of chronic postpartum pain

This exposure variable was created counting the number of body areas that were still painful at the time of interview. The range is from 0 to 5. Again, if a respondent did not report problematic postpartum pain, she was coded as having no pain. Because of the sample size, it was not possible to have more that 4 levels. The levels of this variable are:

1) No chronic pain
2) One chronic pain
3) Two chronic pains
4) Three or more chronic pains

4.3.3 Covariates

All the covariates were selected from studies on the risk factors of pain and PPD following a thorough literature search. All suspected and determined risk factors for postpartum depression were identified from the literature first, and then included in the analyses if possible. All major systematic reviews and meta-analyses consulted reported psychological and psychosocial factors as the strongest risk factors for PPD.(22, 25) Fortunately, the MES contained a wealth of psychosocial and psychological variables that could be included in the analyses. Because of the heterogeneity of quality of studies on PPD, variables for which evidence is inconclusive such as birthing method were also included in this study.

With a total of 33 covariates, it was essential to simplify the process of model building. To simplify the analyses and help build the multivariate models, the covariates were grouped in three main categories:

1) Socioeconomic (SES) and demographic variables
2) Obstetric and health variables
3) Psychosocial and psychological variables

Thesis variable definition

Category	Variable name	Definition	Type	Levels
SES and demographic	Age	Age of mother at time of interview	Categorical	1) 15 to 19 2) 20 to 24 3) 25 to 29 4) 30 to 34 5) 35 to 39 6) 40 +
	Education	Mother's education level	Categorical	1) Less than high school grad. 2) High school graduation 3) Some postsecondary 4) Bachelors degree or +
	Marital Status	Mother's marital status	Categorical	1) Married or Common law 2) Separated/Divorced/ Widowed 3) Single
	Income	Household income for the past 12 months	Categorical	1) Less than $19,999 2) $20,000 to $39,999 3) $40,000 to $59,999 4) $60,000 to $79,999 5) $80,000 to $99,999 6) $100,000 and +
	Region	Region of residence of respondents at time of 2006 census	Categorical	1) Atlantic 2) Quebec 3) Ontario 4) Prairies 5) British Columbia 6) Territories
	Area	Size of area of residence from the 2001 census count	Binary	1) Rural (Less than 30,000) 2) Urban (30,000 +)
	Immigrant	Whether mother is foreign-born or not	Binary	1) Foreign born 2) Canadian born
	Aboriginal status	First Nations, Métis or Inuit	Binary	1) Aboriginal status 2) No
Obstetric and health				

	Birthing method	The final method of delivery: vaginal or cesarean	Binary	1) Vaginal 2) Cesarean
	Use of forceps	Use of forceps to aid in delivery	Binary	1) Yes 2) No
	Use of vacuum	Use of vacuum to aid in delivery	Binary	1) Yes 2) No
	Episiotomy	A cut to enlarge vagina for delivery	Binary	1) Yes 2) No
	Stitches	Stitches to repair a tear or a cut	Binary	1) Yes 2) No
	Parity	Number of live births	Categorical	1) One 2) Two 3) Three 4) Four and +
	Postpartum contact by nurse	Whether respondents were contacted or not by a public health nurse		1) No 2) Yes
	Sex of baby	Sex of baby	Binary	1) Female 2) Male
	Childbirth education	Attended prenatal education	Binary	1) No 2) Yes
	Non medical pain relief	Use of non medical pain relief such as birthing ball, massage, positioning etc	Binary	1) No 2) Yes
	Medical pain relief	Use of medical pain relief such as epidural, Demerol, or nitrous oxide	Binary	1) No 2) Yes
	Postpartum period of interview	Age of baby at time of interview	Categorical	1) Early postpartum (< 6.5 months) 2) Mid postpartum (6.5 months to < 8 months) 3) Late postpartum (8 months and over)

	NICU (Neonatal Intensive Care Unit)	Admission of the baby to NICU	Binary	1) Yes 2) No
	New health problem	New health problem in pregnancy	Binary	1) Yes 2) No
	Previous Health problem	Health problems before pregnancy	Binary	1) Yes 2) No
	BMI	Body Mass Index	Categorical	1) Underweight 2) Normal 3) Overweight 4) Obese
	Smoking	Maternal smoking	Binary	1) Yes 2) No
Psychosocial and psychological				
	Reaction to pregnancy	First reaction to becoming pregnant	Binary	1) Negative 2) Positive
	Stress	Self perceived stress	Binary	1) Stressed 2) Not stressed
	Stressful events	Number of stressful events in the 12 months before birth of baby	Categorical	1) None 2) One 3) Two 4) Three 5) Four +
	Social Support	Perceived social support	Binary	1) Inadequate 2) Adequate
	Previous depression	Previous diagnosis of depression or having been prescribed antidepressants	Binary	1) Yes 2) No
	Alcohol	Use of alcohol during pregnancy	Binary	1) Yes 2) No
	Drugs	Use of street drugs in pregnancy	Binary	1) Yes 2) No
	History of abuse	Experience of any type of violent abuse in the past 2 years	Binary	1) Yes 2) No

The variable "area" which gives the size of area of residence according to the 2001 census count needs further clarifications. At the time of interview, respondents were asked to provide their forward sortation area.(62) With this information, the Census Metropolitan Area – Census Agglomeration (CMACA) variable was derived according to Statistics Canada`s 2001 Standard Geographical Classification (SGC).(61) This derived variable is an attempt to take into consideration potentially high social and economic integration of certain urban and rural areas.(61) In the 2006 Census, which was the sampling frame for the MES, there were 33 Census Metropolitan Areas and 111 Census Agglomerations, and a number of Census Metropolitan Area and Census Agglomeration Influenced Zones (MIZ) that are outside the CMAs and CAs.(61) These are categorized according to the strength of the influence that the CMAs and CAs have on these zones. These zones can be strongly influenced, moderately influenced, weakly influenced, or not influenced at all.(61) The CMACA variable was useful to classify the respondent in terms of the size of the area they were living in at the time of interview.(62) However, in order to have categories with sufficient sample size for analyses in this thesis, the categories were collapsed to create a binary variable (rural/urban). All respondents who were living in a rural area or an urban area with a population of less than 30,000 at the time of interview were classified as rural, while those living in urban areas with at least 30,000 residents were classified as urban.

It is also important to clarify that the "social support" covariate refers to any type of social support during the pregnancy. Respondents were not asked to distinguish between subtypes of support. Survey participants were simply asked how often support was available to them when they needed it.(62) If participants answered none of the time, a little of the time, or some of the time, they were deemed to have had inadequate support. Respondents who reported that that support was available most of the time or all of the time were deemed to have had received adequate support during their pregnancies. Unfortunately, information regarding support in the postpartum period was not captured by the MES.

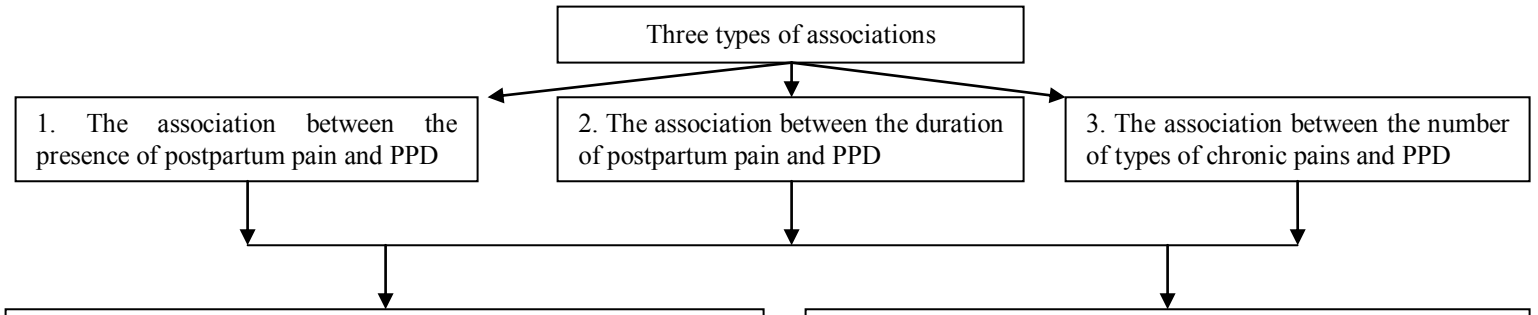
Because of concerns regarding sample sizes and to avoid over-adjustments in the analyses, covariates were not adjusted for other factors. For example, the Public Health Agency of Canada created secondary variables such as "household low income cut-off" to help in their analyses of the MES.(6) This variable was created according to household size, total household income and area of residence of the respondent.(6) Although such variables provide useful information, it would not have been possible to include this secondary variable in this thesis. The variables that are used to create the "household low income cut-off" were recoded, and were also included in the multivariate analyses. Including this secondary variable could have potentially introduced biases due to over-adjustment, thus affecting the precision of study results.(63)

4.4 General analytical strategy

The present study involved the use of descriptive statistics, multivariate logistic regressions and multivariate ordered logistic regressions. These strategies are described in each objective's section (sections 5.0 and 6.0). The data analysis for this thesis was done at the Carleton Ottawa Outaouais Local Research Data Centre (COOL RDC), using the SAS analytical software version 9.2, and the STATA analytical software version 11.

4.4.1 Analytical plan

The following plan attempts to illustrate the complex, comprehensive and exhaustive processes that were integral part of this thesis project.



Objective 1

To describe the nature of the association and determine if exposure is a significant independent risk factor for PPD

Analyses

For each of the three associations under study:

a) Descriptive statistics
   - Sample size
   - Population prevalences:
     1. Exposures
     2. Outcome
     3. Covariates
        i. SES and demographics
        ii. Obstetric and health
        iii. Psychosocial and psychological

b) Confounding, effect modification and additive interaction analyses

c) Measures of associations
   - Crude associations
   - Multivariate logistic regressions models
     1. Full model (all covariates)
     2. SES/demographic covariates only
     3. Obstetric/health covariates only
     4. Psychosocial/psychological covariates only
     5. SES/dem + Obs/health covariates
     6. SES/dem +Psychosocial/psych. Covariates
     7. Obs/health + Psychosocial/psych. covariates

d) Model fit statistics
   - Likelihood Ratio Test
   - Hosmer Lemeshow Test
   - C-statistic

e) Sensitivity analyses
   - Multiply imputed dataset
   - Sample restricted to never previously depressed survey respondents

Objective 2

To explore the use of ordered logistic regression as a valid method to study the associations and to examine what subtype of ordered logistic regression is best

Analyses

For each of the three associations under study:

a) Primary ordered logistic regression

b) Brant test of proportional odds

c) Final partial proportional odds model
   1. Full model (all covariates)
   2. SES/demographic covariates only
   3. Obstetric/health covariates only
   4. Psychosocial/psychological covariates only
   5. SES/dem + Obs/health covariates
   6. SES/dem +Psychosocial/psych. Covariates
   7. Obs/health + Psychosocial/psych. Covariates

d) Model fit statistics
   - Likelihood Ratio test
   - C-statistic

e) Sensitivity analyses
   - Multiply imputed dataset
   - Sample restricted to never previously depressed survey respondents

4.4.2 Missing data

Surveys are not perfect. Respondents do not always answer every single survey question, resulting in missing data. Missing data can be a real problem. It can negatively affect the quality of the study, threaten the validity of results and introduce bias.(64) The present study had a final complete-subject sample size of 5614 compared to the 6421 final MES respondents.(6) A total of 12.6% of respondents were deleted due to missing information. This percentage is due to the large number of variables that were analyzed in this study. The complete-subject approach that was used in the data analyses is described in more details in the following section, and is followed by a description of the multiple imputation approach that was used as a strategy to deal with this problem of missing data and smaller sample size resulting from the complete-subject analysis approach. The variance estimation methods are also described, and this section closes with Statistics Canada Guidelines that were followed in this thesis.

4.4.3 Complete-subject analyses

A complete-subject analysis approach was primarily implemented in this thesis. The complete-subject analysis is a valid method where analyses are done only on records that have complete information for the variables included in the analyses.(65) For this method to be completely valid and to avoid introducing bias in the inferences, the missing information needs to be missing completely at random.(64-66) Wayman(67) warns of the risk of bias if the complete-subject

sample is not representative of the population.(67) The severity of biases in complete-subjects analyses is proportional to the amount of subjects dropped because of missing values.(64) Another issue with complete subject analyses is the loss of power due to smaller sample size.(57, 64)

4.4.4 Multiple imputations by mean of regression analysis

Performing multiple imputations by mean of regression analysis (MI) reduces bias caused by missing data. Rubin (68) explains that it is "the method of choice for addressing problems due to missing values" as well as being "appropriate for complex surveys".(68) When conducting a multiple imputation, available data is analyzed and utilized to predict the missing values.(67) Many imputed datasets are produced (five in this thesis) and are analyzed separately before the results are pooled from these multiply imputed datasets and inferences are made.(67) This method has a number of advantages compared to other methods. It produces unbiased parameter estimates, is robust even when data is not normally distributed, and is adequate for use even with small sample size or when rates of missing data are high.(67) Multiple imputations using the respondent's known characteristics are most likely to produce unbiased results and provide correct standard errors.(66) In the study by Janssen et al.(64), the use of multiple imputations resulted in unbiased regression coefficients compared to complete-subject analyses which underestimated the coefficients. (64)

The IVEware: Imputation and Variance Estimation software developed by Raghunathan et al. (69) from the University of Michigan and available online for free was used to perform the multiple imputations by means of regression analysis.(70) This software uses a sequential regression imputation method.(69) IVEware allows for the imputation of various types of variables: continuous, count, dichotomous, and polytomous which are all found within the MES dataset.(69) It uses a “variable by variable” approach using all the other observed variables included for each respondents of the survey and selects the type of regression that is appropriate for each type of variable.(69) Each imputation is "drawn from the posterior predictive distribution specified by the regression model with a flat or non-informative prior distribution for the parameters in the regression model".(69)

A total of five multiples with 80 iterations each were created to use in this thesis. Variable imputations were mostly polytomous, with some binary logistic, linear, and poisson. In the MES dataset, certain summary variables were derived. For example, the EPDS score is derived from the answers to the 10 EPDS questions that were included in the MES. Missing values for any of the EPDS questions meant that the summary score was not computed for that respondent.(62) Even if 9 out of 10 questions were answered, the summary score was not computed and considered missing.(62) It was therefore decided to impute the missing

values for each individual question before deriving the summary score instead of imputing the missing EPDS summary score. This resulted in more accurate values for PPD.

4.4.5 Estimating the variance

For the first objective, the BOOTVAR program (version 3.1) was utilized with the SAS system to perform unbiased weighted analyses since the survey is of a complex multistage stratified sample design.(6,71,72) BOOTVAR is a variance estimation method by means of bootstrapping.(72) It uses the bootstrap weights which were provided with the MES to estimate the variance, standard errors, confidence intervals and coefficients of variation.(72)

For the second objective, the STATA software was utilized with the OLOGIT and GEOLOGIT2 programs to analyze the data from the MES. It was not possible to use the BOOTVAR program without making complicated major modifications to the coding. Balance repeated replication for survey data (BRR) was therefore chosen as the variance estimator to use with STATA. Again, the bootstrap weights that were provided with the MES were used with the BRR to estimate the variance, standard errors as well as the confidence intervals. As Phillips (73) explains, the bootstrap is a replicate based variance estimation technique, and even if the bootstrap and the BRR do differ in how they build their replicates, "the bootstrap weights can be used to produce bootstrap variance estimates in

software that will accommodate BRR weights".(73) STATA accommodates BRR weights.(73)

4.4.6 Statistics Canada guidelines

Statistics Canada provides guidelines for tabulation, analysis, and release of information so that the estimates obtained correspond to those produced by Statistics Canada.(61) In order to be consistent with the guidelines, the estimates, marginal sub-totals, totals in the tables of this study are therefore presented rounded to the hundred units. Averages, proportions, rates, percentages and ratios are also presented rounded to the decimal. Statistics Canada warns that unrounded estimates "imply greater precision than actually exists".(61)

5.0 PART 1: THE ASSOCIATION BETWEEN POSTPARTUM PAIN AND PPD

5.1 Objective

The first objective was to describe the nature of the association between postpartum pain and PPD in a nationally representative sample of postpartum women, and to determine whether pain is a significant independent risk factor for PPD.

5.2 Research questions and expected findings

Four main research questions guided the analyses of this section. The research questions, along with their expected findings were the following:

Question 1: Is the presence of problematic postpartum pain associated with PPD? It was expected that findings would indicate that women who report problematic postpartum pain or chronic postpartum pain have higher odds of PPD.

Question 2: Is the duration of problematic postpartum pain associated with PPD? An exposure-response relationship between the duration of postpartum pain and PPD was expected to be observed.

Question 3: Is the number of chronic postpartum pain sites associated with PPD? Again, an exposure-response relationship between the number of chronic pain sites and PPD was expected to be observed.

Question 4: Between the scar (genetic predisposition) and consequence (pain causes depression) hypotheses, which hypothesis best explains the association between postpartum pain and PPD in Canadian women? It was expected that the consequence hypothesis, where pain precedes depression would best explain the association between postpartum pain and PPD in Canadian women, which would be consistent with the best evidence in pain-PPD research.(55) This will be examined and answered by running analyses on the sample restricted to never previously depressed respondents.

5.3 Analytical strategy

In this section, the various methods utilized to meet the first objective are described in details. These methods are the use of descriptive statistics, confounding analyses, analyses of effect modification and additive interaction, multivariate logistic regression modeling, sensitivity analyses and model fit statistics. The results obtained by these methods are discussed in the next section.

5.3.1 Descriptive statistics

Population distributions of the important baseline characteristics are reported in the form of proportions with bootstrapped 95% confidence intervals. Results showing high sampling variability (coefficients of variation (CV) between 16.6 and 33.3) are marked with a star. The CV "assesses the reliability and quality of an estimate".(74) Any results showing a large CV should be interpreted with caution as "high levels of error are associated with these estimates".(61,74) The CVs were obtained using the BOOTVAR program.

5.3.2 Confounding analyses

The literature review of this thesis uncovered many risk factors for PPD and chronic pain. Some of these risk factors may in fact be confounding factors of the association between postpartum pain and PPD. The reason is that pain and depression are intimately related. To help in the confounding analyses, the risk factors that were uncovered are grouped according to type of risk factors. The three main types of risk factors are:

1) SES and demographic
2) Obstetric and health
3) Psychosocial and psychological

When there is confounding, "the association between the exposure and outcome is distorted because of the relationship between the confounder and the exposure, and between the confounder and the disease.(75) For a variable to be a confounder, it has to be associated with "the exposure in the population that produced the cases" as well as an independent predictor of the disease, without being part of the causal pathway of the disease.(75) Each of the 33 risk factors was assessed to verify if they were associated with postpartum pain (the main exposure of interest) and PPD (the outcome of interest).

This confounding assessment was done by first computing the prevalences of postpartum pain and PPD for respondents who had the particular risk factor. The prevalences of pain and PPD in those who had the risk factors were compared to the prevalences of pain and PPD in those who did not have the risk factors. Stratified analyses were conducted next. Crude odds ratios and 95% CIs were then obtained for the association between:

1) The risk factor and postpartum pain
2) The risk factor and PPD

A risk factor was deemed a potential confounder of the association between postpartum pain and PPD if:

1) The prevalences of both Pain and PPD were higher for respondents who had the risk factors
2) The crude odds ratios were statistically significant for the association of the risk factor with both postpartum pain and PPD.

Confounding is a major issue and needs to be addressed. After potential confounding factors were identified in this thesis, it was important to limit the damaging effect of confounding. Fortunately, the analytical plan for this thesis called for the use of multivariate logistic regression, which is a method that can adjust for many confounding factors at the same time. However, one must apply caution in the use of multivariate logistic regression as there is a risk of over adjusting as well as performing unnecessary adjustments, which can both introduce biases in the study and affect the precision of the study results. Schisterman et al. (63) provide a definition of over adjustment bias and unnecessary adjustment. Over adjustment bias is defined as "control for an intermediate variable on a causal pathway from exposure to outcome"(63), while unnecessary adjustment is defined as "any adjustment for variables that does not alter the expectation of the average causal effect of interest but may affect precision".(63)

It is impossible to ensure that biases were not introduced in this thesis by over-adjusting for confounders. This is why the risk factors included in the analyses

were carefully chosen prior to the analytical part of this thesis. They were chosen based on evidence and expert opinion. A total of seven logistic regressions with different combinations of risk factors were performed for each of the three studied associations (presence of postpartum pain, duration of postpartum pain, and number of chronic pain sites with PPD). This enabled the observation of changes in parameter estimates, depending on which risk factors were present in the regression, providing clues as to the possibility of confounding and over-adjustments. The seven regression models were:

1) Model with SES and demographic variables only
2) Model with obstetric and health variables only
3) Model with psychosocial and psychological variables only
4) Model with SES, demographic, obstetric and health variables
5) Model with SES, demographic, psychosocial and psychological variables
6) Model with obstetric, health, psychosocial and psychological variables
7) Full model containing all variables

5.3.3 Effect modification and biological interaction

Stratified analyses are very important in epidemiological studies.(65) Stratified analyses are used to analyze data for bias, patterns, confounding and effect modifications.(65) In this study, odds of PPD according to the three main pain exposures of interest (presence of pain, duration of pain, and number of chronic

pains) were stratified by selected SES/demographic, obstetric and health and psychosocial/psychological variables that were suspected of modifying the association. Since there was limited data on the association between postpartum pain and PPD, it was not possible to rely on previous studies to select suspected effect modifiers. Stratification variables were therefore chosen on the basis of whether there existed a plausible explanation for the effect modification. These chosen variables were: immigration status, birthing method, sex of the baby, use of non medical pain relief methods, use of medical pain relief, body mass index, maternal smoking, and social support.

Immigration status

It was thought that immigration status might be an effect modifier of the associations between postpartum pain and PPD for two reasons. First of all, refugees, immigrants, and asylum seekers were found to be at greater risk for PPD than their Canadian-born counterparts.(24) Traumatic backgrounds and lack of social support were cited as key factors.(24). They are also known risk factors for the development of chronic pain.(76) The second reason is that ethnic minorities are more susceptible to vitamin D deficiencies, which may be associated with pain and depression.(77) There is evidence that women of ethnic minorities are less likely to be assessed for pain and treated adequately.(78).

Birthing Method

Birthing method was thought to be an effect modifier of the association between postpartum pain and PPD because operative deliveries cause nerve damage, which is associated with the development of chronic post-surgical pain.(79) If birthing method is indeed an effect modifier, the association between postpartum pain and PPD would be stronger following cesarean section than it would be following non operative vaginal deliveries.

Sex of the baby

In some cultures, baby boys are more desirable than baby girls, and there may be increased stress associated with giving birth to a female baby. A study by Xie et al.(80) showed that Chinese women received much less social support after giving birth to a female infant. It was especially true of support from family members.(81) Also, mothers of female infants had higher odds of PPD (OR: 3.67, 95% CI: 2.31, 5.84) compared to women who gave birth to male infants.(80) These results suggest that sex of the baby might be an effect modifier of the association between postpartum pain and PPD.

Use of non-medical and medical pain relief methods

It was thought that the use of non medical pain relief methods as well as medical pain relief methods would diminish the association between pain and PPD, as intensity of pain has been associated with a greater risk of developing chronic pain.(79)

Body Mass Index

Obese patients have a higher risk of complications following surgery which may increase both pain and odds of PPD. Indeed, obese patients have higher risk of heart attack, peripheral nerve injury, wound infection, and urinary track infection post surgery compared to their non obese counterparts.(82) Not only is there more risk associated with surgery for the obese person, but obese women are more likely to deliver via cesarean section compared to their non-obese counterparts.(83) It is very likely that BMI is an effect modifier of the association between postpartum pain and PPD.

Maternal smoking

There is growing evidence that nicotine may have an effect on pain perception. (84-86) Nicotinic acetylcholine receptors (nAChRs) are activated by nicotine or acetylcholine, and can be found "all over the autonomic and central nervous systems and the neuromuscular junction".(84) These receptors have been found

to be involved in pain modulation.(84) Nicotine is thought to modulate pain through several mechanisms, including the activation of α2-adrenergic receptors which releases norepinephrine, the release of endogenous opioids, and through its anti-inflammatory properties.(84-86)The use of nicotine continues to be investigated in its use as postoperative pain management option.(85) For these reasons, it was hypothesized that maternal smoking could be a modifier of the postpartum pain and PPD association.

Social support

The last hypothesized modifier of the association between postpartum pain and PPD is social support. The relationship between social support and PPD is well established while there is contradicting evidence regarding the association between social support and pain. Social support is a well-known protective factor against PPD. Low social support has been shown to be a strong risk factor for PPD. (87) Social support also diminishes pain in experimental settings.(88) However, social support may act as a positive re-enforcer of pain behaviors that are part of chronic pain syndromes, especially if the support offered is not appropriate.(89) This is especially true regarding support from family members, which may "sustain pain behaviors and encourage disability in individuals with chronic pain".(90) In fact, satisfaction with social support and pain behaviors were found to be positively correlated in a study.(89) Even if there is contradictory evidence in the case of family support, support from outside the

family networks, such as involvement in groups or clubs may have a protective effect on both pain and depression as is associated with the maintenance of a balanced lifestyle.(90)

For each of the analyses of effect modification, crude and adjusted odds ratios are presented as well as bootstrapped 95% confidence intervals. The effect modifications have also been further analyzed on the additive scale, to find evidence of biological interaction. The relative excess risk due to interaction (RERI), the attributable proportion due to interaction (AP), and the synergy index (S) were computed for every effect modification using the Excel sheet provided at www.epinet.se.(91)

5.3.4 Multivariate logistic regression modeling

Crude odds ratios

Odds ratios for PPD as well as problematic pain are presented according to SES/Demographics, Obstetric/Health factors, as well Psychosocial/Psychological factors. They are presented with their bootstrapped 95% confidence intervals.

Adjusted odds ratios

Adjusted odds ratios were obtained by performing multivariate logistic regressions. The multivariate logistic regression is a technique that allows for the analysis of a binary outcome with continuous or categorical covariates.(92) It is not only used to assess the effect sizes of these covariates, but also to rank the importance, investigate effect modification, and control for confounding.(65) The logistic regression is "based on a linear relationship between the natural logarithm (ln) of the odds an event and continuous (or categorical) independent variables".(92) It takes the form of: $\ln(p/1-p) = \beta_0 + \beta_1 X + \ldots + \varepsilon$.(92) p is the proportion of success, β_0 is the intercept, $\beta_1 X$ is an independent variable and its regression coefficient, and ε is the random error.(92) Other assumptions of the logistic regression model are that the outcome follows a binomial distribution and that the values of the outcome are statistically independent. (93) This regression technique was used to examine the independent associations of the presence of problematic postpartum pain, the duration of postpartum pain, and the number of chronic postpartum pains with PPD.

One full model and six nested sub models were created for each of these three associations being examined:

1) Model with main exposure of interest and SES and demographic variables
2) Model with main exposure of interest and obstetric and health variables
3) Model with main exposure of interest and psychosocial and psychological variables
4) Model with main exposure of interest as well as SES/demographic and obstetric variables
5) Model with main exposure of interest as well as psychosocial/psychological and obstetric variables
6) Model with main exposure of interest as well as psychosocial/psychological and SES/demographic variables
7) Full model with all variables

5.3.5 Model fit statistics

The model fit statistics were obtained through the use of the Likelihood ratio test and the Hosmer-Lemeshow test. The c-statistics were also considered.

Likelihood ratio test

Likelihood Ratio tests were done to assess the fit of the final models. The use of the Likelihood Ratio test was appropriate as the six sub-models were nested within the full final models and the sample size stayed constant.(93) All sub models were compared to the main full model using this method. The difference in -2 log L as well as the difference in degrees of freedom were computed for each pairs of model that were compared. The associated p-values were used to assess whether the differences were significant or not.

The Hosmer-Lemeshow test

The Hosmer-Lemeshow test assesses the "goodness of fit" of the model.(93) As Vittinghoff (2006) explains, "the test works by forming groups of the ordered, estimated outcome probabilities and evaluating the concordance of the expected outcome frequencies in these groups with their empirical counterparts".(93) A non significant Hosmer-Lemeshow test signifies that the fit of the model is good.(93)

The c-statistic

The c-statistic, a measure of concordance, provides the measure of the discrimination ability of the models.(93) In logistic regression models, the c-

statistic is the area under the receiver operating characteristic curve, better known as the ROC curve.(94) The c-statistic varies between 0.5 and 1. A c-statistic of 0.5 indicates that the model has no discriminative abilities while a c-statistic of 1.0 indicates perfect discriminative abilities.(94)

5.3.6 Sensitivity analyses

Sensitivity analyses were performed for all final models obtained by means of multivariate logistic regression. Sensitivity analyses evaluate the robustness of the findings and provide information as to the magnitude of possible bias.(75, 95) The sensitivity analyses for this part of thesis were performed with the multiply imputed dataset and the sample restricted to respondents without a history of depression.

5.4 Results

A total of 5615 respondents were included in the final analyses. The results are presented in Table 1 to 5. The tables are organized according to groupings of variables, except for table 5 which contains the results of the investigation of effect modification.

Table 1 presents the descriptive statistics as well as the results from the logistic regressions and sensitivity analyses for the main exposures of interest. Table 2

presents the descriptive statistics, results from the confounding analyses, as well as crude and adjusted ORs for the SES and demographic variables. Table 3 and Table 4 are similar to table 2, but present the results for obstetric and health variables (table 3), and psychosocial and psychological variables (table 4). To help clarify the results, the tables are presented first. A description of the key points emanating from these tables follows the presentation of the tables.

Table 1: Descriptive statistics as well as crude and adjusted odds ratios (OR) and 95% confidence intervals for the associations between the main pain exposures of interest and PPD in Canadian women

Exposure	Total sample size	PPD Prevalence †	Crude OR	Adjusted OR: SES /demographic	Adjusted OR: Obstetric /health	Adjusted OR: Psychological /psychosocial	Adjusted OR: SES/ dem., obstetric /health	Adjusted OR: SES/dem., psychological /psychosocial	Adjusted OR: Obst./health, psychological /psychosocial	**Final Model: OR adjusted for all variables**	Final Model: Multiply imputed dataset	Final Model: never previously depressed sub-sample
1) Presence of pain												
No (ref)	1061	3.7%										
Yes	4553	7.7%	2.2 (1.5,3.1)	2.1 (1.5, 3.1)	2.2 (1.6, 3.2)	1.8 (1.3, 2.7)	2.1 (1.4, 3.1)	1.7 (1.2, 2.5)	1.8 (1.3, 2.6)	**1.7 (1.2, 2.5)**	1.8 (1.4, 2.1)	2.0 (1.2, 3.2)
2) Duration of pain												
None (ref)*	1061	3.7%										
Acute only	3085	5.3%	1.5 (1.0, 2.1)	1.7 (1.0, 2.2)	1.5 (1.0, 2.2)	1.3 (0.9, 1.9)	1.5 (1.0, 2.2)	1.3 (0.9, 1.9)	1.3 (0.9, 2.0)	**1.3 (0.9, 1.9)**	1.4 (0.6, 2.2)	1.5 (0.9, 2.5)
Chronic	1468	12.7%	3.8 (2.6, 5.6)	3.4 (2.3, 5.1)	3.8 (2.6, 5.7)	2.5 (1.6, 3.7)	2.4 (2.3, 5.0)	2.5 (1.6, 3.7)	2.7 (1.8, 4.0)	**2.4 (1.6, 3.6)**	2.4 (1.6, 3.2)	2.8 (1.7, 4.7)
3) Number of chronic postpartum pains												
None	4146	4.9%										
One	1193	10.0%	2.2 (1.7, 2.8)	1.55, 2.58	2.1 (1.6, 2.7)	1.7 (1.3, 2.3)	1.9 (1.5, 2.5)	1.7 (1.3, 2.2)	1.7 (1.3, 2.3)	**1.7 (1.3, 2.2)**	1.6 (1.4, 1.9)	1.7 (1.2, 2.3)
Two	241	22.6%	5.7 (4.0, 8.1)	4.7 (3.3, 6.8)	5.7 (3.9, 8.2)	3.7 (2.5, 5.5)	4.7 (3.2, 6.9)	3.1 (2.1, 4.7)	3.8 (2.6, 5.7)	**3.2 (2.1, 4.9)**	2.6 (2.2, 3.0)	3.4 (2.1, 5.7)
Three +	34	33.5%	9.8 (4.6, 21.1)	7.1 (3.1, 16.0)	8.7 (3.6, 21.0)	5.9 (1.9, 17.9)	6.5 (2.5, 16.7)	4.4 (0.9, 21.0)	5.5 (1.4, 22.7)	**4.2 (0.7, 25.0)**	4.1 (3.0, 5.1)	5.1 (0.0, 8.5)

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All prevalences and odds ratios , as well as 95% CI were obtained using bootstrap weights

Table 2: Descriptive statistics and results from the confounding analyses for the SES and demographic variables

	Outcome: Presence of problematic pain				Outcome: Postpartum depression								
SES and demographics variables	Total sample size	Pain prevalence †	Pain crude OR	95% CI	PPD Prevalence	PPD crude OR	95% CI	Adjusted OR: Model 1‡	95% CI	Adjusted OR: Model 2§	95% CI	Adjusted OR: Model 3‖	95% CI
Maternal age													
15 to 19*	155	87.4%	1.6	1.0, 2.7	14.5%	2.7	1.6, 4.3	1.4	0.7, 2.7	1.4	0.8, 2.8	1.4	0.7, 2.6
20 to 24	680	85.7%	1.4	1.1, 1.8	8.4%	1.4	1.0, 2.0	0.9	0.6, 1.4	0.9	0.6, 1.4	0.9	0.6, 1.4
25 to 29 (ref)	1693	80.9%			6.0%								
30 to 34	1962	81.4%	1.0	0.9, 1.2	6.4%	1.1	0.8, 1.4	1.1	0.8, 1.5	1.1	0.8, 1.5	1.1	0.8, 1.6
35 to 39	921	81.5%	1.0	0.8, 1.3	7.9%	1.3	1.0, 1.7	1.1	0.8, 1.7	1.2	0.8, 1.7	1.2	0.8, 1.8
40 and over*	203	76.7%	0.8	0.6, 1.1	8.7%	1.5	0.8, 2.7	1.0	0.5, 2.0	1.0	0.5, 2.0	1.0	0.5, 2.0
Maternal education													
Less than high school grad.	452	81.9%	1.0	0.8, 1.3	13.0%	2.5	1.7, 3.6	1.5	0.9, 2.5	1.4	0.8, 2.4	1.4	0.8, 2.4
High school graduation	786	81.5%	1.0	0.8, 1.2	8.9%	1.7	1.2, 2.3	1.3	0.8, 2.0	1.3	0.8, 1.9	1.3	0.8, 2.0
Post secondary	2423	81.6%	1.0	0.8, 1.2	6.6%	1.2	0.9, 1.5	1.0	0.7, 1.3	1.0	0.7, 1.3	1.0	0.7, 1.3
Bachelors degree(ref)	1953	81.8%			5.6%								
Maternal marital status													
Married/Common law (ref)	5085	81.5%			6.5%								
Divorced/widowed*	102	77.9%	0.8	0.5, 1.3	16.3%	2.8	1.5, 5.2	1.0	0.5, 2.1	1.1	0.5, 2.2	1.1	0.5, 2.3
Single	427	85.5%	1.3	1.0, 1.8	11.1%	1.8	1.3, 2.5	0.7	0.5, 1.2	0.8	0.5, 1.2	0.8	0.5, 1.3
Household annual income													
Less than $20,000	503	82.2%	1.0	0.8, 1.4	14.1%	3.3	2.2, 5.1	1.6	0.9, 2.7	1.5	0.9, 2.5	1.4	0.8, 2.5
$20,000 to $39,000	998	83.1%	1.1	0.9, 1.4	9.7%	2.2	1.5, 3.2	1.5	0.9, 2.3	1.4	0.9, 2.2	1.3	0.8, 2.2
$40,000 to $59,000	1088	82.1%	1.0	0.8, 1.3	6.3%	1.4	0.9, 2.1	1.0	0.6, 1.6	1.0	0.6, 1.5	0.9	0.6, 1.5
$60,000 to $79,000	1016	81.7%	1.0	0.8, 1.3	5.4%	1.2	0.8, 1.8	1.1	0.7, 1.6	1.0	0.7, 1.6	1.0	0.6, 1.5
$80,000 to $99,000*	716	79.2%	0.8	0.7, 1.1	5.0%	1.1	0.6, 1,7	1.1	0.7, 1.9	1.1	0.7, 1.8	1.1	0.6, 1.8
$100,000 and + (ref)	1034	81.8%			4.7%								

Unknown*	259	80.1%	0.9	0.6, 1.3	9.7%	2.2	1.2, 3.8	1.4	0.7, 2.7	1.3	0.7, 2.6	1.3	0.6, 2.5
Maternal region of residence													
Atlantic	1016	80.3%	0.8	0.7, 1.0	6.0%	0.8	0.6, 1.1	1.0	0.7, 1.4	1.0	0.7, 1.4	1.0	0.7, 1.4
Quebec	1035	82.8%	1.0	0.8, 1.2	7.5%	1.0	0.8, 1.3	1.4	1.0, 1.9	1.4	1.0, 1.9	1.4	1.0, 2.0
Ontario (ref)	1667	82.9%			7.5%								
Prairies	1175	79.7%	0.8	0.7, 1.0	6.1%	0.8	0.6, 1.1	0.9	0.6, 1.3	0.9	0.6, 1.2	0.9	0.6, 1.2
British Columbia	552	79.3%	0.8	0.6, 1.0	6.2%	0.8	0.6, 1.2	0.9	0.6, 1.4	0.9	0.6, 1.4	0.9	0.6, 1.4
Territories	169	77.4%	0.7	0.5, 0.9	9.9%	1.4	0.9, 2.0	1.2	0.7, 2.1	1.3	0.7, 2.3	1.3	0.7, 2.3
Rural dwelling	1255	80.0%	0.9	0.7, 1.0	5.8%	0.8	0.6, 1.1	0.9	0.6, 1.2	0.8	0.6, 1.2	0.9	0.6, 1.2
Urban dwelling (ref)	4359	82.0%			7.2%								
Maternal immigrant status													
Yes	975	84.2%	1.3	1.0, 1.5	11.2%	2.1	1.6, 2.6	2.6	1.9, 3.5	2.5	1.8, 3.3	2.4	1.7, 3.2
No (ref)	4639	81.0%			5.8%								
Maternal aboriginal status													
Yes*	329	80.0%	0.9	0.7, 1.2	10.5%	1.6	1.1, 2.4	1.2	0.7, 1.9	1.2	0.7, 2.0	1.2	0.7, 1.9
No (ref)	5285	81.7%			6.8%								

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All prevalences and odds ratios , as well as 95% CI were obtained using bootstrap weights

‡ Model 1: Multivariate logistic regression predicting PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate logistic regression predicting PPD with the duration of pain as main exposure

|| Model 3: Multivariate logistic regression predicting PPD with the number of chronic pains as main exposure

Table 3: Descriptive statistics and results from the confounding analyses for the obstetric and health variables

	Outcome: Presence of problematic pain				Outcome: Postpartum depression								
Obstetric and health variables	Total sample size	Pain prevalence †	Pain crude OR	95% CI	PPD Prevalence	PPD crude OR	95% CI	Adjusted OR: Model 1‡	95% CI	Adjusted OR: Model 2§	95% CI	Adjusted OR: Model 3‖	95% CI
Birthing Method													
Vaginal birth (ref)	4134	81.2%			7.2%								
Cesarean birth	1480	83.0%	1.1	1.0, 1.3	6.3%	0.9	0.7, 1.1	0.8	0.5, 1.3	0.8	0.5, 1.3	0.8	0.5, 1.2
Operative delivery - Forceps													
Yes	291	87.0%	1.5	1.1, 2.2	8.4%	1.2	0.8, 2.0	1.1	0.6, 2.0	1.1	0.6, 1.9	1.1	0.6, 1.9
No (ref)	5323	81.4%			6.9%								
Operative delivery - Vacuum													
Yes	490	87.5%	1.6	1.2, 2.2	5.4%	0.7	0.5, 1.2	0.7	0.4, 1.1	0.7	0.4, 1.1	0.6	0.4, 1.1
No (ref)	5124	81.1%			7.1%								
Operative delivery - Episiotomy													
Yes	900	87.2%	1.6	1.3, 2.0	8.3%	1.3	0.9, 1.7	1.1	0.8, 1.7	1.2	0.8, 1.7	1.1	0.8, 1.6
No (ref)	4714	80.5%			6.7%								
Maternal stitches													
Yes	2973	84.4%	1.5	1.3, 1.7	7.1%	1.0	0.8, 1.3	1.1	0.8, 1.6	1.1	0.8, 1.6	1.2	0.8, 1.6
No (ref)	2641	78.5%			6.9%								
Maternal parity													
One (ref)	2550	86.2%			6.0%								
Two	2067	79.5%	0.6	0.5, 0.7	6.9%	1.2	0.9, 1.5	1.2	0.8, 1.7	1.2	0.8, 1.7	1.1	0.8, 1.6
Three	693	76.8%	0.5	0.4, 0.7	9.2%	1.6	1.2, 2.2	1.3	0.8, 2.1	1.3	0.8, 2.1	1.3	0.8, 2.0
Four	304	70.0%	0.4	0.3, 0.5	10.7%	1.9	1.2, 2.9	1.2	0.7, 2.3	1.2	0.7, 2.3	1.2	0.7, 2.3
Postpartum contact by public health nurse													
Yes (ref)	5247	81.7%			6.7%								

No	367	81.0%	1.0	0.7, 1.3	10.2%	1.6	1.1, 2.3	1.5	1.0, 2.3	1.5	0.9, 2.3	1.4	0.9, 2.3
Sex of baby													
Male (ref)	2885	81.6%			7.0%								
Female	2729	81.7%	1.0	0.9, 1.2	7.0%	1.0	0.8, 1.2	1.0	0.8,1.3	1.0	0.8, 1.3	1.0	0.8, 1.3
Maternal pre-natal education													
Yes (ref)	1903	85.5%			5.6%								
No	3711	79.8%	0.7	0.6, 0.8	7.7%	1.4	1.1, 1.7	1.1	0.8, 1.5	1.1	0.8, 1.5	1.1	0.8, 1.6
Maternal use of non medical pain relief													
Yes (ref)	4324	81.4%			6.7%								
No	1290	82.7%	1.1	0.9, 1.3	7.8%	1.2	0.9, 1.5	1.2	0.9, 1.8	1.2	0.9, 1.8	1.2	0.9, 1.8
Maternal use of medical pain relief use													
Yes (ref)	4531	83.5%			7.2%								
No	1083	74.4%	0.6	0.5, 0.7	6.3%	0.9	0.7, 1.2	0.8	0.6, 1.1	0.8	0.6, 1.2	0.8	0.6, 1.2
Postpartum period of survey													
Early postpartum	1592	81.1%	0.9	0.7, 1.1	6.3%	0.8	0.7, 1.1	0.9	0.6, 1.2	0.9	0.6, 1.2	0.9	0.6, 1.2
Mid postpartum	2750	81.7%	1.0	0.8, 1.2	7.2%	1.1	0.9, 1.3	1.0	0.7, 1.4	1.0	0.8, 1.4	1.0	0.8, 1.4
Late postpartum (ref)	1272	82.4%			7.5%								
Infant neonatal intensive care unit admission													
Yes	720	82.3%	1.1	0.8, 1.3	8.2%	1.2	0.9, 1.7	1.1	0.7, 1.5	1.0	0.7, 1.5	1.0	0.7, 1.5
No (ref)	4894	81.6%			46.5%								
Maternal previous no-live birth													
Yes	1785	80.8%	0.9	0.8, 1.1	8.3%	1.3	1.1, 1.6	1.0	0.8, 1.3	1.0	0.8, 1.4	1.1	0.8, 1.4
No (ref)	3829	82.1%			6.4%								
Maternal smoking													
Yes	1032	82.1%	1.0	0.8, 1.3	9.9%	1.6	1.2, 2.1	1.0	0.7, 1.5	1.0	0.7, 1.5	1.0	0.7, 1.5
No (ref)	4582	81.6%			6.4%								
Maternal pre-pregnancy health problems													

Yes	893	81.7%	1.0	0.8, 1.2	10.2%	1.7	1.3, 2.1	1.4	1.0, 1.9	1.3	1.0, 1.8	1.3	1.0, 1.8
No (ref)	4721	81.7%			6.4%								
Maternal new health problems													
Yes	1389	84.4%	1.3	1.1, 1.5	9.3%	1.5	1.2, 1.9	1.3	1.0, 1.7	1.3	1.0, 1.7	1.3	1.0, 1.7
No (ref)	4225	80.8%			6.3%								
Maternal body mass index													
Underweight	274	82.1%	1.0	0.7, 1.3	7.5%	1.1	0.7, 1.9	0.8	0.5, 1.4	0.8	0.5, 1.4	0.8	0.5, 1.4
Normal (ref)	3205	82.4%			6.6%								
Overweight	1287	80.0%	0.9	0.7, 1.0	6.8%	1.0	0.8, 1.3	1.0	0.7, 1.3	1.0	0.7, 1.3	1.0	0.7, 1.3
Obese	848	81.0%	0.9	0.7, 1.1	8.6%	1.3	1.0, 1.8	1.0	0.7, 1.4	1.0	0.7, 1.4	1.0	0.7, 1.4

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All prevalences and odds ratios , as well as 95% CI were obtained using bootstrap weights

‡ Model 1: Multivariate logistic regression predicting PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate logistic regression predicting PPD with the duration of pain as main exposure

|| Model 3: Multivariate logistic regression predicting PPD with the number of chronic pains as main exposure

Table 4: Descriptive statistics and results from the confounding analyses for the psychosocial and psychological variables

	Outcome: Presence of problematic pain				Outcome: Postpartum depression								
Psychosocial and psychological variables	Total sample size	Pain prevalence †	Crude OR	95% CI	PPD Prevalence	Crude OR	95% CI	Adjusted OR: Model 1‡	95% CI	Adjusted OR: Model 2§	95% CI	Adjusted OR: Model 3‖	95% CI
Reaction to pregnancy													
Negative	408	82.1%	1.03	0.8, 1.4	13.7%	2.3	1.7, 3.1	1.3	0.9, 1.9	1.2	0.8, 1.8	1.2	0.8, 1.9
Positive (ref)	5206	81.6%			6.5%								
Perceived Stress													
High	3203	84.9%	1.6	1.4, 1.9	10.0%	3.5	2.6, 4.6	2.5	1.8, 3.4	2.5	1.8, 3.4	2.4	1.8, 3.3
Low (ref)	2411	77.4%			3.1%								
Stressful events													
None (ref)	2170	79.9%			3.3%								
One event	1546	82.3%	1.2	1.0, 1.4	6.3%	2.0	1.4, 2.8	1.5	1.1, 2.2	1.5	1.0, 2.1	1.5	1.0, 2.1
Two events	912	80.7%	1.1	0.9, 1.3	7.9%	2.5	1.7, 3.7	1.9	1.3, 2.8	1.8	1.2, 2.7	1.9	1.2, 2.8
Three events	497	84.6%	1.4	1.1, 1.8	13.8%	4.7	3.2, 7.0	2.7	1.8, 4.3	2.7	1.7, 4.1	2.7	1.7, 4.2
Four events or more	489	87.1%	1.7	1.2, 2.3	19.0%	6.9	4.8, 9.8	3.3	2.1, 5.2	3.1	1.4, 4.9	3.1	2.0, 5.0
Social support													
Adequate (ref)	4990	81.5%			5.8%								
Inadequate	624	83.1%	1.1	0.9, 1.4	16.1%	3.1	2.4, 4.0	1.9	1.4, 2.5	1.8	1.3, 2.4	1.7	1.2, 2.3
History of depression													
Yes	895	84.3%	1.3	1.0, 1.5	13.4%	2.5	1.9, 3.2	2.0	1.5, 2.7	2.0	1.5, 2.6	1.9	1.5, 2.6
No (ref)	4719	81.2%			5.8%								
Alcohol use (pregnancy)													
Yes	534	83.9%	1.2	0.9, 1.5	8.0%	1.2	0.8, 1.7	1.2	0.8, 1.8	1.2	0.8, 1.8	1.2	0.8, 1.8
No (ref)	5080	81.4%			6.9%								
Drug use (pregnancy) *													

Yes	51	93.8%	3.4	1.0, 11.6	25.0%	4.5	2.1, 9.7	2.1	0.8, 5.5	2.1	0.8, 5.4	2.2	0.8, 5.6
No (ref)	5563	81.6%			6.8%								
History of abuse													
Yes	674	87.2%	1.6	1.2, 2.0	15.3%	2.8	2.2, 3.6	1.6	1.2, 2.3	1.6	1.1, 2.2	1.6	1.1, 2.2
No (ref)	4940	81.0%			6.0%								

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All prevalences and odds ratios , as well as 95% CI were obtained using bootstrap weights

‡ Model 1: Multivariate logistic regression predicting PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate logistic regression predicting PPD with the duration of pain as main exposure

|| Model 3: Multivariate logistic regression predicting PPD with the number of chronic pains as main exposure

Table 5: Investigation of the modification effect of selected variables on the associations between the main exposures and PPD

Variable	n	1) Presence of problematic postpartum pain		2)The duration of postpartum pain				3) The number of sites of chronic postpartum pain			
				Acute pain only		Chronic pain		One site of pain		Two sites of pain +	
		Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR
1) Immigration status											
Immigrant	975	4.0 (1.3, 12.2)	3.8 (1.0, 13.8)	2.6 (0.8, 8.1)	2.6 (0.7, 9.6)	6.3 (2.0, 19.5)	5.5 (1.4, 21.0)	2.3 (1.5, 3.7)	2.22 (1.2, 4.0)	4.6 (2.7, 8.1)	3.5 (1.5, 8.1)
Canadian born	4639	1.72 (1.2, 2.6)	1.3 (0.8, 1.9)	1.2 (0.8, 1.8)	1.0 (0.6, 1.6)	3.0 (2.0, 4.5)	1.8 (1.1, 2.7)	2.0 (1.5, 2.7)	1.4 (1.0, 1.9)	6.3 (4.3, 9.2)	3.8 (2.3, 6.1)
2) Birthing method											
Caesarean delivery	1480	2.9 (1.0, 7.8)	2.4 (0.7, 7.4)	1.8 (0.6, 5.1)	1.7 (0.5, 5.6)	4.5 (1.6, 12.9)	3.2 (1.0, 10.1)	1.7 (1.0, 2.3)	1.5 (0.8, 2.8)	7.0 (3.9, 12.7)	4.3 (1.8, 10.4)
Vaginal delivery	4134	2.1 (1.4, 3.1)	1.6 (1.0, 2.4)	1.4 (0.9, 2.1)	1.2 (0.8, 1.9)	3.7 (2.4, 5.7)	2.3 (1.5, 3.7))	2.4 (1.8, 3.1)	1.8 (1.3, 2.4)	6.0 (4.0, 8.9)	3.2 (1.9, 5.3)
3) Sex of baby											
Female baby	2729	2.9 (1.6, 5.4)	2.4 (1.3, 4.7)	1.9 (1.0, 3.5)	1.8 (0.9, 3.5)	5.4 (2.9, 10.0)	3.6 (1.8, 7.2)	2.6 (1.8, 3.6)	1.9 (1.3, 2.9)	6.5 (4.1, 10.3)	3.8 (2.1, 6.8)
Male baby	2885	1.7 (1.1, 2.8)	1.3 (0.8, 2.3)	1.2 (0.7, 2.0)	1.0 (0.6, 1.8)	2.9 (1.7, 4.7)	1.8 (1.0, 3.2)	1.8 (1.3, 2.6)	1.4 (0.9, 2.1)	5.8 (3.7, 9.0)	3.4 (1.9, 6.2)
4) Non medical pain relief											
Non medical pain relief use	4324	1.9 (1.3, 2.9)	1.5 (1.0, 2.3)	1.4 (0.9, 2.1)	1.2 (0.8, 1.9)	3.3 (2.1, 5.0)	2.1 (1.3, 3.3)	2.1 (1.5, 2.7)	1.6 (1.1, 2.2)	5.4 (3.6, 7.9)	3.0 (1.8, 4.8)
No use	1290	3.4 (1.1, 10.7)	2.9 (0.7, 10.9)	1.9 (0.6, 6.3)	1.8 (0.4, 7.1)	6.1 (1.9, 19.5)	4.6 (1.2, 18.1)	2.5 (1.5, 4.2)	2.1 (1.1, 4.1)	8.1 (4.4, 14.7)	7.3 (2.6, 20.2)
5) Medical pain relief											
Medical pain relief use	4531	1.9 (1.3, 2.8)	1.6 (1.0, 2.4)	1.3 (0.9, 2.0)	1.3 (0.8, 2.0)	3.0 (2.0, 4.6)	2.1 (1.3, 3.3)	1.8 (1.3, 2.4)	1.4 (1.0, 1.9)	5.6 (4.0, 7.9)	3.2 (2.1, 4.9)
No use	1083	3.7 (1.4, 10.1)	2.3 (0.6, 9.3)	2.0 (0.7, 5.7)	1.6 (0.4, 6.8)	9.0 (3.2, 25.2)	4.8 (1.0, 22.6)	4.8 (2.7, 8.5)	3.1 (1.1, 8.4)	9.1 (3.5, 24.1)	4.5 (0.8, 26.7)
6) Maternal smoking											
Smoker	1032	1.1 (0.6, 2.0)	0.7 (0.3, 1.7)	0.7 (0.3, 1.3)	0.5 (0.2, 1.3)	1.8 (0.9, 3.6)	1.1 (0.4, 2.8)	1.6 (0.9, 2.8)	1.2 (0.5, 2.6)	7.1 (3.7, 13.7)	5.6 (1.8, 17.6)
Non smoker	4582	3.0 (1.9, 4.6)	2.3 (1.4, 3.8)	2.0 (1.2, 3.2)	1.8 (1.1, 2.9)	5.1 (3.2, 8.2)	3.3 (2.0, 5.6)	2.3 (1.8, 3.1)	1.8 (1.3, 2.5)	5.9 (4.0, 8.9)	3.3 (2.0, 5.3)
7) Body Mass Index											
Underweight to normal	3479	1.7 (1.1, 2.6)	1.2 (0.8, 2.0)	1.1 (0.7, 1.7)	0.9 (0.6, 1.5)	2.9 (1.8, 4.7)	1.8 (1.1, 3.1)	2.1 (1.5, 2.9)	1.7 (1.1, 2.4)	5.8 (3.8, 8.7)	3.3 (1.9, 5.6)
Obese to overweight	2135	3.8 (1.9, 7.6)	3.2 (1.5, 6.7)	2.6 (1.3, 5.3)	2.5 (1.1, 5.3)	6.4 (3.1, 12.9)	4.5 (2.1, 9.8)	2.2 (1.5, 3.3)	1.7 (1.1, 2.8)	6.8 (4.0, 11.5)	4.7 (2.3, 9.5)
8) Social support											
Adequate social support	4990	2.4 (1.5, 3.7)	1.8 (1.1, 2.9)	1.7 (1.1, 2.7)	1.4 (0.9, 2.3)	3.9 (2.5, 6.3)	2.5 (1.6, 4.2)	2.0 (1.4, 2.6)	1.5 (1.1, 2.0)	6.3 (4.4, 9.2)	4.2 (2.7, 6.6)
Inadequate social support	624	1.7 (0.9, 3.4)	1.5 (0.6, 3.9)	1.0 (0.5, 2.2)	0.9 (0.3, 2.7)	2.7 (1.3, 5.5)	2.2 (0.8, 6.3)	2.3 (1.4, 3.8)	2.3 (1.1, 4.9)	3.4 (1.8, 6.3)	2.3 (0.7, 7.1)

5.4.1 Descriptive statistics

At the time of the interview, 7.0% of the MES respondents had a score of 13 and more on the EPDS and were therefore deemed to suffer from PPD. Results show that PPD was more prevalent in lower socioeconomic groups.

Fortunately, the MES captured a good sample of foreign-born women and aboriginals. Both of these groups had higher prevalences of PPD compared to their Canadian-born non-aboriginal counterparts. Indeed, 10.5% of aboriginal respondents and 11.2% of immigrant women had PPD. Most of the respondents of the MES were healthy. However, 56.9% of the MES participants reported being stressed at the time of interview. This stress was mostly postpartum onset and associated with taking care of a newborn, as a majority of respondents did not report pre-pregnancy stressful life events such as the death of a loved one or financial pressure. It is also worth noting that 15.4% of the respondents reported a previous episode of depression, which is a key risk factor for PPD.

Problematic postpartum pain was very prevalent among the respondents to the EPDS. Almost all respondents reported problematic postpartum pain at some point postpartum (87.1%) and 27.1% reported chronic pain at the time of the interview. The most commonly reported problematic pain in the acute period (first three months postpartum) was cesarean incision pain (62.6% of women who had

cesarean section), followed by pain in the vagina (51.9% of women who had vaginal delivery), breast pain (50.5%), back pain (35.5%), and migraine pain (10.4%). However, there are differences in reported acute and chronic pain. Cesarean incision pain was the most reported type of chronic pain (20.1% of women who had cesarean deliveries), followed by back pain (16.1%), vagina pain (7.1% of all women who had vaginal deliveries), migraine pain (3.3%) and breast pain (2.8%).

5.4.2 Confounding analysis

Results revealed that maternal age, parity, maternal prenatal education, new health problems in pregnancy, perceived stress, and a history of depression were associated with both PPD and postpartum pain. It is difficult to determine if any of these variables satisfied the causal pathway criteria since the causal pathway between postpartum pain and PPD remains unknown. It is fair to say that these variables were probably the main confounders of the association between postpartum pain and PPD.

Fortunately, the logistic regressions adjusted for most of the confounding for all 21 models. Table 1 shows the variation in adjusted ORs according to sub-models. The biggest variations were observed in the ORs of the models containing psychosocial and psychological variables. The ORs were lower when

these variables are included in the models. Again, these results suggest that psychosocial and psychological factors had a greater confounding effect on the association of postpartum pain with PPD.

5.4.3 Effect modification and biological interaction

Results of the investigation of effect modification (table 5) were inconclusive. The 95% confidence intervals were all overlapping, possibly due to the variance estimation method. Even if the results were inconclusive, interesting trends were observed. Being an immigrant, having had a cesarean section delivery, not using any pain relief methods and being obese were all factors that strengthened the association between postpartum pain and PPD.

A very surprising finding was that adequate social support did not decrease the association between postpartum pain and PPD. On the contrary, the association of postpartum pain and PPD was stronger for women who reported adequate social support. Just as surprising, maternal smoking appeared to be a protective factor of the association between postpartum and PPD. Compared to non-smokers, women who reported chronic postpartum pain had lower odds of PPD. However, the protective effect of nicotine was not observed in women who reported more than one site of chronic pain.

All of these interactions were also analyzed on the additive scale to find evidence of biological interaction. However, no significant additive interactions were found. The RERI, AP, and the S index were all inconclusive.

5.4.4 Multivariate logistic regressions

The main results from the multivariate logistic regressions are presented in Table 1. Results indicate that problematic postpartum pain was an independent risk factor for PPD. After adjusting for all study variables, there remained a strong, statistically significant relationship between 1) the presence of problematic postpartum pain and PPD, 2) the duration of the problematic postpartum pain and PPD, and 3) the number of reported chronic pain sites and PPD in the MES population.

When all the study variables were held constant, odds of PPD were 1.7 times greater (95% CI: 1.2, 2.5) for women who reported problematic postpartum pain compared to women who did not report problematic postpartum pain. Odds of PPD for women who reported chronic pain was 2.4 (95% CI: 1.6, 3.6), while women who had acute pain that eventually resolved had odds of PPD of 1.3 (95% CI: 0.9, 1.9). Results also show that there was a positive exposure-response relationship between the number of chronic postpartum pains and PPD. Odds of PPD for respondents reporting one site of chronic pain was 1.7

(95% CI: 1.3, 3.2) and increased to 3.2 (95% CI: 2.1, 4.9) for those reporting two site of chronic pain, and reached 4.2 (95% CI: 0.7, 25.0) for those reporting three or more sites of chronic pain. Unfortunately, the sample size for the "three or more sites of chronic pain" category was not large enough to have results that were statistically significant.

Of all the study variables, only a few remained statistically significant risk factors for PPD. These risk factors were immigration status, perceived stress, stressful life events, inadequate social support, previous depression, and previous abuse.

5.4.5 Model fit statistics

Model fit statistics were obtained for the final multivariate logistic regression models as well as the six nested sub-models. All p-values obtained from the log likelihood tests were statistically significant, proving that the models were well fitted, and that the full models, containing all the study variables, were better than the nested sub models which contained only subsets of variables. All models had non-significant p-values associated with the Hosmer-Lemeshow test, showing no evidence of a lack of fit for any of the models. The c-statistics associated with the full models for 1) the association of the presence of problematic pains with PPD, 2) the association of the duration of postpartum pain with PPD, and 3) the association of the number of chronic pains with PPD were: 0.791 (acceptable to

excellent discrimination), 0.798 (acceptable to excellent discrimination), and 0.800 (acceptable discrimination).

5.4.6 Sensitivity analyses

The sensitivity analyses were performed on the multiply imputed dataset as well as the sample restricted to MES respondents who were never previously depressed. The results are presented in Table 1.

Prior to creating the multiply imputed dataset, the MES dataset was analyzed for patterns of missing data in order to determine if data was missing at random for PPD, the outcome variable. The variables that were chosen for this analysis were mother's age at the time of interview, the province of residence, immigration status, parity, and years of formal education. Between survey participants who responded to all the questions pertaining to the EPDS and those who did not complete the EPDS, there were no significant differences observed in terms of age, parity and education. Those who did not complete the EPDS were more likely to be foreign-born and to come from Nunavut or Alberta. The information was not missing completely at random; however, it is probably safe to assume

that the information was missing at random. The multiple imputation method requires that the information be missing at random.

The sensitivity analyses showed that the results of the logistic regressions were robust. The imputed estimates were slightly higher than the estimates of the final model (OR: 1.8, 95% C.I.: 1.4, 2.1). It can be concluded that the final model's estimates were probably fairly conservative. Interestingly, the restricted analysis (with a sample without respondents who had been previously depressed) showed a much stronger association between problematic postpartum pain and postpartum depression (OR: 2.0, 95% CI: 1.2, 3.2). This finding would favor the consequence theory, where pain causes depression.(55)

6.0 PART 2: THE ASSOCIATION BETWEEN POSTPARTUM PAIN AND PPD USING ORDERED LOGISTIC REGRESSION MODELLING

6.1 Objective

The second objective of this thesis project was to explore the use of the ordered logistic regression as a valid method to study the association between postpartum pain and PPD, and to examine what subtype of ordered logistic regression is best suited for this type of research (ex: proportional odd modeling) when the outcome is divided into three PPD categories:

1. No PPD (EPDS scores of 0-9)
2. At risk for PPD (EPDS scores of 10-12)
3. PPD (EPDS scores of 13 and +)

6.2 Research questions

The particular research questions that guided the analyses were the following:

1) For any given risk factor for PPD, are the effects proportional?
2) If the odds are not proportional, are different variables involved the lowest categories of PPD to the at risk category, compared to moving from the at risk category of PPD to the highest?

3) Does the researcher gain accuracy by using the OLR to study PPD instead of the normally used binary logistic regression?

6.3 Hypotheses

It was expected that the odds would not be proportional, and that certain risk factors, such as previous depression, would be associated with higher PPD categories. It was also expected that more accuracy would be gained by using ordered logistic regression modelling to explore the association between postpartum pain and PPD.

6.4 Analytical Strategy

6.4.1 Ordered logistic regression

These questions were answered by means of ordered logistic regression, which is an "extension of the binary logistic regression".(96) In the previous section, the analyses were conducted with a binary outcome. PPD was defined as a score 12/13 (13 or more) on the EPDS. However, reality is never so clear cut. Some women, although they do not score 13 on the EPDS, may still suffer from a mild form of PPD, or may be at great risk for PPD. Important information was potentially sacrificed in order to use the binary logistic regression modeling technique in the first chapter.(97) For example, it may be that particular risk

factors have a more important impact on the less severe forms of PPD than they have on the more severe cases.

The ordered logistic regression with a cumulative mode of comparison is the perfect method to investigate the impact of the risk factors on different levels of the PPD continuum.(97) A cumulative mode of comparison is preferred since the independent variable "is an ordinal scale that represents an underlying continuous measure (EPDS)".(97) The three following levels of PPD are based on the continuous scores to the EPDS scale:

Level 1: No PPD (EPDS score of 0 to 9)
Level 2: Increased risk /possible depression (EPDS score of 10-12)
Level 3: Presence of PPD (EPDS score of 13 and +) (6)

The ordered logistic regression with a cumulative approach compares "the probability of being at a given point compared to the probability of being beyond that point: pr[y = m]/pr[y > m])".(97) For M outcome categories, there are M-1 binary logit equations formed.(97) Since this study compares three categories, two binary logit equations are formed, giving two cut point odds ratios.(97) The first equation would be level 1 versus 2,3, and the second equation would be levels 1,2 versus 3.(98)

6.4.2 The proportional odds model

The proportional odds model is the most well known and widely utilized type of ordered logistic regression.(97) The proportional odds model assumes that the coefficients of all binary logit equations are the same. This assumption is called the "proportional odds assumption or parallel regression assumption".(98) Under this model, only one odds ratio would be presented for each risk factor. This odds ratio would be valid for all cut points. However, this assumption of proportionality is not always correct and the odds ratios that describe the relationships (1 versus 2,3 and 1,2 versus 3) are different.(97) If this is the case, the proportional odds ratio is a biased estimate, even if most researchers will chose to keep running a proportional odds model.(97)

6.4.3 The Brant test of proportionality of odds ratios

To test the assumption of proportionality, one can conduct the Wald test developed by Brant.(99) In the Brant method, all underlying binary logistic regressions correlated fits are compared.(99) A significant Brant test means that the assumption of proportional odds does not hold and there needs to be two different coefficients for each variables that violate this assumption: one for 1 versus 2,3 and the second for 1,2 versus 3.(98) If some of the variables violate the assumption while others do not, a partial proportional odds model can be fitted.(97) This model will estimate two coefficients for variables that violate this

assumption. If all independent variables violate the assumption of proportionality, then a generalized ordered model should be fitted.(97) This model will estimate two different coefficients for all variables in the model.

6.4.4 Model fit statistics

Log likelihood tests were performed on all final models as well as nested sub-models. It was not possible to perform the Hosmer-Lemeshow test in this section as this test requires a binary outcome. The c-statistics were once again obtained in order to gage the discrimination ability of the models.(93)

6.4.5 Sensitivity analyses

The same sensitivity analyses that are described in objective 1 were repeated for this objective. Sensitivity analyses were performed on the multiply imputed dataset as well as on the sample restricted to never previously depressed MES respondents.

6.5 Results

6.5.1 Brant test for the assumption of proportional odds

Brant tests were performed for the full ordered logistic regression models of the three main associations of interest. The Brant tests revealed that almost all

variables met the proportional assumption, except for three variables. The dummy variables for cesarean section and street drug use in pregnancy did not satisfy the parallel line assumption for all three models, while the dummy variable for territories as area of residence did not meet the parallel line assumption for the model of the association of the presence of postpartum pain with PPD and the model of the association of the duration of postpartum pain with PPD. Two odds ratios are presented for each of these three dummy variables. The first odds ratio describes the relationship of no PPD versus probable and definitive PPD, while the second odds ratio describes the relationship of definitive PPD versus no PPD to probable PPD. One single odds ratio is presented for each study variable that meet the proportional assumption.

6.5.2 Results of the multivariate ordered logistic regressions

The results are presented once more according to groups of variables. Table 6 contains the main results of the multivariate ordered logistic regression by means of partial proportional odds modeling. It contains the results of the fully adjusted models, sub models, as well as sensitivity analyses for each of the three main exposure of interest:

1) Presence of problematic postpartum pain
2) The duration of problematic postpartum pain
3) The number of sites of chronic postpartum pain

Table 7 contains the results of the multivariate logistic regressions for the SES and demographic variables. Table 8 presents the results of the multivariate logistic regressions for the obstetric and health variables, while Table 9 presents the results for the psychosocial and psychological variables. The tables are presented first, and a description of the key points emanating from these tables follows the presentation of the tables.

Table 6: Main results from the multivariate ordered logistic regression of the association between the three pain exposures and PPD in Canadian women: proportional odds ratios and 95% confidence intervals

Main Exposure variables	Adjusted OR: SES /demographic †	Adjusted OR: Obstetric /health	Adjusted OR: Psychological /psychosocial	Adjusted OR: SES/ dem., obstetric /health	Adjusted OR: SES/dem., psychological /psychosocial	Adjusted OR: Obst./health, psychological /psychosocial	Final Model: OR adjusted for all variables	Final Model: never previously depressed sub-sample	Final Model: Multiply imputed dataset
1) Presence of problematic postpartum pain									
Yes	2.1 (1.7, 2.7)	2.2 (1.7, 2.8)	1.9 (1.5, 2.4)	2.1 (1.6, 2.7)	1.8 (1.4, 2.4)	1.9 (1.5, 2.4)	**1.8 (1.4, 2.3)**	2.0 (1.4, 2.7)	1.7 (1.3, 2.2)
No (ref)									
2) Duration of postpartum pain									
None* (ref)									
Acute pain only	1.6 (1.2, 2.1)	1.6(1.3, 2.1)	1.5 (1.1, 1.9)	1.6 (1.3, 2.1)	1.5 (1.1, 1.9)	1.5 (1.1, 1.9)	**1.5 (1.1, 1.9)**	1.6 (1.2, 2.2)	1.4 (1.1, 1.7)
Chronic pain	3.3 (2.6, 4.3)	3.5 (2.7, 4.6)	2.7 (2.1, 3.5)	3.2 (2.5, 4.2)	2.5 (1.9, 3.3)	2.7 (2.0, 3.5)	**2.4 (1.9, 3.2)**	2.6 (1.9, 3.7)	2.3 (1.8, 2.9)
3) Number of chronic postpartum pains									
None (ref)									
One	1.9 (1.6, 2.2)	1.9 (1.6, 2.3)	1.6 (1.4, 2.0)	1.8 (1.5, 2.1)	1.6 (1.3, 1.9)	1.6 (1.4, 2.0)	**1.5 (1.3, 1.9)**	1.6 (1.3, 2.0)	1.6 (1.0, 2.2)
Two	4.3 (3.2, 5.8)	4.9 (3.7, 6.6)	3.5 (2.5, 4.8)	4.1 (3.0, 5.6)	2.9 (2.1, 4.1)	3.4 (2.5, 4.7)	**2.9 (2.0, 4.0)**	2.9 (1.9, 4.3)	2.6 (1.8, 3.4)
Three or more	6.9 (3.4, 14.2)	8.3 (4.0, 17.4)	5.8 (2.8, 12.2)	6.3 (2.9, 13.4)	4.3 (2.0, 9.2)	5.3 (2.4, 11.9)	**4.2 (1.9, 9.2)**	4.6 (1.6, 13.6)	4.0 (1.4, 6.7)

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All odds ratios as well as 95% CI were obtained using population weights and BRR re-sampling method

Table 7: Proportional odds ratios and 95% confidence intervals for SES/demographic variables

SES and demographic variables	Total sample size	Adjusted OR: Model 1†‡	95% CI	Adjusted OR: Model 2§	95% CI	Adjusted OR: Model 3‖	95% CI
Maternal age							
15 to 19*	155	1.3	(0.8, 2.1)	1.3	(0.8, 2.1)	1.3	(0.8, 2.1)
20 to 24	680	0.8	(0.6, 1.1)	0.8	(0.6, 1.1)	0.9	(0.6, 1.2)
25 to 29 (ref)	1693						
30 to 34	1962	1.0	(0.8, 1.2)	1.0	(0.8, 1.2)	1.0	(0.8,1.3)
35 to 39	921	1.1	(0.8, 1.4)	1.1	(0.8, 1.4)	1.1	(0.8, 1.5)
40 and over*	203	1.0	(0.6, 1.6)	1.0	(0.6, 1.6)	1.0	(0.6, 1.56)
Maternal education							
Less than high school graduation	452	1.4	(1.0, 2.1)	1.4	(0.9, 2.1)	1.4	(0.9, 2.1)
High school graduation	786	1.3	(1.0, 1.8)	1.3	(0.9, 1.7)	1.3	(1.0, 1.8)
Post secondary	2423	1.1	(0.8, 1.3)	1.1	(0.8, 1.3)	1.1	(0.9, 1.3)
Bachelors degree(ref)	1953						
Maternal marital status							
Married/Common law (ref)	5085						
Divorced/widowed	102	1.1	(0.6, 1.8)	1.1	(0.7, 2.0)	1.1	(0.7, 2.0)
Single	427	0.7	(0.5, 0.9)	0.7	(0.5, 1.0)	0.7	(0.5, 1.0)
Household annual income							
Less than $20,000	503	2.0	(1.3, 3.0)	1.9	(1.3, 2.9)	1.8	(1.2, 2.8)
$20,000 to $39,000	998	1.5	(1.1, 2.1)	1.5	(1.1, 2.1)	1.4	(1.0, 2.0)
$40,000 to $59,000	1088	1.3	(0.9, 1.8)	1.3	(0.9, 1.8)	1.3	(0.9, 1.7)
$60,000 to $79,000	1016	1.2	(0.8, 1.6)	1.1	(0.8, 1.6)	1.1	(0.8, 1.6)
$80,000 to $99,000	716	1.3	(0.9, 1.8)	1.3	(0.9, 1.8)	1.2	(0.9, 1.8)
$100,000 and + (ref)	1034						
Unknown	259	1.7	(1.1, 2.7)	1.7	(1.1, 2.7)	1.6	(1.0, 2.6)
Maternal region of residence							
Atlantic	1016	1.0	(0.8, 1.3)	1.0	(0.8,1.3)	1.0	(0.8, 1.3)
Quebec	1035	1.1	(0.9, 1.5)	1.2	(0.9,1.5)	1.2	(0.9, 1.5)
Ontario (ref)	1667						
Prairies	1175	0.8	(0.6, 1.0)	0.8	(0.6, 1.0)	0.8	(0.6, 1.0)
British Columbia	552	1.0	(0.7, 1.3)	1.0	(0.7, 1.3)	1.0	(0.7, 1.3)
Territories	169	1) 1.7 2) 1.1	1) (1.0, 3.0) 2) (0.6, 2.0)	1) 1.8 2) 1.1	1) (1.0, 3.0) 2) (0.6, 2.1)	1.6	(1.0, 2.7)
Rural dwelling	1255	0.9	(0.7, 1.2)	0.9	(0.7, 1.1)	0.9	(0.7, 1.1)
Urban dwelling (ref)	4359						

Maternal immigrant status							
Yes	975	2.5	(2.0, 3.1)	2.4	(1.9, 3.0)	2.3	(1.9, 2.9)
No (ref)	4639						
Maternal aboriginal status							
Yes	329	1.2	(0.8, 1.5)	1.2	(0.8, 1.8)	1.2	(0.8, 1.7)
No (ref)	5285						

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All odds ratios as well as 95% CI were obtained using population weights and BRR re-sampling method

‡ Model 1: Multivariate ordered logistic regression predicting level of PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate ordered logistic regression predicting level of PPD with the duration of pain as main exposure

|| Model 3: Multivariate ordered logistic regression predicting level of PPD with the number of chronic pains as main exposure

Table 8: Proportional odds ratios and 95% confidence intervals for the obstetric and health variables

Obstetric and health variables	Total sample size	Adjusted OR: Model 1†‡	95% CI	Adjusted OR: Model 2§	95% CI	Adjusted OR: Model 3‖	95% CI
Birthing Method							
Vaginal birth (ref)	4134						
Cesarean birth	1480	1) 1.1 2) 0.9	1) (0.8, 1.5) 2) (0.6, 1.2)	1) 1.1 2) 0.8	1) (0.8, 1.5) 2) (0.6, 1.2)	1) 1.1 2) 0.8	1) (0.8, 1.5) 2) (0.6, 1.2)
Operative delivery - Forceps							
Yes	291	1.2	(0.8, 1.7)	1.1	(0.8, 1.6)	1.1	(0.7, 1.6)
No (ref)	5323						
Operative delivery - Vacuum							
Yes	490	0.9	(0.7, 1.3)	0.9	(0.7, 1.3)	0.9	(0.6, 1.3)
No (ref)	5124						
Operative delivery - Episiotomy							
Yes	900	1.0	(0.8, 1.4)	1.0	(0.8, 1.4)	1.0	(0.8, 1.3)
No (ref)	4714						
Maternal stitches							
Yes	2973	1.1	(0.9, 1.4)	1.1	(0.9, 1.5)	1.2	(0.9, 1.5)
No (ref)	2641						
Maternal parity							
One (ref)	2550						
Two	2067	1.2	(0.9, 1.6)	1.2	(0.9, 1.6)	1.2	(0.9, 1.5)
Three	693	1.3	(0.9, 1.8)	1.3	(0.9, 1.8)	1.3	(0.9, 1.8)
Four	304	1.1	(0.7, 1.4)	1.1	(0.7, 1.7)	1.0	(0.7, 1.6)
Postpartum contact by public health nurse							
Yes (ref)	5247						
No	367	1.2	(0.9, 1.7)	1.2	(0.8, 1.7)	1.2	(0.8, 1.7)
Sex of baby							
Male (ref)	2885						
Female	2729	0.9	(0.8, 1.1)	0.9	(0.8, 1.1)	0.9	(0.8, 1.1)
Maternal pre-natal education							
Yes (ref)	1903						
No	3711	1.1	(0.8, 1.4)	1.1	(0.8, 1.3)	1.1	(0.8, 1.4)
Maternal use of non medical pain relief							
Yes (ref)	4324						
No	1290	1.2	(0.9, 1.5)	1.2	(0.9, 1.5)	1.2	(0.9, 1.6)
Maternal use of medical pain relief use							
Yes (ref)	4531						

No	1083	0.8	(0.6, 1.0)	0.8	(0.6, 1.1)	0.8	(0.6, 1.0)
Postpartum period of survey							
Early postpartum	1592	0.9	(0.7, 1.1)	0.8	(0.7, 1.1)	0.9	(0.7, 1.1)
Mid postpartum	2750	1.0	(0.8, 1.2)	1.0	(0.8, 1.2)	1.0	(0.8, 1.2)
Late postpartum (ref)	1272						
Infant neonatal intensive care unit admission							
Yes	720	1.1	(0.9, 1.4)	1.1	(0.8, 1.4)	1.1	(0.8, 1.4)
No (ref)	4894						
Maternal previous no-live birth							
Yes	1785	1.1	(0.9, 1.3)	1.1	(0.9, 1.3)	1.0	(0.9, 1.3)
No (ref)	3829						
Maternal smoking							
Yes	1032	1.2	(0.9, 1.5)	1.2	(0.9, 1.5)	1.2	(0.9, 1.5)
No (ref)	4582						
Maternal pre-pregnancy health problems							
Yes	893	1.2	(0.9, 1.5)	1.2	(0.9, 1.5)	1.2	(0.9, 1.5)
No (ref)	4721						
Maternal new health problems							
Yes	1389	1.3	(1.1, 1.6)	1.3	(1.0, 1.5)	1.3	(1.0, 1.5)
No (ref)	4225						
Maternal body mass index							
Underweight	274	0.8	(0.5, 1.2)	0.8	(0.5, 1.2)	0.7	(0.5, 1.1)
Normal (ref)	3205						
Overweight	1287	0.8	(0.7, 1.1)	0.8	(0.7, 1.1)	0.9	(0.7, 1.1)
Obese	848	1.1	(0.9, 1.4)	1.1	(0.8, 1.4)	1.1	(0.8, 1.4)

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All odds ratios as well as 95% CI were obtained using population weights and BRR re-sampling method

‡ Model 1: Multivariate ordered logistic regression predicting level of PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate ordered logistic regression predicting level of PPD with the duration of pain as main exposure

|| Model 3: Multivariate ordered logistic regression predicting level of PPD with the number of chronic pains as main exposure

Table 9: Proportional odds ratios and 95% confidence intervals for the psychosocial and psychological variables

Psychosocial and psychological variables	Total sample size	Adjusted OR: Model 1[†‡]	95% CI	Adjusted OR: Model 2[§]	95% CI	Adjusted OR: Model 3[‖]	95% CI
Reaction to pregnancy							
Negative	408	1.2	(0.9, 1.7)	1.2	(0.9, 1.6)	1.2	(0.8, 1.6)
Positive (ref)	5206						
Perceived Stress							
High	3203	2.4	(1.9, 3.0)	2.3	(1.9, 2.9)	2.3	(1.9, 2.9)
Low (ref)	2411						
Stressful events							
None (ref)	2170						
One event	1546	1.3	(1.0, 1.7)	1.3	(1.0, 1.6)	1.3	(1.0, 1.6)
Two events	912	1.6	(1.2, 2.1)	1.6	(1.2, 2.1)	1.6	(1.2, 2.1)
Three events	497	2.3	(1.7, 3.1)	2.3	(1.7, 3.1)	2.3	(1.7, 3.1)
Four events or more	489	2.7	(2.0, 3.8)	2.6	(1.9, 3.7)	2.7	(1.9, 3.7)
Social support							
Adequate (ref)	4990						
Inadequate	624	2.0	(1.6, 2.5)	1.9	(1.5,2.4)	1.8	(1.5, 2.3)
History of depression							
Yes	895	1.9	(1.6, 2.4)	1.9	(1.6, 2.4)	1.9	(1.5, 2.3)
No (ref)	4719						
Alcohol use (pregnancy)							
Yes	534	1.1	(0.8, 1.5)	1.1	(0.8, 1.5)	1.1	(0.8, 1.5)
No (ref)	5080						
Drug use (pregnancy)							
Yes	51	1) 1.1 2) 2.1	1) (0.5, 2.3) 2) (0.9, 4.9)	1) 1.1 2) 2.2	1) (0.5, 2.4) 2) (1.0, 4.9)	1) 1.2 2) 2.2	1) (0.5, 2.5) 2) (1.0, 5.0)
No (ref)	5563						
History of abuse							
Yes	674	1.7	(1.3, 2.2)	1.7	(1.3, 2.1)	1.6	(1.3, 2.1)
No (ref)	4940						

* Interpret with caution, 16.6 < CV <= 33.3: high sampling variability

† All odds ratios as well as 95% CI were obtained using population weights and BRR re-sampling method

‡ Model 1: Multivariate ordered logistic regression predicting level of PPD with presence of postpartum pain as main exposure

§ Model 2: Multivariate ordered logistic regression predicting level of PPD with the duration of pain as main exposure

|| Model 3: Multivariate ordered logistic regression predicting level of PPD with the number of chronic pains as main exposure

Table 6 shows that the main results were very similar to those obtained in the previous section of this thesis. Indeed, there was a strong statistically significant association between the main exposures of interest and PPD.

When all the study variables were held constant, odds of PPD for women who reported problematic postpartum pain were 1.8 (95% CI: 1.4, 2.3) compared to women who did not report problematic postpartum pain. Women who reported chronic postpartum pain had even greater odds of PPD (OR=2.4 95% CI: 1.9, 3.2). There was also an exposure-response relationship between number of sites of chronic postpartum pain and PPD in Canadian women, with odds of PPD reaching 4.2 (95% CI: 1.9, 9.2) for those reporting three or more sites of chronic pain.

The variables that remained independent predictors of PPD in this section of the thesis were similar to those uncovered in the previous section. Once again, immigration status, perceived stress, stressful life events, inadequate social support, previous depression as well as previous abuse were all significant independent predictors of PPD. Along with these variables, two other variables were found to be independent predictors of PPD: new maternal health problems in pregnancy and low annual income.

6.5.3 Model fit statistics

Log likelihood tests were performed on all three final models as well as all nested sub-models. All the p-values were statistically significant, meaning that the final models of the three associations under study were better fitted than the sub-models. It was not possible to perform the Hosmer-Lemeshow tests in this section because the outcome variable, PPD, was a three level variable. The Hosmer-Lemeshow tests can only be performed on binary outcomes. The c-statistics of the three main models were similar and indicated that the three full models had acceptable discrimination abilities. The c-statistics associated with the model of the association of postpartum pain with PPD, the model of the association of the duration of pain with PPD, and the model of the association of the number of chronic pain sites and PPD were 0.761, 0.766, and 0.767.

6.5.4 Sensitivity analyses

The sensitivity analyses performed on the multiply imputed dataset and on the sample restricted to the never previously depressed respondents are presented in Table 1. Once again, the sensitivity analyses showed that the results of the multivariate ordered logistic regressions were robust and probably fairly conservative. Consistent with finding in the previous section, the restricted analysis showed a much stronger association between problematic postpartum pain and postpartum depression, favoring the consequence theory (pain precedes depression).(55)

7.0 DISCUSSION

7.1 Main findings

7.1.1 Prevalences of acute and chronic postpartum pain

Pain after childbirth is very common. Most of the MES respondents (81.7%, 95% CI: 79.1%, 84.3%) experienced at least one site of problematic pain caused by childbirth. For 27.1% (95% C.I.: 25.8%, 28.3%) of these women, pain was still present at the time of interview, at an average of 7.3 months postpartum. The most commonly reported problematic pain in the acute period (first three months postpartum) was cesarean incision pain (62.6% of women who had cesarean section), followed by pain in the vagina (51.9% of women who had vaginal delivery). In this study, breast pain was the third most reported pain by Canadian mothers (50.5%), followed by back pain (35.5%) and migraines pain was the rarest (10.4%).

Similar results regarding the sequence of reported pain in the acute period were found in the "Listening to mothers II" national survey of American mothers.(100) Although the American prevalences of pain were higher than in the MES, cesarean incision pain was the most often reported postpartum pain (79%) followed by vaginal pain (72%), breast pain (59%), back pain (36%), and migraine pain (10.4%).(100) The American self-reports of pain were gathered at

two months postpartum, whereas Canadian data was gathered at three months postpartum.(62,100) This could explain the higher prevalences of pain for American mothers, and highlight the need for consistency when gathering and comparing postpartum data.

For Canadian mothers, most of the problematic pain had resolved within three months postpartum. However, some pain persisted and was still present at the time of interview (mean 7.3 months postpartum). One in five Canadian mothers (20.1%) who had delivered their baby via cesarean section still experienced pain at the site of incision at the time of the interview while persistent vaginal pain was reported by 7.1% of women who had vaginal deliveries. Back pain was a persistent problem for 16.1% of new Canadian mothers, while persistent migraine pain and breast pain were rare in Canadian women (3.3% and 2.8%).

Canadian prevalences of chronic cesarean incision pain and chronic breast pain were similar to those observed in Finland and in the United States.(53, 100, 101) Back pain prevalence in Canadian women was much lower than the 45% prevalence of back pain reported in the Australian study by Thompson et al.(101) However, it was closer to the 24% prevalence reported in the United States.(100) Persistent migraine was rare in Canadian women (3.3%) but more common in

other studies (16% to 22.5%).(100-103) Again, the variance in results could be secondary to methodological differences such as timing of survey interview.

7.1.2 The association between pain and PPD using logistic regression modeling

Results of this study showed that problematic postpartum pain was an important risk factor for PPD, which affected up to 7.0% (95% C.I.: 6.3%, 7.7%) of the MES respondents. After adjusting for all study covariates (SES and demographic, obstetric and health, as well as psychosocial and psychological variables), women who experienced any type of postpartum pain that they felt was problematic were almost twice as likely to have PPD compared to women who do not report problematic postpartum pain. Odds of PPD were even greater for women whose pain persisted. Indeed, odds of PPD were 2.4 for women who experienced chronic pain, compared to women who never experienced problematic postpartum pain. Furthermore, odds of PPD increased according to the number of body sites where pain persisted in an exposure-response type of relationship.

The relationships of 1) the presence of problematic postpartum pain with PPD, 2) the duration of the problematic postpartum pain with PPD, and 3) the number of

reported chronic pain sites with PPD were not only strong, but also statistically significant.

It is impossible to ensure that the pain reported in the MES was not associated with other pre-existing conditions un-related to childbirth as there is always a possibility that respondents misinterpreted the survey questions. However, the risk is very small and it is very unlikely that bias was introduced because of misinterpretation. The survey questions clearly state that the pain they were referring to was due to the childbirth. It is therefore safe to presume that most cases of pain are indeed brought on by childbirth, and that the results truly describe the association between postpartum pain and postpartum depression.

Very few study variables remained statistically significant independent predictors of PPD when all variables were included in the regression models. Along with the pain variables, the covariates that consistently remained independent predictors of PPD were: 1) immigration status, 2) perceived stress, 3) number of past stressful a life events, 4) lack of social support, 5) a history of depression, and 6) a history of abuse. These risk factors were similar to the strong to moderate predictors of PPD reported in the systematic reviews by Robertson et al.(22) and Beck (2001).(22, 25) These reviews also found that socioeconomic status, some obstetric factors and marital status were significant, independent predictors of PPD.(22, 25) These risk factors were not found to be significant in the present

study, but perhaps because of differences in health care systems between countries.

Another important finding was that birthing method, and obstetric factors in general, were not associated with PPD in this study. This is consistent with other large sample studies on predictors of PPD. Robertson et al. (22) explain that studies showing associations between obstetric factors and PPD may actually be "reflecting trends within the sample rather than an etiological relationship between postpartum depression and obstetric variables".

It was an unexpected finding that immigrant status would be amongst the best independent risk factors for PPD. Stewart et al.(24) conducted a study that examined PPD in refugees, nonrefugee immigrants, asylum seekers as well as Canadian-born women, in the three main urban centres of Montreal, Toronto, and Vancouver.(24) The study, conducted at 7 to 10 days postpartum, revealed that compared with Canadian-born women, refugees (OR 4.80; 95% CI 1.57, 14.69), immigrant (OR 4.58; 95%CI 1.61, 13.02) and asylum seekers (OR 3.06; 95%CI 1.06, 8.82) were more likely to have EPDS scores of over 10 (at risk for depression).(24) This could be due to many factors, such as traumatic backgrounds and lack of present social support.(24) What is extremely alarming is that "racial and ethnic minorities are at risk for inadequate pain care, including pain assessment and treatment".(78)

The confounding investigation was inconclusive as it was impossible to ensure that the potential confounders of the association of postpartum pain with PPD were not part of the causal pathway. Bivariate analyses showed that maternal age, parity, maternal prenatal education, new health problems in pregnancy, perceived stress, as well as a history of depression were significantly associated with both PPD and postpartum pain. Age, parity and maternal prenatal education are probably the truest confounders of the association. The other variables may be part of the causal pathway in the form of stressors that may precipitate the development of chronic pain and PPD.(49) It is impossible to ascertain with confidence the confounding factors of the association between pain and PPD. A recent study by Jardri et al. (104) suggests that pain, instead of being a risk factor for PPD, would actually be a confounder in PPD screening. In their small study on 316 women, pain measured between the third and 5th day postpartum was not associated with PPD at 8 weeks postpartum.(104) However, it is very likely that no associations were found because the study did not capture the psychological wearing down that is a result of the suffering associated with postpartum pain.(49) Results could have been much different if pain measurements would have been taken further in the postpartum period. The present thesis study revealed that chronic pain following childbirth is definitely strongly associated with PPD.

7.1.3 The association between postpartum pain and PPD using ordered logistic regression modelling

The second objective of this thesis project was to explore the use of the ordered logistic regression as a valid method to study the association between postpartum pain and PPD, and to examine what subtype of ordered logistic regression is best suited for this type of research (ex: proportional odd modeling) when the outcome is divided into three PPD categories:

1) No PPD
2) At risk for PPD
3) PPD

Encouragingly, the proportional odds assumption held for the majority of the risk factors. Only three variables violated the proportional odds assumption: cesarean section, living in the territories and drug use in pregnancy. Proportionality is a desired quality in ordinal models, as proportional models are easier to interpret and report.(97) In this study, a partial proportional odds model was fitted to accommodate the three variables that did not meet the proportional assumption. According to Fullerton(97), partial proportional odds models are a good middle ground between fitting a proportional odds models which is more parsimonious and fitting an unconstrained model which may be more accurate.(97)

Estimates obtained from the logistic regressions and ordered logistic regressions were essentially the same. This is due to the fact that the proportional assumption held for most of the independent variables. The estimates are not completely identical because they were obtained using two different software packages: SAS and STATA. No matter how they were obtained, results do support the pain-depression association in Canadian women who have just given birth.

Both the logistic regression and ordered logistic regression modeling techniques appear to be valid methods to investigate PPD. This may seem obvious, but this writer has not found papers describing the use of ordered logistic regression to investigate PPD.

7.2 Mechanism and interpretations

The body of research on pain and depression is showing results that satisfy many of Bradford Hill criteria for causality.(105) The results of this study satisfied the strength of the association, consistency, biological gradient, plausibility and coherence criteria and the temporality criteria to some extent.(105) No matter how the results of the present study satisfied the causality criteria, no conclusion can be made regarding a causal association between postpartum pain and PPD, since this study is based on cross-sectional data.

Fishbain et al.(55) conducted a famous systematic review of studies investigating the causal association between chronic pain and depression.(55) There were five main causal hypotheses:

1) The antecedent hypothesis: Depression causes pain
2) The consequence hypothesis: Depression is caused by pain
3) The scar hypothesis: Genetic predisposition to recurrent depression
4) The cognitive-behavioral mediation hypothesis
5) Common pathogenetic mechanism hypothesis .(55)

Fishbain et al.(55) consider the antecedent, consequence and scar hypotheses as the three main hypotheses concerning the timing and causality in the pain-depression relationship, as the cognitive-behavioural mediation hypothesis would fall under the consequence hypothesis while the common pathogenetic mechanism hypothesis is similar to the scar hypothesis.(55) Fishbain et al.(55) also found that there is strong evidence supporting the consequence hypothesis and mixed results for the scar hypothesis, while the antecedent hypothesis is mainly refuted.(55)

Further clarifications of the association between pain and depression were provided by the Diathesis-Stress model proposed by Banks and Kerns(106),

which is essentially an extension of Gatchel's model of transition from acute pain to chronic pain that was presented in the literature review of this thesis.(49, 106) In the context of the proposed model, a diathesis is a biological or psychological characteristic, such as negative thought patterns, that predisposes an individual to suffer from depression, while the stressor is an event which the person feels threatens their well-being and surpasses their coping abilities, such as suffering from persistent pain.(106) Banks and Kerns (106) propose that the chronic pain-cognition interaction is reciprocal and dynamic, and can escalate into major depressive disorder.(106)

The Diathesis-Stress model can be used to explain the association between pain and PPD. A new mother can be overwhelmed by pain (stressor). She may be anxious (diathesis) that her pain will interfere with her ability to take proper care of her newborn, and she may also be fearful that she may be misunderstood by her health care provider who keeps dismissing her concerns by repeating that pain after childbirth is normal. The anxiety and fear may in turn exacerbate the pain and perpetuate it which in turn will affect the mood. It is a spiral that can quickly develop into a major depressive disorder. It is very unfortunate that the MES did not capture any information on the respondent`s personality and psychological characteristics, which could have been helpful in examining the mediating effects of these characteristics.(49)

Dersh et al.(107) explain that the results obtained in Fishbain's systematic review support the Diathesis-Stress model.(55, 106, 107) They emphasize that the Diathesis-Stress model is "consistent with the consequence, scar, and cognitive-behavioral mediation hypotheses"(107), and could also be consistent with the scar hypothesis if "it could be broadened to include not only a genetic predisposition to recurrent major depression but also to include psychological predispositions such as negative schemas or a depressive attributional style".(107)

Between the consequence hypothesis and the scar hypothesis, the consequence hypothesis would best describe the association between pain and PPD in Canadian women. The events under study in this thesis project followed a set timeline. PPD is a condition that develops within a few weeks following birth, whereas the pain studied was a direct consequence of birth, preceding the development of PPD. It is impossible to rule out the possibility that some of the women were already depressed prenatally, but evidence would suggest that pain causes depression more than the opposite.(55)

In order to verify that the consequence hypothesis is the one that best explains the pain-depression association in puerperal Canadian women, further analyses were done on a sub-sample of the MES that excluded women who had previously lived through a depressive episode (15.4% of the MES respondents).

This eliminated instances that support the scar hypothesis.(55) Interestingly, the results of the logistic regression with the sample restricted to respondents who had never been previously depressed showed a much stronger association between the three pain exposures and PPD, compared to the complete subject sample. Odds of PPD for women who reported chronic pain were 2.8 (95%CI: 1.7, 4.7) in the restricted sample compared to women who did not report chronic pain, while the odds of PPD were 2.4 (95%CI: 1.6, 3.6) in the complete-subject sample for the same women. This finding would favor the consequence hypothesis.(55)

In reality, all three hypotheses probably describe the association between pain and PPD in a Canadian puerperal population. The consequence hypothesis would describe the majority of the instances of PPD, and would be followed by the scar hypothesis and the antecedent hypothesis. Fishbain et al.(55) believe that "the scar hypothesis may apply more to patient with major depression, and the consequence hypothesis to pain of the neuropathic type (ex: cesarean section or operative vaginal deliveries)".(55)

In this study, three different types of associations were observed. The presence of problematic pain, the duration of postpartum pain and the number of painful body sites were all associated with PPD. According to Fishbain(55), three more

associations would remain to be observed to confirm causality.(55) There associations are:

1) The severity of perceived pain and PPD,

2) The frequency of pain/pain intrusion/pain breakthrough and PPD

3) The percentage of body affected by pain and PPD.(55)

7.2.1 Biological evidence for the pain-PPD association

If theoretical models are true, then they should be supported by biological evidence. Research has unveiled biological evidence supporting the pain-depression causal association hypotheses. The biologic pathways of chronic pain and depression are similar and include the serotonergic and noradrenergic systems.(45, 108) Depression is associated with the deregulation of both the serotonergic and noradrenergic systems pathways that project to different brain areas: frontal cortex, basal ganglia, hypothalamus, and limbic area in the serotonin pathways, and frontal cortex, limbic area, hypothalamus and cerebellum in the norepinephrine pathways.(45) All of these regions produce distinct clinical manifestations of depression.(45) The serotonergic and noradrenergic pathways also include descending neurons which are involved in pain modulation at the peripheral neurons.(45) The descending neurons originate in the brain stem and enter the spinal cord at the dorsal horn. The mechanisms

of pain modulation also involve the action of other neurotransmitters such as gamma-aminobutyric acid (GABA) and peptides in order to modulate pain.(45) Both persistent pain and depression have been treated by tricyclic antidepressants, which inhibit the reuptake of the noradrenalin and 5-hydroxytryptamine neurotransmitters.(45, 108)

There may also be biological evidence supporting the finding that foreign-born women are more at risk for both chronic pain and PPD, compared to their Canadian-born counterparts. Straub et al.(109) explain that "immigrants and members of ethnic minorities are especially at risk of 25-OH vitamin D deficiency due to darker skin colour, low sun exposure, diet, and traditional dress".(109) Vitamin D deficiency has been associated with higher incidence of both chronic pain and depression.(77) However, the systematic review by Straube et al.(109) on vitamin D and chronic pain in immigrants and ethnic minority populations was inconclusive due to a lack of evidence.(109) Nonetheless, further research in this area sounds promising and could offer a plausible explanation as to why chronic pain and depression seems to be especially associated with immigrant populations, and how this alarming problem could be addressed.

7.3 Strengths and limitations

7.3.1 Strengths

The main strength of this thesis is that it was the first study to examine the direct association between postpartum pain and PPD in a Canadian puerperal population. The association between postpartum pain and PPD was investigated using both binary logistic regression, and ordered logistic regression which is not usually seen in PPD research.

The MES, which is the source of data for this study, is of a high quality and provided population data that has never before been available for Canada.(6) The MES contained the EPDS, which is a validated self-report PPD screening tool.(29, 30) The correct cuts off scores for the EPDS were used to classify PPD in this study, which diminished the likelihood of misclassification bias.(30) Many studies of PPD do not use the correct cut offs as defined by the original authors of the EPDS, which are 12/13 (13 or more) to identify women with major depression, and a cut off of 9/10 (10 or more) to identify women with minor depression.(29) Matthey et al.(30) warn of the increase use of invalidated EPDS cut-off score in PPD research, as well as invalidated changes that are made to the original EPDS format and wording which threaten validity of the results.(30) This could explain the wide range of reported PPD prevalences, since a one

point variation in the cut off score can significantly affect the estimates of PPD.(5, 30)

Finally, the EPDS captured a good number of cases of PPD resulting in a sample size that was big enough to provide statistically significant results. The sensitivity analyses of both objectives showed that the results were not only conservative, but also fairly robust. With some exceptions, the results of the present study can be generalized to all Canadian women who have just given birth.(6) The results of this thesis corroborate with other pain-depression association studies. (55)

7.3.2 Limitations

The most important limitation was the difficulty of comparing the results of this study with results from other studies. There is a definite lack of studies that examine the association of postpartum pain with PPD. There are many population-based studies on maternal health during pregnancy and after birth, but the measurements of key factors like PPD and postpartum pain are taken at different times and with different tools or are simply missing, making the study results not directly comparable with each other.(6, 57, 100, 101, 110, 111) For example, the American Pregnancy Risk Assessment Monitoring System (PRAMS) uses two questions to evaluate postpartum depressive symptoms

(PDS) in their survey respondents, where as the EPDS (10 questions) was used to assess PPD in the Canadian MES.(6, 111)

Another major limitation was the methodological weaknesses of many PPD studies. This is especially true of clinical trials of antidepressants.(31) Considering the gestalt of studies of PPD, there is tremendous heterogeneity in the methodologies. They do not include the same risk factors, and important ones such as psychosocial factors are often omitted. Studies are inconsistent in their case definitions of PPD and in their measurements of key variables. For example, many different instruments measure social support, but no consensus exists regarding a gold standard.(112) These issues are pointed out by some of the most prominent PPD researchers.(31, 40) This heterogeneity present in PPD research made the task of basing the present study on sound and robust scientific knowledge very difficult.

The present study was limited by the fact that it is a secondary data analysis. The source survey was not constructed to gather information on every single PPD risk factor. Data was simply not gathered for some suspected PPD risk factors. For example, twin births were excluded from the Maternity Experiences Survey.(10) Choi et al.(10) found higher odds of moderate to severe PPD (OR: 1.43 95% CI: 1.12-1.84) for multiple births versus singletons in a nationally representative sample in the United States at nine months postpartum.(10)

A discussion of the strength and limitations of this study would not be complete without a comprehensive review of the potential biases that could have been present in this study.

7.3.3 Bias assessment

Bias is a "systemic error that results in an incorrect or invalid estimate of the measure of association".(75) Bias may have been introduced early in the study, during the literature review.(26) Papers that were not written in either French or English were excluded. Also, bias could have been introduced in the literature search itself.(26) Every step was taken to avoid the possibility of literature review bias. All appropriate databases were searched (Medline, Embase, Cinhal, Psychinfo, Pubmed) and help was requested from the University of Ottawa Faculty of Medicine research librarian.

The most important bias in this study was probably recall bias. Sackett (113) warns researchers that recall bias inflates the effects so that it biases the results away from the null.(113) In order to diminish the likelihood of recall bias in the MES, the respondents were chosen from a three month birth cohort close to the 2006 Canadian Census which was the sampling frame for the MES.(6) Biases could have also been introduced due to response fatigue, and due to the fact that

PPD can be considered an "unacceptable disease", as there is much stigma associated with mental health issues.(26)

Another important bias that could have been introduced is non-response bias. Non-response bias happens when the respondents differ from the non-respondents.(113) In order to mitigate response bias, Sackett (113) recommends a response rate of 80% and a comparison of respondents and non-respondents.(113) Research by Posmontier et al.(9) demonstrated that women who refused to participate were more likely to have PPD, but "there were no significant differences in PPD prevalence between completers and non completers".(9) Because of the scope of the survey, the Cross-cultural validity of the MES was never assessed, and this could definitely be a source of response bias.(6) Van de Vijer(114) explains that method bias can happen when a cultural factor affects the way that some questions are answered.(114) Zinke (2007) reports that "cross-cultural variations have been observed in terms of report of pain intensity, interference with work, emotional distress and pain expressiveness, qualitative descriptors of pain, healthcare workers' assessment of pain, differences in pain tolerances in laboratory settings, and coping styles".(78)

Misclassification bias (measurement error) is another well-known bias in epidemiological research. It is defined as "an error in the classification of the

exposure or the disease".(75) In the case of this study, there was probably a greater risk of misclassification of PPD than pain. The EPDS is a screening tool and does not necessarily lead to a diagnostic of PPD.(29) There are false negatives as well as false positives associated with the use of the EPDS. Overall, the misclassification was probably non-differential and the results mostly biased towards the null.(75) In case of differential misclassification, the results are biased either upwards or downwards.(75) Further misclassification may have occurred because respondents may have misunderstood the survey questions, or because they simply chose not to answer certain questions, resulting in missing data.(26) It was not possible to ensure that the respondents answered the EPDS questions alone. The presence of a family member when answering the EPDS questions can negatively affect the sensitivity and specificity of the tool, thus resulting in higher rates of false negatives and false positives.(29)

Reverse cause-effect bias means that the opposite of an association might be true. In this case, it could well be that PPD causes some pain. However, evidence strongly supports the theory that pain causes PPD more than the opposite.(55) The truth is probably not so clear cut. It is safe to assume that most cases of PPD were caused by problematic postpartum pain, while some of the respondents did have a predisposition for PPD, and some PPD sufferers did recall more pain. The PPD etiology is multifactorial and does not have one single cause.(7)

Publication bias is the tendency to publish positive findings.(26) The topic of PPD must have been a victim of Publication bias as well as Hot Topic bias at one point in time. Many risk factors have been found to be associated with PPD, but only a few remain independent predictors of PPD in systematic reviews and in this study.

Along with bias, confounding is definitely a concern in any epidemiological study, as it threatens the validity of the results.(75) There is confounding when a third variable influences and distorts the relationship observed between an exposure and the outcome.(75) For a variable to be a confounder, it has to be associated with "the exposure in the population that produced the cases" as well as an independent predictor of the disease, without being part of the causal pathway of the disease.(75) Confounding was mostly controlled for in the multivariate regression analysis. As advises Dorak(26), great care was taken in this study to include all acknowledged and suspected risk factors for both PPD and pain.(26) It is remarkable that the association between postpartum pain and PPD remained strong and statistically significant after adjusting for all the other variables.

Random error is the final threat to the validity of the present study. It is the "probability that the observed result is due to chance".(75) The results of this

study corroborate with other research in pain and depression.(55) Although there was definitely some random error in this study, the association between pain and PPD is one that is observed time and time again and therefore is probably a real phenomena and not the result of chance.

7.4 Future research needs

More longitudinal studies are needed to settle this chicken and egg question of which comes first, the pain or the depression. It would not be possible to study this association using randomized-control trials as such studies would definitely not be ethical. However, a prospective cohort study could be implemented. Althuser,(115) advocates more prospective studies from pre-conception to a long postpartum period.(115) A cohort study could provide a clear and answer to this chicken and egg question. Let's not forget that qualitative studies could also provide more insights into how pain could be related to PPD.

Finally, there is a need to develop clear guidelines for PPD research so that there is a consensus regarding the case definition and gold standard methods of assessing the risk factors. This would yield studies of higher methodological quality, and provide clearer evidence to guide not only the patient and the health care workers, but also policy makers, and other major stakeholders.

8.0 Conclusion

This thesis demonstrated that there exists a significant relationship between postpartum pain and PPD in Canadian women. Indeed, the presence of postpartum pain, the duration of postpartum pain, and the number of sites of chronic postpartum pain are all associated with PPD. Postpartum pain should therefore be closely monitored and treated adequately. At the postpartum follow-up with their health care providers, new mothers experiencing high levels of pain should also be systematically screened for PPD. This may not only prevent the development of chronic pain, but may also prevent the development of PPD. More research into the association between postpartum pain and PPD is needed in order to establish clear causality.

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Appendix A

The Edinburgh Postnatal Depression Scale (EPDS)

In the past 7 days:

1. I have been able to laugh and see the funny side of things.

   As much as I always could
   Not quite so much now
   Definitely not so much now
   Not at all
2. I have looked forward with enjoyment to things.

   As much as I ever did
   Rather less than I used to
   Definitely less than I used to
   Hardly at all

3. * I have blamed myself unnecessarily when things went wrong.

   Yes, most of the time
   Yes, some of the time
   Not very often
   No, never

4. I have been anxious or worried for no good reason.

   No, not at all
   Hardly ever
   Yes, sometimes
   Yes, very often

5. * I have felt scared or panicky for not very good reason.

   Yes, quite a lot
   Yes, sometimes
   No, not much
   No, not at all

6. * Things have been getting on top of me.

   Yes, most of the time I haven't been able to cope at all
   Yes, sometimes I haven't been coping as well as usual
   No, most of the time I have coped quite well
   No, I have been coping as well as ever

7. * I have been so unhappy that I have had difficulty sleeping.

   Yes, most of the time
   Yes, sometimes
   Not very often
   No, not at all

8. * I have felt sad or miserable.

   Yes, most of the time
   Yes, quite often
   Not very often
   No, not at all

9. * I have been so unhappy that I have been crying.

   Yes, most of the time
   Yes, quite often
   Only occasionally
   No, never

10. * The thought of harming myself has occurred to me.

    Yes, quite often
    Sometimes
    Hardly ever
    Never

Response categories are scored 0, 1, 2, and 3 according to increased severity of the symptoms. Items marked with an asterisk are reverse scored (i.e. 3, 2, 1, and 0). The total score is calculated by adding together the scores for each of the ten items.

Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-6

Appendix B

Literature search strategy

Database: PsycINFO <1806 to October Week 3 2009>

Search Strategy:

1 postpartum depression/ (2154)
2 pain/ or back pain/ or chronic pain/ or headache/ or pain perception/ (28153
3 birth/ or "labor (childbirth)"/ (4668)
4 ("c section" or "episiotomy").mp. [mp=title, abstract, heading word, table of contents, key concepts] (82)
5 4 or 3 or 2 (32667)
6 1 and 5 (177)
7 "chronic pain associated depression antecedent".fc_titl. (2)
8 "postpartum depression".mp. [mp=title, abstract, heading word, table of contents, key concepts] (2355)
9 8 or 1 (2355)
10 9 and 5 (192)

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1950 to Present>

Search Strategy:

1 Depression, Postpartum/ (2200)
2 "postpartum depression".mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (1077)
3 1 or 2 (2553)
4 pain/ or back pain/ or headache/ or labor pain/ or neuralgia/ (132038)
5 delivery, obstetric/ or cesarean section/ or episiotomy/ (43933)
6 "breast pain".mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier] (487)
7 6 or 4 or 5 (175664) 3 and 7 (88)