Nausea and Vomiting in Pregnancy: Prevalence and Relationship with Psychosocial Determinants of Health

A Thesis Submitted to the College of Graduate Studies and Research
in partial fulfillment of the
Requirements for the Degree of Master of Nursing in the
College of Nursing
University of Saskatchewan,
Saskatoon, Saskatchewan

By Jennifer Kramer, BSN, RN

Permission to Use

In presenting this thesis in partial fulfillment of the requirements for the Master of Nursing Degree from the University of Saskatchewan, I agree that the Libraries of this University may make it freely available for inspection. I further agree that permission for copying of this thesis in any manner, in whole or in part, for scholarly purposes may be granted by the professor or professors who supervised my thesis work or, in their absence, by the Dean of the College of Nursing in which my thesis work was done. It is understood that any copying or publication or use of this thesis or parts thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and to the University of Saskatchewan in any scholarly use which may be made of any material in my thesis.

Requests for permission to copy or to make other use of material in this thesis in whole or part should be addressed to:

Dean of the College of Nursing
University of Saskatchewan
107 Wiggins Road
Saskatoon, Saskatchewan
Canada S7N 5E5

Abstract

Nausea and vomiting are commonly experienced by women in pregnancy (NVP). Symptoms are usually limited to the first trimester, but can persist until birth. Both mild and more severe symptoms can have negative effects for the mother, her unborn child, and the family. Despite the frequency of NVP and associated distress, the exact cause is unknown and the condition remains poorly understood.

This secondary analysis explores nausea and vomiting in pregnancy, as determined by the Nausea and Vomiting in Pregnancy Instrument (NVPI), in a cohort of Canadian pregnant women at two gestational time points. The data analyzed in this study were originally from a longitudinal and epidemiological study of depression in pregnancy and into the postpartum. A population health approach has been used to examine psychosocial determinants of nausea and vomiting in pregnancy.

During the second trimester, the prevalence of nausea and vomiting in this sample of 551 women was 63.3%, with 24% of women reporting moderate nausea and vomiting and 18.9% reporting severe symptoms. These rates are similar to other studies of women during the first and second trimester of pregnancy. In the final model, nausea and vomiting in pregnancy was associated with gestation (weeks), antiemetic medication use, employment status, worry, and symptoms of major depression.

During the third trimester, the prevalence of NVP in this sample of 575 women was 45.4%, with 8.2% reporting moderate nausea and vomiting and 14.3% reporting severe symptoms. These results exceed previous reports on prevalence beyond 20 weeks in pregnancy. In the final model, nausea and vomiting in pregnancy was associated with antiemetic medication use, worry, and symptoms of major depression. The presence of support and maternal smoking were found to have a protective effect.

The co-morbidity of nausea and vomiting, worry, and symptoms of major depression in this sample of pregnant women represents a significant public and mental health problem. Care providers need to screen pregnant women for nausea and vomiting and also screen women for depression in the presence of more severe NVP symptoms. Supportive measures that address both conditions may be necessary in

order to improve the quality of life of pregnant women, their families, and to protect the unborn child from the effects of both nausea and vomiting and depression in pregnancy.

Acknowledgements

This thesis would no have been possible without the expert knowledge, kind support, and patient guidance of my thesis supervisor Dr. Angela Bowen. Whether it was through e-mail, on the phone, or in person, I was honoured to have her on-going encouragement and professional insight. Her leadership and dedication towards improving the health and lives of women, children, and families is inspirational. I could not have hoped for a better supervisor, and I will always think of her as an exceptional mentor. I would also like to express my gratitude to the members of my thesis committee Dr. Norma Stewart and Dr. Nazeem Muhajarine for their contribution to this project.

I would also like to acknowledge those who are closest to me. I will always be grateful for the on-going support of my family, with a special thanks to my mother Joanne for giving me perspective and for always being my confidant. Thanks also to my partner Shaun for always encouraging me and for making me laugh. I am eternally grateful for your love and absolute confidence in me. Finally, I would like to dedicate this thesis to my son Ronin, who has enriched my life with more joy and love than I ever thought possible.

Table of Contents

List of Tables

List of Figures

Page

Chapter 1

Introduction

Nausea and vomiting is a common experience for women in pregnancy (NVP). Symptoms are usually limited to the first trimester, but can continue throughout pregnancy and even persist until the birth (O'Brien & Zhou, 1995). The severity of nausea and vomiting may affect the physical and emotional health of the pregnant women (Deuchar, 1995), family, social and occupational functioning (Chou, Chen, Ku, & Tseng, 2006; Locock, Alexander, & Rozmovits, 2008), the stages of maternal role attainment (Meighan & Wood, 2005), and even outcomes for the unborn child (e.g., low birth weight) (Zhou, O'Brien, & Relyea, 1999). The cause is unknown, but it is widely agreed that NVP is a multifaceted condition with genetic, physiological, behavioural, social, and psychological contributing determinants. However, the reports regarding these determinants continue to be contradictory and are often restricted to either the first trimester of pregnancy or hyperemeis gravidarum (HG), the most severe form of NVP (Broussard & Richter, 1998).

The extent of the distress associated with nausea and vomiting on the daily lives of women is substantial. Women with NVP report concerns about economics and employment (Poursharif et al., 2008), have high levels of stress (O'Brien & Zhou) and worry that the symptoms could adversely affect their baby (Mazzootta, Stewart, Atanackovic, Koren, & Magee, 2000). Women suffering severe and prolonged nausea and vomiting in pregnancy have reported depressive and anxious feelings (Poursharif et al., 2008), changed plans for future children, considered termination of otherwise wanted pregnancies (Mazzotta et al., 2000; Mazotta, Magee, & Koren, 1997), and have reported characteristics of Posttraumatic Stress Disorder (PTSD) after the birth of their baby (Fejzo et al., 2009). Pregnant women who are depressed or who did not intend to become pregnant are both more likely to use cigarettes, alcohol, and drugs during pregnancy and are less likely to have adequate prenatal care (Hellerstedt et al., 1998; Naimi, Lipscomb, Brewer, & Gilbert, 2003; Zuckerman, Amaro, Bauchner, & Cabral, 1989). The literature has shown that worry, stress, anxiety (Austin, Leader, & Reilly 2005; O'Keane & Scott, 2005; Teixeira, 1999), depression (Chung, Lau, Yip, Chiu, & Lee, 2001), and unintended pregnancy (Brown, & Eisenberg, 1995) as well as cigarette (U.S. Department of Health and Human Services, 1990), alcohol

and drug use (Allen & Feeney, 1997) can all have deleterious effects on the health of the fetus, the baby, and the mother. The full extent and implications of NVP warrant early intervention, which is thought to decrease the severity and duration of the condition as well as prevent complications. However, due to the nonlife-threatening nature and commonality of the condition, both care providers and pregnant women often tend to minimize the impact of NVP (Attard et al., 2002; O'Brien & Naber, 1992), thus the condition is often inadequately treated.

It is anticipated that this research will add to the growing body of knowledge about nausea and vomiting in pregnancy. Increased understanding about the prevalence and determinants associated with nausea and vomiting at multiple time points will inform care givers and researchers about the factors affecting the well-being of the mother, the family, and the unborn child throughout pregnancy. Screening and early intervention of nausea and vomiting may help to prevent more severe symptoms in later pregnancy. In addition, early intervention of secondary conditions such as anxiety and depression may help to prevent their negative effects and associated obstetrical complications for the mother and her baby. Finally, it is hoped that the findings will increase awareness of pregnant women suffering from nausea and vomiting, a very common condition in pregnancy.

1.1 Purpose

The purpose of this project is to increase our understanding of nausea and vomiting in pregnancy in a group of mostly urban Canadian women. It will determine the prevalence, as well as the sociodemographic, obstetrical/biological, psychological, and behavioural determinants of moderate and more severe nausea and vomiting symptoms. Determining the prevalence and determinants of NVP can help us to target women at increased risk for screening and treatment. There is increased opportunity in pregnancy to anticipate those women at risk for nausea and vomiting and consequently to improve the quality of life for the mother, her baby, and her family.

1.2 Research Questions and Hypotheses

This study will investigate the following four research questions and respective hypotheses. These questions begin with an estimation of prevalence rates and then progress to more specific questions to identify the determinants of nausea and vomiting in

this sample. The symptom profile of nausea and vomiting in the total sample of women will be explored and compared among women with different degrees of symptoms: those with mild or less than mild symptoms, moderate symptoms, and more severe symptoms.

1.2.1 Question 1. What is the prevalence of nausea, retching, and vomiting at two gestational time points in this sample of pregnant women and is this prevalence different from rates reported in the literature?

The prevalence of nausea, retching, and vomiting prior to 20 weeks in pregnancy will be comparable to prevalence reported in the literature for women in the first and second trimester of pregnancy (50% to 90%). The prevalence of nausea, retching, and vomiting beyond 20 weeks in pregnancy will also be comparable to the prevalence reported in the literature for these women (10-32%).

Hypothesis. Pregnant women taking medication to relieve nausea at Time 1 will report less severe nausea and vomiting in pregnancy. Similarly, pregnant women taking medication to relieve nausea at Time 2 will report less severe nausea and vomiting in pregnancy.

1.2.2 Question 2. What sociodemographic, biological/obstetrical, psychological, and behavioral determinants are associated with moderate and severe nausea and vomiting at Time 1 in this group of pregnant women?

Hypothesis. Pregnant women at Time 1 with more severe nausea, retching, and vomiting symptoms will be of younger age, lower level of education, lower level of income or not working, have fewer pregnancies, have fewer supports, have more worry, more stressors, more mood swings, more psychological problems, and are not engaged in risk behaviours compared to women with mild or less than mild nausea and vomiting symptoms.

1.2.3 Question 3. What sociodemographic, biological/obstetrical, psychological, and behavioral determinants are associated with moderate and severe nausea, retching, and vomiting at Time 2 in this group of pregnant women?

Hypothesis. Pregnant women at Time 2 with more severe nausea, retching, and vomiting symptoms will be of younger age, lower level of education, lower level of income or not working, have fewer pregnancies, have fewer supports, have more worry, more

stressors, more mood swings, more psychological problems, and are not engaged in risk behaviours compared to women with mild or less than mild nausea and vomiting symptoms.

1.2.4 Question 4. What is the nature of the relationship between nausea and vomiting and psychological determinants, as well as antiemetic and psychotropic medications, as evidenced by two time points in pregnancy?

Hypothesis. Pregnant women with more severe nausea and vomiting symptoms will have more psychological symptoms in pregnancy and women taking mediation to relieve nausea will have less psychological symptoms in pregnancy. In addition, women who report severe nausea and vomiting and symptoms of major depression at Time 1, as well as no symptoms of major depression at Time 2, will be associated with less severe NVP at Time 2.

Chapter 2

Literature Review

Chapter two describes the epidemiology and the effects of nausea and vomiting during pregnancy on the woman, the fetus, and the family. The sociodemographic, obstetric/biological, psychological, and behavioural determinants of NVP as well as the etiology of the condition are discussed. The chapter ends with an examination of preventative measures and treatment guidelines for women whose pregnancy experience is dominated and often diminished by nausea and vomiting.

2.1 Epidemiology of Nausea and Vomiting in Pregnancy

Since the time of Hippocrates, nausea and vomiting in pregnancy (NVP) has been recognized as a sign of early pregnancy. Nausea is a subjective and disagreeable feeling experienced in the back of the throat, which usually results in vomiting (Grant, 1987; Lang, 1990). Vomiting is the reflex causing the forceful expulsion of the contents of the stomach or intestine or both (Davis, Lake-Bakaar, & Grahame-Smith, 1986). Retching or dry heaving without vomiting has also been recognized as a distinct symptom of the condition that is increasingly measured separately (Lacasse, Rey, Ferreira, Morin, & Berard, 2008; O'Brien, Relyea, & Taerum, 1996; Zhou, O'Brien, & Soeken, 2001).

In contemporary Western populations, the prevalence of nausea and vomiting in early pregnancy ranges from 50% to 90% and may include mild to severe nausea and retching, with or without vomiting (Broussard & Richter, 1998; Miller, 2002; Woolhouse, 2006). Hyperemesis gravidarum (HG) is the most extreme manifestation of the condition (Hod, Orvieto, Kaplan, Friedman, & Ovadia, 1994) and occurs in approximately 0.5%-2% of pregnancies (American College of Obstetrics and Gynecology, 2004). HG is characterized by persistent nausea resulting in vomiting severe enough to interfere with nutrition and fluid intake, and may require close medical monitoring. Whether NVP and HG are independent conditions or a part of a continuum of illness remain unclear.

The lay term 'morning sickness' is based on the assumption that symptoms commonly occur in the morning. However, only 17% of those with nausea experience it solely in the morning; for others, it can occur at any time and last all day (Whitehead, Andrews, & Chamberlain, 1992). The onset of symptoms is typically between four to eight

weeks after conception, and begins to decline around the twelfth week, with symptoms disappearing by week 20 for most women (Gadsby, Barnie-Adshead, & Jagger, 1993; Klebanoff, Koslowe, & Kaslow, 1985; Lacroix, Eason, & Melzack, 2000; Whitehead et al., 1992). A prospective study in 160 American women that examined patterns of symptoms daily throughout pregnancy found that 90% of women experienced the onset of symptoms by week 8 of gestation, and 90% experienced relief of symptoms by week 22 (Lacroix et al., 2000). More recently, it has been reported that symptoms of NVP can persist into late pregnancy for up to 32% of women (Lindseth & Vari, 2005).

2.2 Etiology

The cause remains unknown, thus NVP is a diagnosis of exclusion. Fever, abdominal pain (unless caused by retching) and diarrhea are not associated with NVP (Davis, 2004). Other pathological causes of nausea and vomiting must be considered and excluded before concluding that the symptoms are triggered from pregnancy. These include peptic ulcers, cholecystitis, gastroenteritis, appendicitis, hepatitis, thyroid disease, adrenocortical insufficiency, genitourinary disorders such as pyelonephritis, metabolic and neurological disorders (Koch, 2002; Quinlan, 2003).

Changing maternal circulatory levels of reproductive hormones early in pregnancy have been implicated as potential mechanisms triggering nausea and vomiting. The endocrine factor most commonly implicated is human chorionic gonadotropin (hCG) and is based on two arguments. First, the pattern of hCG secretion in early pregnancy tends to parallel the onset, peak and decline of NVP symptoms. Second, conditions with higher levels of hCG, such as multiple pregnancies and molar pregnancies, have been associated with a higher risk of nausea and vomiting (Goodwin, 2002). Hormonal studies of women with and without NVP indicate that higher levels of hCG are more often associated with NVP symptoms. Of the 17 studies published since 1977, 13 reported a positive association between hCG and NVP compared to women without NVP (Goodwin). It has been suggested that the lack of consistency of some studies to show a relationship may be explained by the complex interactions between different forms of hCG and biologic activity (Goodwin, 2000).

Estrogen has also been held responsible in producing NVP as indirect evidence points to an increased likelihood of NVP in women with higher estrogen levels (Goodwin,

2002). Variations in postoperative nausea and vomiting by menstrual cycle (Beatie, Buckley, & Forrest, 1991) and the dose related nausea and vomiting related to birth control pills suggest that estrogen is involved (Jarnefelt-Samsioe et al., 1985; O'Brien & Zhou, 1995). However, relatively few studies have explicitly examined estrogen concentrations in women with and without NVP, and they have not found consistent associations. Two studies of NVP and estrogen reported higher levels of estrogen in symptomatic women (Jarnfelt-Samsioe, Bremme, & Eneroth, 1986; Lagiou et al., 2003) and one study reported no association (Masson, Anthony, & Chau, 1985). Three studies reported positive associations between hyperemesis gravidarum and estrogen (Depue, Bernstein, Ross, Judd, & Henderson, 1987; Goodwin, Montoro, Mestman, Pekary, & Hershman, 1992; Youneyama et al., 2002) and one found no association (Jordan et al., 1999). There is considerable variation across studies in the timing of data collection, ranging between 4 and 38 weeks. This is problematic as hormonal levels and symptoms are change significantly from week to week in pregnancy. In addition, women were sampled more than once in pregnancy, during the second and third trimesters, in only two of these studies (Jarnefelt-Samsioe et al., 1986; Lagiou et al., 2003).

Other endocrine factors proposed to play a role in the development of NVP include progesterone, adrenal and pituitary hormones. One study found lower levels of progesterone among women who vomited in pregnancy (Jarnefelt-Samsioe et al., 1986), two other studies found no difference in progesterone levels and NVP (Lagioue et al., 2003; Masson et al., 1985), and one study reported higher levels of progesterone in women with hyperemesis gravidarum (Yoneyama et al., 2002). Few reports have examined adrenal, and pituitary hormones and currently there is no conclusive evidence implicating either of them (Borgeat, Fathi, & Valiton, 1997).

Theories regarding beneficial effects relate NVP to safe digestive behaviours. Certain foods, caffeinated beverages and alcohol may be teratogenic and it has been suggested that pregnant women are sensitized to vomit by persistent nausea in order to protect the developing fetus in early pregnancy (Profet, 1988). Flaxman and Sherman (2000) hypothesized that women with NVP tend to avoid animal products that are more likely to harbor parasites or other pathogens that could potentially endanger their health and the health of the developing fetus. Food aversions to meat, fish, eggs, and fatty foods are

common and this pattern is consistent with the ethnographic evidence of little or no NVP in population groups relying on grain and plant-based diets. In addition, many women with NVP also complain of an increased sense of smell (Swallow, Lindow, Masson, & Hay, 2005), which may lead to aversion of noxious or toxic substances in pregnancy. However, an increased sensitivity to certain smells and tastes frequently triggers nausea in these women and is no longer protective when nausea and vomiting results.

It has been speculated that NVP might be a response to infection. Five women with HG who did not respond to standard HG management reported complete relief of symptoms after *Helicobacter pylori* management (El Younis, Abulafia, & Sherer, 1998; Jacoby & Porter, 1999). However, there are no randomized controlled trials evaluating the efficacy of this treatment strategy to date.

A genetic influence is supported by observations that NVP shows ethnic variation (Minturn & Weither, 1984), is more frequent in monozygotic twins (Cory, Berh, Solaas, & Nance, 1992), is more common in women whose sisters and mothers are affected (Gadsby, Barnie-Adshead, & Jagger, 1993), and is associated with genetically determined conditions such as taste sensation (Sipiora, Murtaugh, Gregoire, & Duffy, 2000) and glycoprotein receptor defects (Akerman, Zhenmin, Rao, & Nakajim, 2000; Rodien et al., 1998). Genetic predisposition may also a explain link between a history of migraine headaches and the increased risk of hyperemesis gravidarum (Heinrichs, 2002).

Common gastric changes during pregnancy include decreased gastric emptying and lowered esophageal pressure (Walsh, Hasler, Nugent, & Owyang, 1996). Gastric changes may exacerbate NVP, but are unlikely the sole cause of the condition (Nelson-Piercy, 1997). History of motion sickness has also been associated with NVP (Whitehead et al., 1992) and suggests that a pregnancy stimulus may lower the threshold for vestibular mediated nausea and vomiting in some women.

Early theories attributed more severe nausea and vomiting and psychological conflict regarding the pregnancy; however, most studies suggesting this link are older and have flawed methodologies that discredit the findings. The finding that women with NVP are more hypnotizable (Apfel, Kelly, & Frankel, 1986) led researchers to suggest that vomiting may be

a conditioned response to specific environmental cues, just like chemotherapy patients who develop anticipatory vomiting.

2.3 Outcome

2.3.1 Fetal. A review of the literature did not reveal an increased incidence of congenital malformations reported in children born to women affected by NVP (Klebanoff & Mills, 1986). Several studies suggest that NVP is a favorable prognostic sign, with a decreased risk of miscarriage, preterm delivery, low birthweight, stillbirth and fetal and perinatal mortality (Czeizel & Puho, 2004; Weigel & Weigel 1989), although later studies have challenged these claims (Louik, Hernandez-Diaz, Werler, & Mitchell, 2006). Hyperemesis gravidarum has been linked to fetal growth restriction (Chin & Lao, 1988; Gross, Librach, & Cecuti, 1989) and Wernicke's encephalopathy resulting in fetal death in 40% of cases (Rotman, Hassin, Mouallem, Barkai, & Farfel, 1994).

Few studies have examined the long-term effects of NVP on child development. Nausea and vomiting in the second and third trimesters of pregnancy has been found to be associated with effects on child's emotions, increased motor activity, and attention and learning problems at 12 years of age (Martin, Wisenbaker, & Huttunen, 1999). Interestingly, one study reported an association between NVP and improved neurodevelopment in the offspring (Nulman et al., 2009). Children aged 3 to 7 born to mothers with NVP had significantly higher nonverbal intelligence, verbal processing, and forward digit span scores. The authors also found that exposure to diclectin did not adversely affect children's cognitive abilities, which is congruent with other reports of no adverse morphological effects of the doxylamine-vitamin B6 combination in women with NVP (Huxley, 2000; Sherman & Flaxman, 2002; Weigel & Weigel, 1989).

2.3.2 Maternal. Before the availability of modern treatments, severe NVP was important contributor to maternal mortality (Sonkusare, 2008). While rarely life threatening now, women report considerable physical and psychological effects with altered family, social or occupational functioning (Attard et al. 2002; Chou, Lin, Cooney, Walker, & Riggs, 2003; Chou, Kuo, & Wang, 2008; O'Brien & Naber,1992; O'Brien, Relyea, & Lidstone, 1997; Swallow, Lindow, & Masson, 2004). The misery associated with persistent nausea and vomiting and the serious disruption to everyday life are often underestimated by care

providers (Attard et al., 2002; O'Brien & Naber, 1992), and woman have reported that they would like their symptoms and resulting suffering acknowledged to a greater extent (Locock, Alexander, & Rozmovits, 2008).

The socioeconomic burden of NVP on women and society is substantial. The complete spectrum of NVP results in 47% to 50% of working women with NVP believing that their job efficiency is reduced (O'Brien & Naber, 1992; Vallacott, Cooke, & James, 1988), 35% lose work time (mean loss of 62 working hours per woman) (O'Brien & Naber), and 25% lose time from housework (mean lose of 32 hours per woman (Gadsby, Barnie-Adshead, & Jagger, 1993; Jarnfelt-Samsioe, Samsioe, & Velinder, 1983; Mazzota et al., 2000, O'Biren & Naber). Severe NVP is the most common cause of hospitalization in the first half of pregnancy and the second most common cause of antenatal hospitalization during pregnancy overall, second only to preterm labor (Gazmararian et al., 2002).

Little is known about the long-term impact of NVP on mothers who bear the condition. Hyperemesis gravidarum and hospitalization during pregnancy have both been reported as factors related to Posttraumatic Stress Disorder (PTSD) after delivery (Maggioni, Margola, & Fillippi, 2006). Another study found that women with HG were more likely to report that recovery from their pregnancy took longer than 1 month and continued to report gallbladder dysfunction, food aversions, muscle pain, nausea, and symptoms characteristic of PTSD into the postpartum period (Fejzo et al., 2009). The authors suggest that food aversions may be the result of behavior modification over the months of pregnancy, and other symptoms may be a sign of the marked nutritional deprivation these women undergo.

2.4 Determinants

Numerous reports have examined various treatments for NVP (Niebyl & Goodwin, 2002; Mazzotta & Magee, 2000) or the relationship between NVP and pregnancy outcome (Klebanoff & Mills, 1986; Sherman & Flaxman, 2002), but few studies have considered risk factors for either the development or severity of NVP itself. Among those studies that have explored the correlates of NVP, no clear consensus has emerged. An overview of the studies comparing nausea and vomiting in pregnancy and psychosocial determinants of health is included in Appendix E.

2.4.1 Sociodemographic. A review of the literature reveals that NVP is more common in Westernized civilizations, in predominantly urban compared with rural populations, and is rare in African, Native American, Eskimo, and some Asian populations except for the industrialized Japanese (Fairweather, 1968; Minturn & Weiher; Semmens, 1971; Walker, Walker, Jones, Vervardi, & Walker, 1985). Living alone (Gertraude, Strunz-Lehner, Egen-Lappe, Lack, & Hasford, 2007) or living in overcrowded or unfamiliar circumstances (Deuchar, 1995) are predictors for NVP. Some studies report that women who are younger (Klebanoff, Koslowe, Kaslow, & Rhoads, 1985; O'Brien & Zhou), with a lower level of education (Klebanoff et al., 1985; Lacroix et al., 2000), and who are not working or who are housewives are more likely to have NVP (Kallen, Lundberg, & Aberg, 2003). However, others have revealed that NVP affects all socioeconomic strata (Tierson, Olsen, & Hook, 1986) and may not be associated with education level (Fitzgerald, 1984; O'Brien & Zhou, 1995) or age (Fitzgerald, 1984).

2.4.2 Obstetrical/biological. Certain obstetrical and biological factors may also influence the development of nausea and vomiting in pregnancy. NVP is more common in women who are obese (O'Brien & Zhou, 1995) and who have a history of nausea when taking estrogen-containing oral contraceptives (Järnfelt-Samsioe, Samsioe, & Velinder, 1983). Prior infertility and a history of the condition in a previous pregnancy also increase the likelihood of NVP (Gadsby, Barnie-Adshead, & Jagger, 1997; Weigel & Weigel, 1988). In women seeking an abortion, ultrasound assessments revealed that vomiting was associated with corpus luteum on the right ovary, but not the left (Samsioe, Crona, Enk, & Järnfelt-Samsioe, 1986). The authors suggested that venous drainage, which differs between the right and the left side, might be responsible for the fact that the same woman can either suffer from or be free from nausea during pregnancy. NVP may increase in duration with each successive pregnancy (Einarson, Navioz, Matlepe, Einarson, & Koren, 2007), although some women experience higher, lower, or similar incidences (Gadsby, Barnie-Adshead, & Jagger, 1993; Rhodes, 1990). Jarnfelt-Samsioe and colleagues (1983) reported that nausea was more pronounced in women with allergies, symptomatic gallbladder disease, or gastritits, but these concurrent conditions did not affect the duration of nausea. NVP appears to be uncorrelated with other complications of pregnancy, including

diabetes, hypertension, preeclampsia, anemia, and proteinuria (Jarnfelt-Samsioe et al.; Klebanoff, Koslowe, Kaslow, & Rhoads, 1985).

Intriguingly, a female fetus is most often associated with NVP. Three studies have found and association between NVP and female offspring (Hsu & Witter, 1993; O'Brien & Zhou, 1995; Vilming & Nesheim, 2000), although earlier studies disagree with this assertion (Vallacott, Cooke, & James, 1988; Whitehead, Andrews, & Chamberlain, 1992). Three studies have found an association between hyperemesis gravidarum and increased odds of having a female fetus compared with controls (Askling, Erlandsson, Kaijser, Akre, & Ekbom, 1999; Kallen, 1987; Schiff, Reed, & Daling, 2004). The usual explanation for the increased incidence of female fetuses is related to higher estrogen concentrations.

2.4.3 Psychological. Nausea and vomiting in pregnancy might be explained by recent evidence which supports biological pathways linking stress to body changes. Hormones that are involved in the stress response (e.g., adrenocortico-tropic hormone and cortisol) were positively correlated with the severity of nausea reported among pregnancy women (Otto, Riepl, Klosterhalfen, & Enck, 2006). Reactions to stress during pregnancy can be somatic and include vomiting (Morgan, 1985). Somatic complaints including vomiting have been reported more often in women with high levels of anxiety during pregnancy compared to pregnant women without anxiety (Martin, 1987). Emotionally disturbing events have also been associated with vomiting in pregnancy (Georgas, Giakoumake, Georgoulias, Koumandakis, & Kaskarelis, 1984). Based on a 'specially constructed questionnaire' administered to 102 women in the first trimester, NVP were associated with stress, lack of information about pregnancy, childbirth and health of the fetus, and poor communication with the husband and physician (Iatrakis, Sakellaropoulos, Kourkoubas, & Kabounia, 1998). On the other hand, studies have found no differences in marital status, whether the infant was planned, or positive feelings about the pregnancy between women with and without nausea and vomiting in pregnancy (Vallacott, Cooke, & James, 1988; Wolkind & Zajicek, 1978). The rapid improvement of some women on admission to hospital and consequent removal from a stressful home environment (American College of Obstetricians and Gynecologists, 2004) suggests that stressors and maternal coping skills may play a role in the development of NVP. Having a supportive relationship with either a partner, mother, or

friend has been shown to mediate both stress (Chou, Avant, Kuo, & Fetzer, 2008; Chou, Kuo, & Wang, 2008) and anxiety in pregnancy (Jesse, Walcott-McQuigg, Mariella, & Swanson, 2005), although the effect of social support on NVP is less understood.

Mood changes and depression have been associated with nausea and vomiting in pregnancy. Women who experience NVP report occurrences of tearfulness, irritability, lowered mood, sleep disturbance that undermined their self-esteem (O'Brien & Naber, 1992; Deuchar, 1995). When quality of life measures are used in research studies, the scores for women with NVP are worse than the scores of women who report chronic depression (Attard et al., 2002). A diagnosis of depression in pregnancy is difficult due to the similarity in symptoms between the two conditions. Nonetheless, depression has been reported to affect up to 20% of pregnant women (Marcus, Flynn, Blow, & Barry, 2003) and nausea and vomiting have been independently associated with anxiety (Andersson, Sundstrom-Poromaa, Wulff, Astrom, & Bixo, 2004; Swallow, Lindow, Masson, & Hay, 2004) depression (Chou, Lin, Cooney, Walker, & Riggs, 2003; Kitamura, Sugawara, Sugawara, Toda, & Shima, 1996; Mazzotta et al., 2000) and social dysfunction (Swallow et al., 2004) in pregnancy. While these studies clearly associate NVP with psychological morbidity, the temporal relationship is unclear, for example, if depression in pregnancy preceded or resulted from nausea and vomiting.

Historically there was thought to be an association between NVP and psychological conflict regarding the pregnancy, although the finding has never been corroborated. This perspective stems from the favorite Freudian diagnosis of hysteria. Vomiting was viewed as an attempt to expel the unwanted fetus orally (Katon, Ries, Bokan, & Kleinman, 1980) and also represented a physical rejection of the woman to accept the transition into motherhood, symbolized the woman's relationship with her husband, and was even a means of the woman rejecting her own mother (Pines, 1990). Psychoanalysts have characterized women suffering from NVP as emotional, attention-seekers, seductive, dependent, helpless, self-dramatizers, and with chameleon-like personality and sexual problems (Buckwalter & Simpson, 2002). A link between pathological personality types and NVP has never been proven and the concept that NVP reflects a conversion disorder has most likely impeded the progress toward a greater understanding of the condition (American College of

Obstetricians and Gynecologists, 2004). More recent studies have suggested that psychological symptoms are the result of the stress and the burden of daily and persistent nausea and vomiting rather than the cause (Verberg, Gillott, Al-Fardan, & Grudzinskas, 2005). It has also been suggested that psychologic responses to the physiologic stimuli could become entrenched or conditioned with the 2 interacting to exacerbate NVP (Buckwalter & Simpson, 2002), thus interventions aimed at treating psychological symptoms might be helpful.

2.4.3 Behavioural. FitizGerald (1984) reported an association between NVP and unintended pregnancy, although two other studies found no difference in whether or not the infant was planned (Vallacott, Cooke, & James, 1988; Wolkind & Zajicek, 1978). Women who are not actively planning their pregnancy may be more likely to experience NVP as early multivitamin supplementation has been linked to a decrease in risk of the condition (Kallen, Lundberg, & Aberg, 2003).

Similar to women with depression, women with unintended pregnancies are less likely to start prenatal care early and are more likely to use cigarettes, alcohol, and drugs in pregnancy (Hellerstedt et al., 1998; Naimi, Lipscomb, Brewer, & Gilbert, 2003; Zuckerman, Amaro, Bauchner, & Cabral, 1989). Women who use drugs during pregnancy are more likely to be depressed, have fewer social supports, less stable living arrangements, and are more likely to smoke and drink alcohol (Lindenberg, Alexander, Gendrop, Nencioli, & Williams, 1991; Robins & Mills, 1993). Prenatal smoking was found decrease the chance of having vomiting (Klebanoff et al., 1985) or both nausea and vomiting in early pregnancy (Kallen, Lundberg, & Aberg, 2003; Weigel & Weigel, 1988). Alcohol consumption has been associated with a decreased probability of nausea and vomiting in early pregnancy (Little & Hook, 1979) as well as with increased stress levels after 20 weeks in gestation (Lindseth & Vari, 2005). Lacroix et al. (2000) did not find that cigarette and alcohol use in pregnancy were associated with nausea and vomiting, although other studies report an association with cigarette and alcohol use and emotional problems during pregnancy (Stewart & Steiner, 1994).

There is an abundance of literature on the negative effects of cigarette (US Department of Health and Human Services, 1990), alcohol, and drug use (Allen & Feeney,

1997), as well as unintended pregnancy (Brown & Eisenberg, 1995) on the health of the mother, the fetus, and future child. Whether or not cigarette and alcohol use are associated with NVP or are reflective of the amount of stress experienced by the pregnant woman warrant further exploration.

2.5 Prevention

A randomized double-blind controlled trial of peri-conceptional multivitamin supplementation prior to 6 weeks gestation found a significant decrease in the rate of moderate nausea and vomiting in pregnancy. There was also a significant reduction in the occurrence of hyperemesis gravidarum, 3% in the supplemented group versus 6.6% in the unsupplemented group (Czeizel, 1996). Therefore, all sexually active women of childbearing age should be encouraged to take a multivitamin prior to known pregnancy for prevention of nausea and vomiting of pregnancy.

2.6 Treatment

The approach to treatment of NVP focuses on reducing the symptoms, while minimizing the maternal and fetal risks of antiemetic or non-medication measures. In the absence of a standardized assessment tool, the best assessment of the degree of symptoms is to ask the woman to share her view of the illness. Early intervention is thought to decrease the severity and duration of NVP, prevent complications, and likely improves the quality of life for the pregnant woman and her family. Thus, women with mild or moderate symptoms should be counseled early in their pregnancy on safe and effective treatments, as well as provided reassurance regarding the teratogenic risk of antiemetic medications in early pregnancy (Arsenault & Lane, 2002).

2.6.1 Dietary and lifestyle modifications. Alterations to diet and lifestyle are common first line interventions for pregnant women with less severe nausea and vomiting. Although there are no clinical trials of these recommendations, women have reported that these measures can be beneficial in reducing the severity of NVP (Chandra, Magee, Einarson, & Koren, 2003; O'Brien & Naber, 1992). In a recent international survey of 765 women with HG, 22% reported that dietary changes were either maybe effective or effective in relieving their symptoms (Goodwin et al., 2008).

Common dietary and lifestyle recommendations include small, dry, bland, frequent meals rich in easily digestible carbohydrates (e.g., soda crackers, biscuits), and avoidance of fibrous, spicy and fatty foods. Pregnant women are encouraged to eat whenever they feel hungry, as nausea is likely to be less severe at that time. Eating before rising in the mornings and eating a high-protein snack before going to bed may reduce symptoms. Drinking fluids can exacerbate nausea (Jewell & Young, 2003); therefore, drinking small amounts regularly between meals may help maintain hydration. Sleep requirements increase in early pregnancy (Santiago, Nolledo, Kinzler, & Santiago, 2001) and fatigue seems to exacerbate NVP (Chou et al., 2003). Therefore, pregnant women should increase their rest and lie down when feelings of nausea occur. They should also avoid smells, foods, and activities or situations (e.g., time spent in the kitchen) that they find nauseating (Ornstein, 1995). Lastly, any iron supplements should be temporarily discontinued as they can cause nausea, vomiting, and epigastric pain in some women.

2.6.2 Antiemetics. Antiemetic therapy should be considered in women who have continued nausea and vomiting despite dietary and lifestyle changes. Medications that have been found to be safe and effective include dopamine antagonists (metoclopramide and domperidone) (Milkovich & Van Den Berg, 1976), phenothiazines (chlorpromazine and prochlorperazine (Godet & Marie-Cardine, 1991) and histamine H1 receptor blockers (promethazine and cyclizine) (Seto, Einarson, & Koren, 1997). However, both pregnant women and their doctors fear the possibility of medications affecting the development of the fetus and effective medications for nausea are often underutilized in early pregnancy (Koren & Levichek, 2002; Ornstein, 1995).

Teratogenicity concerns primarily stem from the thalidomide tragedy in the early 1960's. Thalidomide was a drug held responsible for babies born with phocomelia, resulting in shortened, absent, or flipper-like limbs (McCredie, 1973). In 1983, extensive litigation concerning allegations of the teratogenicity of Benedictin (vitamin B6-doxylamine), despite the lack of evidence to substantiate these claims, led the manufacturer to voluntarily withdraw the drug from the market (Pastuszak, 1995). Following this withdrawal, the rate of hospitalizations for women with NVP doubled during the next eight years in Canada and

similar trends were seen in the US. (Pastuszak, 1995). Currently Benedictin is available in Canada, but remains off the US market (Brent, 2002).

2.6.3 Alternative therapies. Ginger, chamomile, peppermint, and red raspberry leaf tea are the most commonly cited herbal remedies from nonmedical sources of advice for "morning sickness" (Wilkinson, 2000). Only the effectiveness of ginger (1g/day) has been studied under randomized controls. Powdered root of ginger given to 30 women was significantly better than the comparison group at diminishing or eliminating symptoms of hyperemesis gravidarum (Fisher-Rasmussen, Kjaer, Dahl, & Asping, 1990). Ginger is a nonregulated food product and is available in a number of forms such as tea, biscuits, confectionary, and crystals or sugared ginger, although the purity and concentrations of most forms is uncertain. As the possibility of teratogenicity has not been excluded, large quantities of ginger should not be recommended as a treatment for NVP (Arsenault & Lane, 2002).

More and more pregnant women are increasing interested in acupuncture and acupressure measures for relief of NVP. These measures involve stimulation of the P6 Neiguan point located three-fingers' breadth proximal to the wrist, between two easily palpated tendons. Acupuncture requires a trained practitioner to insert thin needles over this site, whereas acupressure involves stimulation of the point either manually (using fingers or thumbs) for 5 minutes every 4 hours, or with wristband devices that provide steady pressure from a small button on the site. According to the American College of Obstetricians and Gynecologists (2004), evidence supporting or refuting acupuncture and acupressure is mixed. However, the safety of these measures has not been called to question and manual acupressure is readily available and without cost.

2.6.4 Psychological support. It is common for mood disorders to accompany NVP, along with tearfulness and sleep disturbances (O'Brien & Naber, 1992; Deuchar, 1995. Anxiety and depression may require treatment with safe therapeutic medications, such as antidepressants. Although tricyclic antidepressants (amitriptyline, nortriptyline, and imipramine) have shown no teratogenic effects when used in the first trimester (Nulman et al., 1997), their narrow therapeutic index, life-threatening cardiotoxicity in overdose, and severe anticholinergic effects make them less appealing (Arsenault & Lane, 2002). On the

other hand, selective serotonin re-uptake inhibitors (fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram) are effective, not cardiotoxic, are safe even if used in excess (with the exception of citalopram) (Arsenault & Lane), and are not associated with an increased risk for major malformations when used in the first trimester (Marcus, Barry, Flynn, Tandon, & Greden). When women do not respond to medical and supportive care, psychiatric consultation is recommended (Hod, Orvieto, Kaplan, Friedman, & Ovadia, 1994).

Psychotherapy, hypnotherapy, and behavioural therapy have been reported to diminish the symptoms of hyperemesis gravidarum (Iancu, Kotler, Spivak Radwan, & Weizman, 1994). Supportive counseling or enlisting the support and understanding of close friends and family in order to deal with the personal distress and social or occupational disruption from NVP may also be of benefit (Deuchar, 1995; Hod, Orvieto, Kaplan, Friedman, & Ovadia, 1994). The purpose of supportive therapy is not to develop deep insights into the psychological factors contributing to the condition, but rather to develop commonsense, practical approaches to the problem through encouragement, explanation, reassurance, and the opportunity to vent emotions (Deuchar, 1995).

Chapter 3

Theoretical Perspectives

The purpose of this chapter is to describe the theoretical perspective that has guided this research. The underlying perspective is a population health approach that recognizes the interaction of multiple influences that shape the health of populations.

3.1 Population Health Approach

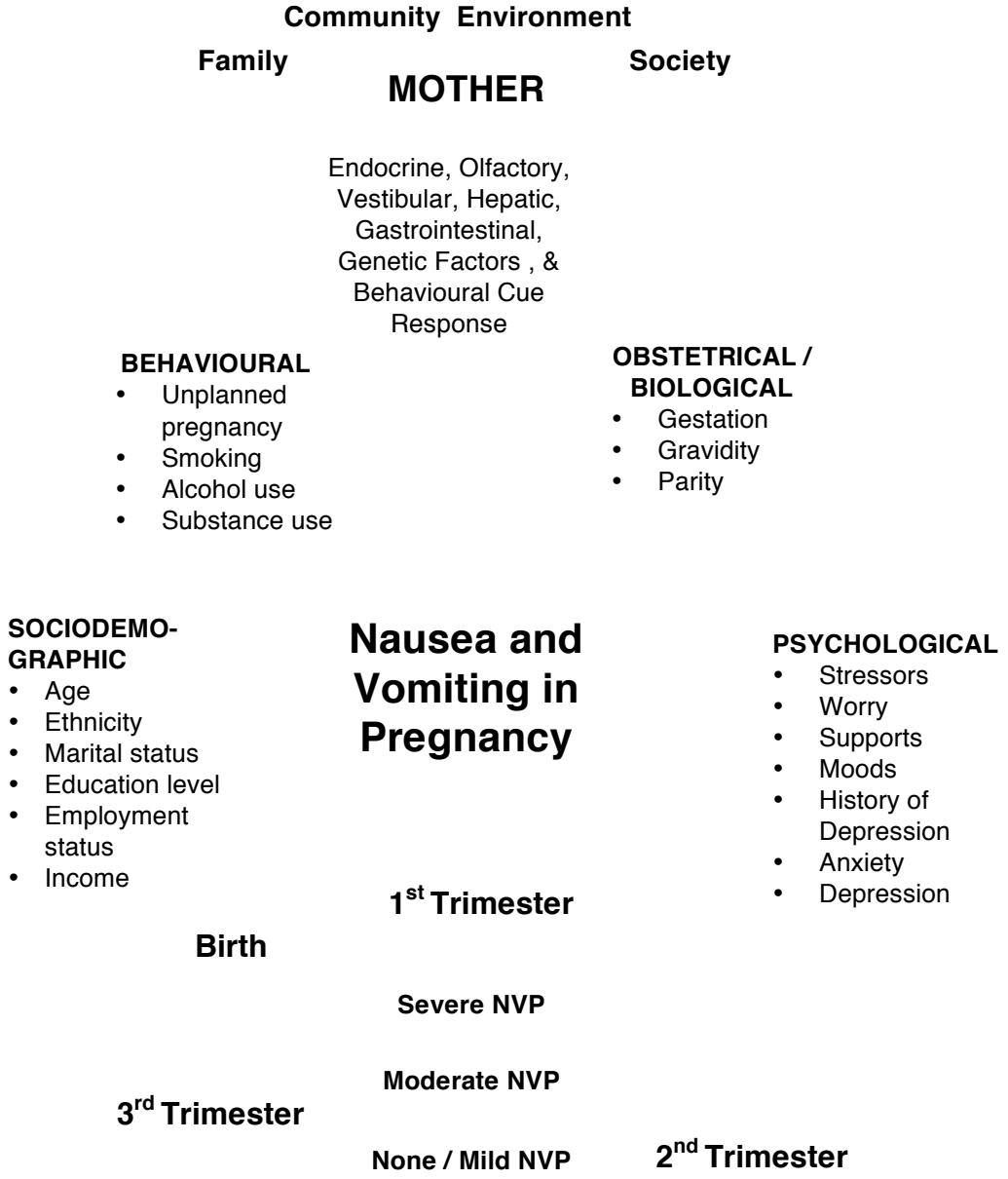
Population health is a perspective that focuses on the entire range of individual and collective factors and the interactions among them that determine health and well-being over the life course (Public Health Agency of Canada, 2005). These factors are referred to as determinants of health and currently include: income, supports, education, employment, social environment, physical environment, personal health practices and coping skills, healthy child development, biology and genetic endowment, health services, gender, and culture (Public Health Agency of Canada). The goal of population health is to improve the health of the entire population at every stage of life and reduce health inequities among different groups of people (Shah, 2003). Health inequalities refer to the broad determinants of health that are different at different social strata (Kindig & Stoddart, 2003). By focusing on determinants of health, policies and services are directed toward improving the overall health status of the population (Public Health Agency of Canada, 2005).

Population health lends a different way of understanding health and may have more impact than the traditional biomedical model (Public Health Agency of Canada, 2005). Health involves emotional, social and physical well-being and is determined by the social, political and economic context of their lives, as well as by biology (Health Canada, 2003). This perspective broadens the scope of what it means to be healthy and differs from the traditional model's narrow focus on individuals that were already sick or those that were at the greatest risk of developing a health problem. The population health perspective focuses on the existing health inequalities and complexities of women's lives and is therefore a fitting approach to the study of nausea and vomiting in pregnancy. Moreover, a lack of attention to health inequalities has led to a systematic devaluation and neglect of women's health (Sen & Östlin, 2008).

Nausea and vomiting in pregnancy is a multifaceted condition and several determinants may aggravate its presence and severity. Previously identified determinants include: genetic (American College of Gynecology Practice Bulletin, 2004), physiological (Goodwin, 2002), and biological factors (Ornstein et al., 1995; Huxley, 2000; Sherman & Flaxman, 2002); social characteristics, including stress, lack of social support (Chou et al., 2003; Paalberg et al., 1996), environment, work status, and certain anxious attitudes or beliefs about the fetus or about pregnancy and motherhood (Atanackovic, Koren, & Magee, 2000); behavioural factors including unintended pregnancy (FitzGerald, 1984), maternal smoking and alcohol consumption (Barkai et al., 1994; Weigel & Weigel 1989; Zhou, O'Brien, & Relyea, 1999), and the psychological factors of anxiety and depression (Anderson et al., 2004; Chou, 2003; Kitamura et al., 1996; Mazzotta et al., 2000). However, as the literature revealed, the evidence is varied and at times contradictory due to the varied factors associated with nausea and vomiting in pregnancy.

For this study, a population health approach has been used to examine nausea and vomiting as well as the risk factors and correlates of moderate and severe symptoms in pregnant women during two gestational time points. A conceptual model, shown in Figure 3.1, was constructed based on the theory of population health (Public Health Agency of Canada, 2005) and adapted from the model titled, *Determinants of Antenatal Depression and the Fetus*, developed by Bowen (2007) for her study on the prevalence and determinants of antenatal depression among high-risk women in Saskatoon, Saskatchewan, Canada. Physiological factors that interrelate with determinants to affect the duration and severity of nausea and vomiting in pregnancy are included in the conceptual model. The anticipated determinants of nausea and vomiting are grouped and named as sociodemographic, obstetrical/biological, psychosocial, and behavioural. Each determinant is discussed in more detail, in relation to how they are measured in this study, in Section 4.7.1 to 4.7.4 of Chapter 4. By exploring these determinants the resulting knowledge may be used to try to explain women's susceptibility for nausea and vomiting in pregnancy.

Figure 3.1. The Population Health Approach Illustrating the Interrelated Determinants of NVP



Chapter 4

Methodology

The chapter describes the study location, design, population and setting, inclusion and exclusion criteria, and ethical considerations. Next the chapter details the outcome variable and independent variables of interest. Finally, the data preparation, analytical procedures, and limitations of the study are described.

4.1 Study Location

This study was conducted at the University of Saskatchewan, Saskatoon, Saskatchewan in the College of Nursing.

4.2 Study Design

The dataset used in this secondary analysis was a sub-set of a larger clinical database of Canadian pregnant women enrolled in a longitudinal study of antenatal and postnatal depression called, *The Feelings in Pregnancy and Motherhood Study (FIP)*, in Saskatoon, Saskatchewan, Canada between November 2005 and December 2008. The co-principal investigators of the FIP study, Dr. Nazeem Muhajarine and Dr. Angela Bowen, were supported for three years under the Canadian Institutes for Health Research (CIHR) strategic research priority, *Analyzing and Reducing Health Disparities* (Grant #145179). The FIP study included a cohort of 649 pregnant women interviewed on three different occasions, in early and late pregnancy, and once again after their babies were born for the purposes of examining depression and its correlates in pregnant and early postpartum women.

4.3 Population and Setting

Participants from the original study spoke English and were recruited from physician's offices or responded to poster, newspaper, and radio advertising.

4.4 Inclusion and Exclusion Criteria

The dataset used for this secondary analysis was restricted to women who completed the NVPI questionnaire after 5 weeks gestation, coinciding with the usual onset of nausea, vomiting and retching in pregnancy. The objective measure of NVP was added to the questionnaire after study commencement and participants who did not complete the measure were removed from the dataset. No pregnant woman refused to complete the

questionnaire once the NVPI measure was added. However, 40 women miscarried or delivered prior to data collection during the second time point and were removed from the dataset. Therefore, the dataset analyzed in this study contained 551 participants at Time 1, and 575 participants at Time 2.

4.5 Ethical Considerations

The FIP study received ethical approval from the University of Saskatchewan and participating health regions prior to study commencement. On August 12, 2009, the Behavior Research Ethics Board of the University of Saskatchewan approved this secondary analysis of the FIP dataset (see Appendix A).

4.6 Outcome Variable

The variable of interest for this study was nausea and vomiting in pregnancy as measured by the Nausea and Vomiting in Pregnancy Instrument (NVPI) (Swallow, Lindow, Masson, & Hay, 2002). Verbal reports of 'slight' and 'severe' symptoms without definition were common in the literature and led to the development of a tool to define and quantify NVP (Swallow et al., 2002). This tool screens for nausea, retching and vomiting over a 1-week time period, and addresses the very real misery of the woman who is severely nauseated throughout the day or who retches repeatedly but does not vomit.

The NVPI is a 6-point Likert scale that includes 3 scales of nausea, retching and vomiting in the past week. The three items of the NVPI include:

1. How often have you felt like being (nauseous) in the past week?
2. How often have you retched (but without actually being sick) in the past week?
3. How often have you been physically sick during the past week?

Each item is scored on a six-point Likert scale: 'not at all', 'occasionally', '3-6 days during the week', 'daily', 'more than once a day' and 'all the time'. Scores range from 0, 'not at all' to 5, 'all the time'. The items are summed to form a NVPI severity score ranging from 0 to 15. The measure is presented in Appendix C.

Swallow et al. (2002) validated the ability of the three scales forming the NVPI to discriminate between different levels of NVP symptoms. The 'not at all' responses appeared to be an objective measure and at the other end of the scale, in five cases where the woman had been admitted to hospital with hyperemesis gravidarum the scores were

substantially above the mean. The instrument had acceptable internal reliability at two gestational time periods with a Cronbach's alpha coefficient of 0.76 and 0.82, respectively. The test-retest reliability was high, although only a small sample completed the instrument twice (0.83; 95% confidence intervals 0.71-0.90).

The NVPI is used as both a continuous and categorical variable in this analysis. Due to the negatively skewed distribution of the NVPI score at Time 1 and Time 2, the variable was collapsed into severity categories that allowed for a focus on pregnant women with more nausea and vomiting. Scores of zero were separated from the NVPI score while remaining scores were divided into three equal groups. Scores of zero were then added to the first group to form the group 'none/less than mild NVP'. The second and third tertiles, excluding scores of 0, were termed 'moderate NVP' and 'severe NVP', respectively.

4.7 Independent Variables: Determinants of NVP

4.7.1 Sociodemographic

Age. Age (years) was treated as continuous in this analysis.

Marital status. Women were categorized as non-partnered for the purposes of this study if they were single, divorced, or widowed and partnered if they were married or in a common-law relationship.

Ethnicity. Women who self-identified as Caucasian were categorized as such and women who self-identified as First Nations, Métis or other were categorized as Aboriginal or other in this analysis.

Education. Education level was collected as a categorical variable. It was further collapsed into the following categories: having grade 11 or less, having a grade 12 education, and attending or graduated from university or a post-secondary institution.

Employment. Women were categorized as working or not working for the purposes of this study.

Income. Family income was assessed through four categories: under $20,000 per year; $20,000 to $39,999 per year; $40,000 to $59,999 per year; and >$60,000 per year. Income assistance, social and band, was grouped with <$20,000 per year.

4.7.2 Obstetrical/biological

Gestation. Gestation (weeks) was recorded by staff or calculated from the expected due date and the date of the interview. Gestation was treated as a continuous variable in the analysis.

Gravida or total number of pregnancies. The actual number of pregnancies was used as both a continuous and categorical variable in the analysis. Categories included one pregnancy, two pregnancies, three pregnancies, four pregnancies, and five or more pregnancies.

Parity or total number of live births. The actual number of viable and live-born children the mother has delivered was assessed through two categories: primiparous as defined as a woman who has given birth to one live infant, and multiparous as defined as a woman who has delivered more than one live infant.

4.7.3 Psychological

Stressors. From a list of specific sources of stress, women were asked to indicate with a check mark as many of the stressors that they were presently experiencing. Potential responses included: Pregnancy, Partner, Money, Children, Family, Where I live, Health of my baby, Birth of my baby, Own health, Work, School, and Other stressors. The 12 items were summed into one composite variable by assigning 1 to each positive response to a stressor and 0 to the negative responses. This summed variable was also categorized into: lowest (0-1 stressors), middle (2-3) stressors, and highest (4+ stressors) numbers of stressors. This was determined by attempting to create equal numbers of stressors for each of the three categories.

Worry. The Cambridge Worry Scale (CWS) is a tool developed to determine the major worries of women during pregnancy (Stathem, Green, & Snowdon, 1993). The validity and reliability of the tool was confirmed in a longitudinal study of 1207 pregnant women (Green, Kafetsios, Statham, & Snodon, 2003), and a Swedish version of the CWS was validated in a sample of 200 pregnant women in Stockholm (Georgsson, Ohman, Grunewald, & Waldenstrom, 2003). Women indicated their response to 16 items on a 5-point Likert scale with the anchors described as 1, not a worry, and 5, major worry. The 16 items included: Housing, Money, Law, Partner, Family, Own health, Health of others,

Employment, Baby, Going to the hospital, Internal examinations, Birth, Coping with baby, Giving up work, Partner present at birth, and Miscarriage. Women also had the opportunity to add other concerns in an open-ended question following the scale coded as Other. The 17 items were summed into one composite variable and treated as both continuous and categorical in this analysis. In addition, three potential items of worry were treated as a separate item: Own health, Baby, and Miscarriage. Each of these items were summed and divided into three equal categories: low (scores of 0 and first third), moderate (second third) and high (final third) worry in this analysis. The measure is presented in Appendix D.

Support. Participants were asked whether they have someone from whom they received emotional support and, if so, were asked to indicate with a check mark those sources of support (partner, mother, friend, relative, or other) of whom they feel they can count on no matter what. The variable was divided into four groups: no support (0 support), low support (1 support), medium support (2 supports), and high support (3 or more supports). The groups no support and low support were combined for regression analysis.

Moods up and down. Mood fluctuation is seen in people who are depressed (Bowen, Clark, & Baetz, 2004). Women were asked two questions including, whether or not their moods went up or down, and if they had mood swings that occurred for no reason. These questions were combined into a continuous composite variable and categorized into low moods up and down, moderate moods up and down, and high moods up and down.

History of depression. This variable consisted of self-reported questions about the woman's history of depression, including antenatal and/or postnatal depression, and was treated as a dichotomous item.

Depression. The Edinburgh Postnatal Depression Scale (EPDS) (Cox, Holden, & Sagovsky, 1987) includes 10 items on a Likert-like scale ranging from 0 to 3, for a maximum score of 30. Originally developed to assess postpartum symptoms, the EPDS has also been validated in prenatal samples (Adouard, Glangeaud-Freudenthal, & Golse, 2005). Using a cutoff score of 10, the EPDS has a sensitivity of 90% and specificity of 78-88% for the identification of both minor and major depression (Gaynes et al., 2005; Adouard et al., 2005). Previous research with similar samples of pregnant women has found that when using a cutoff of 10, 74% of women met diagnostic criteria for depression using the Mood

Disorders Module of the Structured Clinical Interview for DSM-IV (SCID) (Flynn, O'Mahen, Massey, & Marcus, 2006).

An EPDS score of 10 or more (≥10) represents minor depression (Horowitz et al., 2001) and a cut-off score of 13 or more (≥13) has been validated and recommended for detecting major depression in pregnancy (Murray & Cox, 1990) and is used most often to report the prevalence of major depression in antenatal women in the literature (Da-Silva, Moraes-Santos, Carvalho, Martins, & Teixeira, 1998). Thus, a score of ≥13 was used to determine and report the prevalence of major depression in this study. In this analysis, the EPDS was used as a continuous variable. It was also dichotomized into two separate derived variables: minor depression as defined by EPDS score greater or equal to 10, and major depression as defined by EPDS scores greater or equal to 13. The measure is presented in Appendix E.

Anxiety. The EPDS may not measure a single expression of mood or depression. A depression subscale (items 1, 2, and 8) and an anxiety subscale (items 3, 4, and 5) have been identified in the EPDS in women in pregnant and postpartum women (Brouwers, van Baar, & Pop, 2001). The validity of the EPDS as a tool to identify anxiety was affirmed by Stuart, O'Hara and Blehar (1998) who found a strong correlation between the State Anxiety Scale of the State-Trait Anxiety Inventory and the EPDS (r=0.73 at 14 weeks postpartum, r=0.82 at 30 weeks postpartum, n=107). Brouwers et al. (2001) also tested the validity of the EPDS for measuring anxiety and depression (2001), and they confirmed the presence and validity of the subscales but found the overall EPDS most accurately measured both depression and anxiety.

Items 3, 4 and 5 of the EPDS were summed to form one composite variable. A score of 4 or greater represents possible anxiety. The variable was treated as both continuous and categorical in this analysis.

4.7.4 Behavioural

Unintended pregnancy. Women were asked if they had planned their pregnancy. This question had a yes or no choice for response but also included a response of 'sort of' which was coded as 'yes' for the analysis.

Smoking. Participants were asked if they smoked, if they had ever smoked, the amount smoked per day in the last month, or if they had quit before or since becoming pregnant. Smoking was recoded into three categories: never smoked, current smoking, or quit smoking (before or during pregnancy) for analysis.

Alcohol use. Alcohol use was determined using questions that encompass the risk criteria for Fetal Alcohol Spectrum Disorder (FASD): e.g., drinking 5 or more drinks at one sitting (binge drinking), and drinking 1-2 drinks every day in the last month, or if they had quit using alcohol during or before pregnancy (Public Health Agency of Canada, 2004). Women could mark a check for more than one category (e.g., occasional drink and binge drink). The variable was recoded into three categories of alcohol use: never used, current use, or quit use (before or during pregnancy).

Substance abuse. Participants were asked how often they had used illicit drugs such as cocaine, crystal methamphetamine, and marijuana in the past month or if they had quit during or before pregnancy. The variable was recoded into three categories: never used, current use, or quit use (before or during pregnancy).

4.7.5 Potential confounding factors

A confounding factor is an independent factor that distorts the association between another independent factor and the outcome of interest, as it is related to both (Agresti, 2002).

Antiemetic medication. Women were assessed for use of medications for nausea and vomiting in pregnancy. Antiemetic mediation was treated as a dichotomous variable.

Psychotropic medication. Women were assessed for anxiety, depression, and antipsychotic medications. Psychotropic medication use was treated as a dichotomous variable.

4.8 Data Preparation

Variables of interest were transferred from a Statistical package for Social Sciences (SPSS ver. 18.0 for Macintosh) system file. Data were cleaned and edited using frequency runs to check for errant and unusual values as well as logical inconsistencies. These inconsistencies were then checked against the original questionnaire and resolved with the assistance of the co-principal investigator and research assistant of the original study.

4.9 Analytical Procedures

The method of analysis is reported by each research question to address the hypothesis outlined in section 1.2.

4.9.1 Question 1. What is the prevalence of nausea and vomiting at two gestational time points in this sample of pregnant women and is this prevalence different from rates reported in the literature?

Analysis. Following data preparation, descriptive statistics including the mean, mode, median, interquartile range, standard deviation, and frequencies were assessed on each continuous variable and frequencies and percentages were assessed for categorical factors at both time periods (Time 1 and Time 2).

The distribution of the dependent variable was assessed and dichotomized to determine the prevalence of nausea and vomiting (no symptoms versus having NVP) at both time periods. In order to determine the prevalence for severe and moderate nausea and vomiting, participants with a NVPI score between 1 and 15 were divided into three equal groups. None and mild NVP was then defined as a NVPI score of zero plus the first third. Moderate NVP was defined by the second tertile (excluding scores of zero), and severe NVP was defined as the third tertile (excluding scores of zero).

In addition, to the prevalence for severe and moderate nausea and vomiting at both time periods, prevalence was also determined in pregnant women who experienced either of these symptoms at Time 1 and continued to have moderate or severe NVP at Time 2. Data between participants were compared for differences by using Crosstabs. Wilcoxon-Sum Ranks test were performed to assess the degree of difference across both time periods between each of the scale indices: nausea, retching, and vomiting; as well as the total NVPI score.

Differences in psychological determinants between Time 1 and Time 2 were also examined. Women who completed the NVPI at both time periods (n=511) were matched for analysis. Paired observations of continuous variables were analyzed with the Wilcoxon signed ranks test. One continuous psychological variable, worry, was excluded from analysis as a result of its sum of negative ranks equaling the sum of its positive ranks.

4.9.2 Question 2. What sociodemographic, biological/obstetrical, psychological, and behavioral determinants are associated with moderate and severe nausea and vomiting at Time 1 in this group of pregnant women?

Analysis. Descriptive analyses were performed on each determinant at Time 1 and Time 2. Bivariate analyses using binomial statistics were then performed with the categorical dependent variable (Agresti, 2002). A series of logistic regressions each containing a single independent variable was conducted to obtain Odds Ratios (OR), 95% Confidence Intervals (CI), and p-values for each determinant.

Determinants which had bivariate associations at p-value significance ≤ 0.25 were then entered into a logistic regression procedure to determine the final model for moderate and severe NVP in each of the determinants (sociodemographic, biological/obstetrical, psychological, and behavioural). However, following this criterion for the final model would have resulted in a large number of variables, greater than the recommended 10-15 (Hosmer & Lemeshow, 2000). Therefore, only those variables with a bivariate association significant at ≤ 0.10 were entered stepwise into the final logistic regression. Factors that were considered to be potentially confounding, including antiemetic and psychotropic medications, were also entered in the final model.

Variables in the final model for moderate and severe NVP at Time 1 were tested for interaction, linearity of the logit, independence of errors, and multicollinearity. For variables perceived to measure the same concept, a 10% difference was used to determine the presence of confounding (Menard, 1995; Myers, 1990). All cases were included in the initial model and agreement between observed and fitted values was determined with the goodness-of-fit test (Hosmer, Hosmer, Cessie, & Lemeshow, 1997). Next, outliers and influential cases were identified and solutions without these cases were interpreted where these cases were found to be unduly influencing the fit of the data. A 0.05 criterion of statistical significance was used in the final model.

In the final model, no interactions were present and the assumptions of logistic regression were satisfied. Multicollinearity among psychosocial correlates was not a concern. The goodness-of-fit test demonstrated that the baseline model was a good fit of the data. A combined total of 13 outlying and influential cases were identified and removed

from the data set before the analysis was repeated. When these cases were excluded there was little change in the overall fit of the data and only a 2.1% increase in accuracy compared to the baseline model was observed. Therefore the final model used for interpretation included all outlying and influential cases.

4.9.3 Question 3. What sociodemographic, biological/obstetrical, psychological, and behavioral determinants are associated with moderate and severe nausea and vomiting at Time 2 in this group of pregnant women?

Analysis. Similar analyses were done as in Question 2 for pregnant women at Time 2. The NVPI total score at Time 1, collapsed into moderate and severe categories, was also included in the Time 2 model to explore the possible intercorrelation of more severe NVP symptoms at Time 1 and Time 2.

In the final model, no interactions were present and the assumptions of logistic regression were satisfied. Multicollinearity among psychosocial correlates was not a concern. The goodness-of-fit test demonstrated that the model was a good fit of the data. A combined total of 17 outlying and influential cases were identified and removed from the dataset before the analysis was repeated. When these cases were excluded there was little change in the overall fit of the data and only a 4.9% increase in accuracy compared to the baseline model was observed. Therefore the final model used for interpretation included all outlying and influential cases.

4.9.4 Question 4. What is the nature of the relationship between nausea and vomiting and psychological determinants, as well as antiemetic and psychotropic medications, as evidenced by two time points in pregnancy?

Analysis. Differences in NVP severity and symptoms of major depression were compared among three different groups of woman. First, comparisons between psychotropic medication use and NVP severity were made with chi-square analysis for both time periods (n=551, 575). Similarly, comparisons between antiemetic medication use and symptoms of major depression (EPDS≥13) were also conducted. Finally, chi-square was also used to analyze women who completed the NVPI at both time periods (n=511) and who had symptoms of major depression at Time 1 but no longer had these symptoms at Time 2.

4.10 Limitations

The main limitations in this study focus on the measures used and secondary study design.

4.10.1 Study tools. The Nausea and Vomiting in Pregnancy Instrument has been validated in the United Kingdom, a region where English is also the primary language. However, the tool remains to be validated in different settings and cultures. The NVPI was not validated in this particular population, in which 15.5% of the women were of Aboriginal ancestry.

4.10.2 Study design. Three limitations are noted regarding study design. First, the question used to measure mood fluctuation was asked during Time 1 but not asked during the second time point, thus we were only able to examine mood swings and nausea and vomiting in pregnant women for the first time point in this study. Second, the original survey did not record symptom onset and we therefore do not know when nausea and vomiting symptoms first occurred in this sample. Third, the lack of an additional time point either in pregnancy or postpartum limits the ability to establish causality or to explore further the nature of the relationship between health determinants and nausea and vomiting in this sample of pregnant women.

Chapter 5

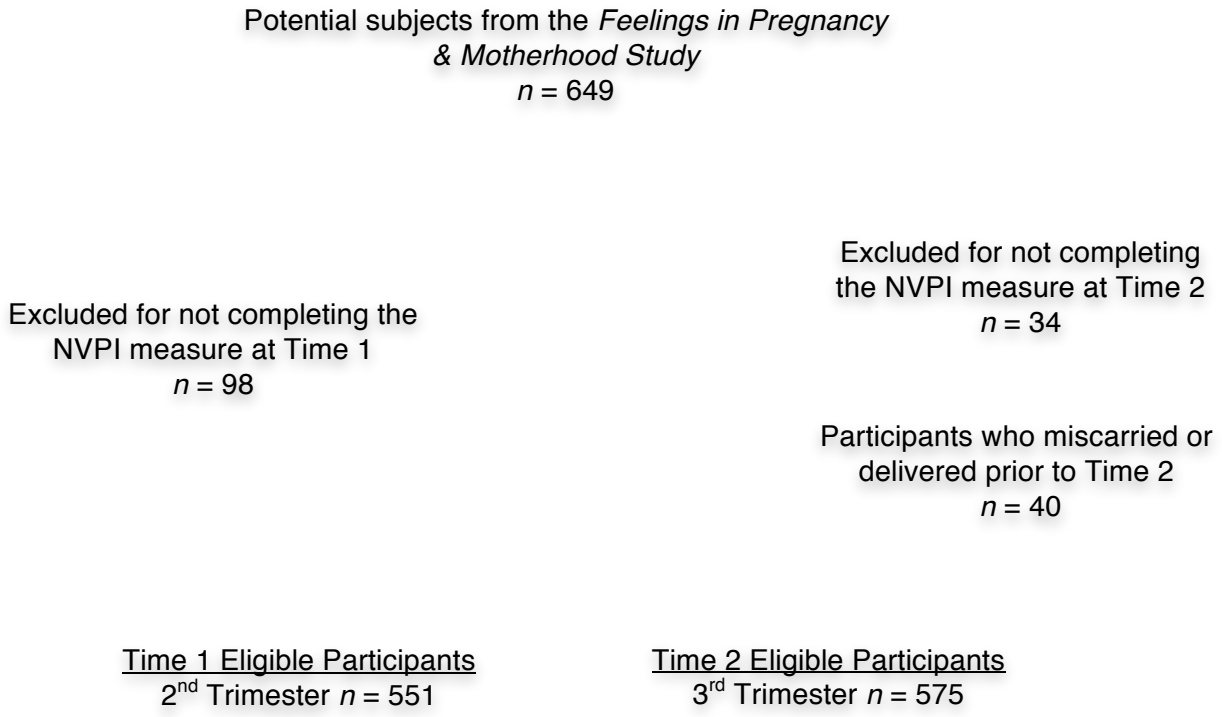
Results

This chapter presents a description of the study participants and the sociodemographic, biological/obstetrical, psychosocial, and behavioral determinants associated with nausea and vomiting in pregnancy. The chapter begins with a profile participant characteristics, followed by addressing the questions posed in the thesis; it presents the prevalence, comparative, and analytic findings for the data. Unless otherwise indicated, a significance level of $p<0.05$ was used to determine statistical significance.

5.1 Participant Characteristics

As Figure 5.1 depicts, approximately 649 women from the original study would have been potential participants during both time periods.

Figure 5.1. Study Sample



Five hundred and fifty one pregnant women were available for data analysis at Time 1 and 575 women were available for analysis at Time 2. In total, these data represent 84.9% and 88.6% of the original 649 participants during the period of the study. The sociodemographic, obstetrical/biological, psychological, and behavioural determinants are provided in detail in Tables 5.1 to 5.4.

Table 5.1 describes the sociodemographic characteristics of study participants. The majority of women in this group were between the ages of 25 and 34 (mean age 29.3 ± 4.65), of Caucasian ancestry (84.5%), partnered (90.3%), and completed post secondary education (68.7%). 81% were working and 47.6% were living on an income greater than $60,000 per year.

Table 5.1. Sociodemographic Characteristics

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n	%	n	%
Age (years)				
<20	18	3.3	14	2.5
20-24	72	13.1	69	12.0
25-29	210	38.1	223	38.9
30-34	177	32.1	194	33.6
35-39	68	12.3	68	11.8
>40	6	1.1	7	1.3
Marital Status				
Single	44	8.0	49	8.5
Common law	89	16.2	82	14.3
Married	411	74.6	437	76.0
Separated/divorced/widowed	7	1.3	7	1.2
Ethnicity				
Aboriginal//Métis/other	82	14.9	89	15.5
Caucasian	469	85.1	486	84.5
Education				
<Grade 8	1	0.2	1	0.2
Grade 9-12	24	4.4	21	3.7
Completed grade 12	70	12.7	65	11.3
Some post secondary	85	15.4	93	16.2
Completed post secondary	371	67.3	395	68.7
Employment				
Not working	111	20.1	109	19.0
Working	440	79.9	466	81.0
Income (per year)				
<$20,000	63	11.6	67	11.8
$20,000-$39,999	106	19.5	102	18.0
$40,000-$59,999	120	22.1	127	22.4
>$60,000	254	46.7	270	47.6
Other	1	0.2	1	0.2

Table 5.2 describes the obstetrical and biological determinants of the women. The average gestation of the pregnancy at the time women completed the questionnaires was 17.6 weeks (± 5.1 weeks), with a range of 5 to 30 weeks at Time 1; and 30.7 weeks (± 2.6 weeks), with a range of 23 to 39 weeks at Time 2. Gravidity ranged from 1 to 8 pregnancies (median 2.0 ± 2 pregnancies), approximately 38% of women were pregnant for the first time and 52.3% had yet to give birth to a live/viable infant. At Time 1, 25% of women reported moderate NVP and almost 24% reported severe NVP.

Table 5.2. Obstetrical/Biological Characteristics

	Time 1 (n=551)		Time 2 (n=575)	
	n	%	n	%
Gestation (weeks) (Mean ± SD)	17.6 ± 5.10		30.7 ± 2.6	
Total number of pregnancies				
1	211	38.3	218	37.9
2	182	33.0	197	34.3
3	94	17.1	97	16.9
4	37	6.7	36	6.3
5+	27	4.9	27	4.8
Live born children*				
Nulliparous	291	53.0	301	52.5
Primiparous	176	32.1	186	32.5
Multiparous	82	14.9	86	15

* Total does not equal to 575 due to missing data

Table 5.3 describes the psychological health determinants. The cumulative stress score was an average of 2.48 ± 1.88 stressors at Time 1, and 2.23 ± 1.74 at Time 2. As Table 5.3 shows, most of the women experienced medium (2-3 stressors) to high levels of stressors (4+ stressors). Approximately 34% report the health of the baby as a stressor at Time 1. Over 35% report the birth of the baby as a stressor at Time 2. The cumulative worry score was an average of 28.76 ± 8.01 points at Time 1, and 28.77 ± 8.10 points at Time 2. Most of the women experienced medium (20-29 score) to high levels of worry (30+ score). Similarly to stressors, women report the health of the baby as middle to major worry approximately 73% at both time periods. Of the 90.3% of women who said they were married or in a common-law relationship, about 84% at Time 1 and 85% at Time 2 reported

their partner as a source of support. Over 98% of the women stated that overall they generally felt supported. The cumulative support score was an average of 2.73 ± 1.17 supports at Time 1, and 2.60 ± 1.17 supports at Time 2.

Thirty-six percent of the women at Time 1 and 35% of the women at Time 2 had a history of depression. Approximately half of the women at Time 1 report moods going up and down; however, the question was not available for response on the Time 2 questionnaire. The cumulative EPDS anxiety subscale score was 3.37 ± 2.06 at Time 1, and 2.96 ± 1.93 at Time 2. Approximately 47% and 39% of women reported an anxiety subscale greater than or equal to 4 for both time periods, indicating possible anxiety. The cumulative EPDS score was 6.82 ± 4.57 at Time 1, and 6.24 ± 4.33 at Time 2. The prevalence of minor antenatal depressive symptoms (EPDS ≥ 10) in this sample, in the last seven days, was 12.7% and 11.8% at both time periods, respectively Major depressive symptoms (EPDS ≥ 13) were reported by 11.4 % and 7.8% of women at Times 1 and 2.

Table 5.3. Psychological Characteristics

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n*	%	n*	%
Stressor score				
Lowest (0-1 stressors)	181	32.8	231	40.2
Middle (2-3 stressors)	238	43.2	234	40.7
Highest (4+ stressors)	132	34.0	110	19.1
Specific stressors				
No stressors right now	51	9.3	67	11.7
Pregnancy	115	20.9	136	23.7
Partner	98	17.9	65	11.3
Money	105	19.1	128	22.3
Children	105	19.1	85	14.8
Family	98	17.9	73	12.7
Where I live	72	13.1	45	7.8
Health of my baby	188	34.2	143	24.9
Birth of my baby	137	25.0	203	35.4
Own health	95	17.3	94	16.4
Work	225	41.0	145	25.3
School	38	6.9	31	5.4
Other	129	23.5	134	23.3
Worry score				
Lowest (0-19 score)	42	7.6	40	7.8
Middle (20-29 score)	306	55.5	285	55.8
Highest (30+ score)	203	36.8	186	36.4
Own health worry score (0-5)				
Lowest (0-1 worries)	245	44.5	269	46.8
Middle (2-3 worries)	261	47.4	269	46.8
Highest (4+ worries)	45	8.2	37	6.4
Health of my baby worry score (0-5)				
Lowest (0-1 worries)	148	26.9	157	27.4
Middle (2-3 worries)	308	56.0	326	56.8
Highest (4+ worries)	94	17.1	91	15.9
Miscarriage worry score (0-5)				
Lowest (0-1 worries)	219	39.7	260	45.2
Middle (2-3 worries)	250	45.3	244	42.4
Highest (4+ worries)	82	14.9	71	12.4
Support score				
No support	9	1.6	6	1.0
Low (1 support)	87	15.8	111	19.3
Medium (2 supports)	143	26.0	171	29.7
High (3+ supports)	312	56.5	287	48.0

Table 5.3. Psychological Characteristics (continued)

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n*	%	n*	%
Specific sources of support				
Support in general	542	98.4	565	98.3
Partner	461	83.8	486	84.7
Mother	345	63.0	351	61.4
Friend	356	64.7	377	65.7
Female relative	249	45.3	259	45.1
Other (father, mother-in-law, etc.)	89	16.2	98	17.1
Do your moods go up and down				
Yes	275	49.8	**	**
History of Depression				
Yes	196	35.6	202	35.1
Anxiety(EPDS subscale ≥ 4)				
Yes	258	46.8	222	38.6
Mild Depression (EPDS ≥ 10)				
Yes	70	12.7	68	11.8
Major Depression (EPDS≥13)				
Yes	63	11.4	45	7.8

* Total may not equal 551 or 575 due to missing values

** Question not included on questionnaire at Time 2

Women who completed the NVPI at both time periods (n=511) were examined for differences in psychological determinants across both time periods. The results of the Wilcoxon signed ranks test indicated that the 511 pregnant women who completed the NVPI at both time periods significantly reduced their median EPDS levels (Md=6.0 to 5.0) (Table 5.4) as their pregnancy progressed. A significant reduction was also noted for stressors (p=0.004) and anxiety (p=0.001) at Time 2.

Table 5.4. Wilcoxon Signed Ranks Analysis for NVPI and Psychological Determinants (n=511)

	Mean	Median	SD	*p*-value
Stressors score total				0.004
Time 1 (17.6 ± 5.10 weeks)	2.55	2.0	1.93	
Time 2 (30.7 ± 2.6 weeks)	2.30	2.0	1.79	
Support score total				0.051
Time 1 (17.6 ± 5.10 weeks)	2.72	3.0	1.17	
Time 2 (30.7 ± 2.6 weeks)	2.64	3.0	1.16	
EPDS anxiety subscale score total				<0.001
Time 1 (17.6 ± 5.10 weeks)	3.37	3.0	2.06	
Time 2 (30.7 ± 2.6 weeks)	2.97	3.0	1.92	
EPDS score total				0.002
Time 1 (17.6 ± 5.10 weeks)	6.82	6.0	4.57	
Time 2 (30.7 ± 2.6 weeks)	6.23	5.0	4.27	

Table 5.5 describes the behavioural determinants of health. Approximately 79% of women intended to become pregnant. Sixty-seven percent of the women reported to have never smoked and about 21% reported that they had quit either before or during the pregnancy. The majority of the women reported that they had never used substances (81.3%), with 2.7% reporting to be current users and 16% reported that they had quit either before or during the pregnancy. The number of women who stated that they presently use alcohol was 6.5%. However, in the original study women were able to mark more than one category as a response in order to try to distinguish the woman who might occasionally drink but also have binge episodes that would potentially contribute to problems for the fetus (e.g., Fetal Alcohol disorder). Therefore, some women who reported that they were drinking a certain amount but also that they had quit were categorized as having quit using alcohol in the original study.

Table 5.5. Behavioural Characteristics

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n	%	n	%
Pregnancy Planning				
No	125	22.7	108	21.2
Yes	426	77.3	453	78.8
Smoking				
Never smoked	369	67.0	465	81
Quit before or during pregnancy	115	20.9	50	8.5
Current smoker	67	12.2	60	10.5
Alcohol Use				
Never drank alcohol	172	31.2	446	77.7
Quit before or during pregnancy	343	62.3	93	16.0
Current drinker	36	6.5	36	6.3
Substance Use				
Never took drugs	447	81.3	470	81.9
Quit before or during pregnancy	88	16.0	89	15.7
Current illicit drug use	15	2.7	15	2.4

Table 5.6 describes the frequency of antiemetic and psychotropic medications used by women in this sample. Approximately 14% of women at Time 1 and 5% of women at Time 2 were taking medication to relieve nausea. Few women were using medications to relieve anxiety or depression symptoms, with about 4% and 3% reported for each time period respectively.

Table 5.6. Antiemetic and Psychotropic Medications

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n	%	n	%
Antiemetic Medication	76	13.8	29	4.9
Psychotropic Medication	23	4.1	19	3.3

5.2 Prevalence of Nausea and Vomiting in Pregnancy

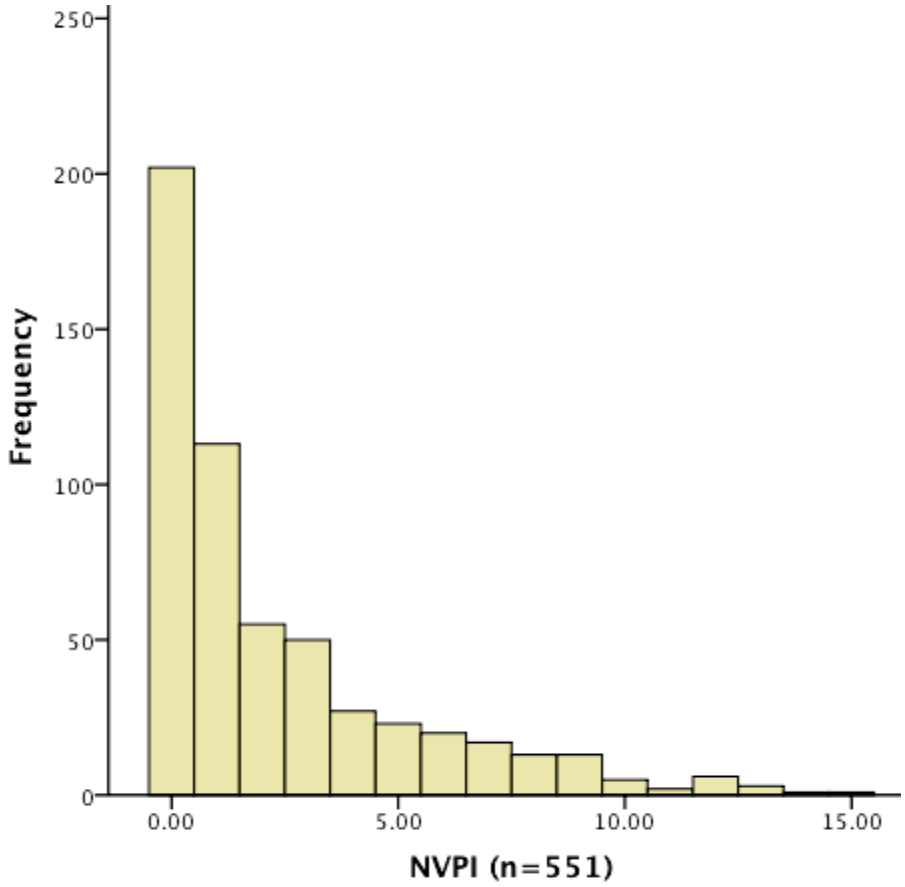
Table 5.7 describes the prevalence of nausea and vomiting at both time periods. Over 63% of pregnant women experienced nausea and vomiting at Time 1. More than 45% of pregnant women experienced nausea and vomiting at Time 2. Of those women who experienced NVP at Time 1 (n=320), 181 pregnant women (56.6%) continued to have nausea and vomiting in later pregnancy.

Table 5.7 Prevalence of NVP

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n	%	n	%
No NVP (score of 0)	202	36.7	314	54.6
NVP Symptoms (score > 0)	349	63.3	261	45.4

Figure 5.2 depicts a histogram of the NVPI score for Time 1 and reports the mean, median, and mode scores. Similarly, Figure 5.3 illustrates the NVPI score histogram for Time 2.

Figure 5.2. NVPI Score at Time 1

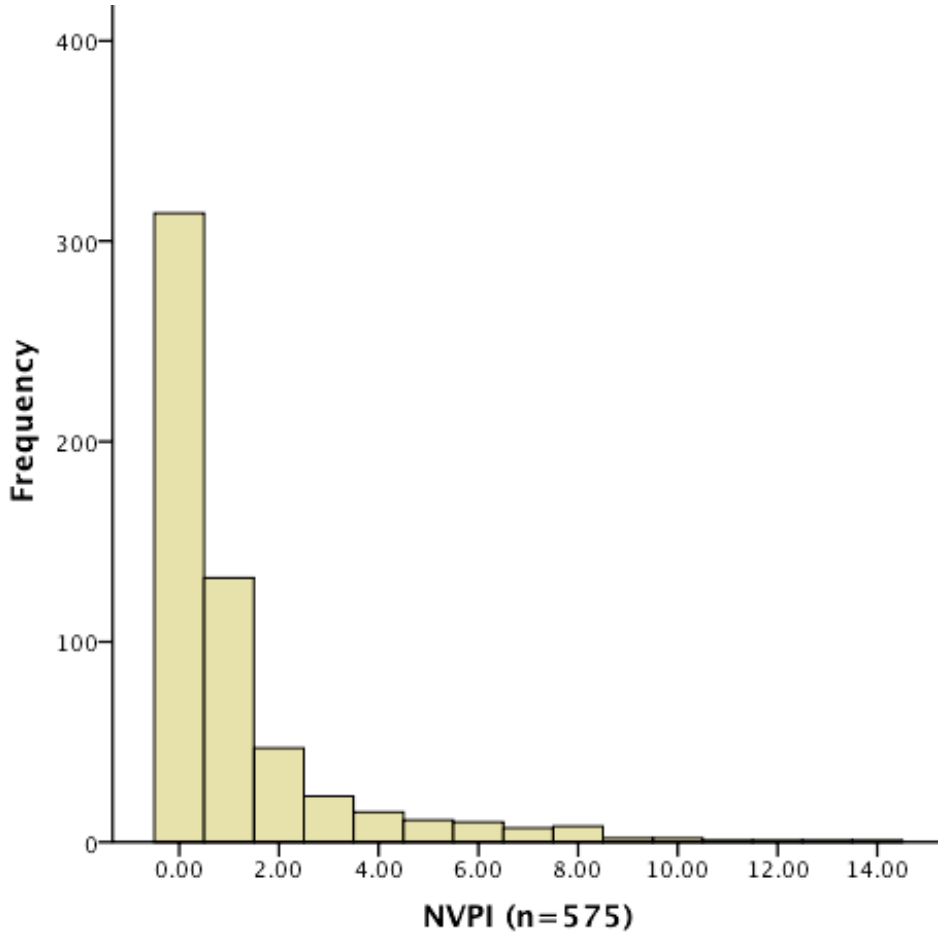


Mean= 2.3 ± 2.97

Median= 1.0

Mode= 0.0

Figure 5.3. NVPI Score at Time 2



Mean= 1.17 ± 2.07

Median= 0.0

Mode= 0.0

The distribution of the NVPI score at both time periods was severely negatively skewed. Therefore, to better understand the determinants of women with more severe NVP symptoms, scores of 0 were separated from the NVPI score while remaining scores were divided into three equal groups. Scores of 0 were then added to group 1 to form the category 'none/mild NVP'. Moderate NVP was then defined as group two, and severe NVP defined as group three. From Table 5.8 we can see that the prevalence of moderate nausea and vomiting symptoms, in the last seven days, in this sample of 551pregnant women at Time 1 was 24%, and 8.2% in the sample of 575 pregnant women at Time 2. Severe nausea and vomiting were reported by 18.9% of women at Time 1, and 14.3% of women at

Time 2. Of those women with moderate and severe NVP at Time 1, 13.8% go on to have moderate NVP and 21.7% go on to have severe NVP symptoms in later pregnancy.

Table 5.8. Frequency of Reported None/Mild, Moderate and Severe NVP

	Time 1 (n=551) (17.6 ± 5.10 weeks)		Time 2 (n=575) (30.7 ± 2.6 weeks)	
	n	%	n	%
None/Mild NVP (Tertile 1 and 0 scores)	315	57.2	446	77.6
Moderate NVP (Tertile 2)	132	24.0	47	8.2
Severe NVP (Tertile 3)	104	18.9	82	14.3

Table 5.9 describes the nausea, retching and vomiting data, collected in the preceding seven days, for Time 1 and Time 2. The range for scale indices during each time period ranged from 0 to 5 and the modal response for each index was 0 for both periods. The highest index was nausea, with a mean score at Time 1 of 1.28 ± 1.47. For Time 1, it is notable that approximately 78% of women did not vomit and about 67% had no retching; yet 30.6% experienced nausea 3 to 6 days during the week or more. At Time 2, almost 89% of women did not vomit and 80% had no retching, but 12.9% of women experienced nausea 3 to 6 days during the week or more. When comparing the same women at Time 1 to Time 2 (n=511), a significant reduction was noted in the severity of reported nausea (Z= -9.54, p< 0.001), retching (Z= -5.82, p< 0.001), and vomiting (Z = -4.99, p< 0.001), as well as the total NVPI score (Z= -9.01, p< 0.001), with a significant reduction in median NVPI levels (Md=1.0 to 0.0) reported.

Table 5.9. Women's Responses to the NVPI at Time 1 (n=551) and Time 2 (n=575)

	Not at all	Occasionally	3-6 days /wk	Daily	> Once /day	All the time	Mean ± SD
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	
Time 1							
Nausea	219 (39.7)	164 (29.8)	51(9.3)	50(9.1)	45(8.2)	22(4.0)	1.28 ± 1.47
Retching	368 (66.8)	100 (18.1)	26(4.7)	29(5.3)	25(4.5)	3(0.5)	0.64 ± 1.14
Vomiting	431 (78.2)	67 (12.2)	32(5.8)	9(1.6)	10(1.8)	2(0.4)	0.38 ± 0.86
Time 2							
Nausea	342 (59.5)	159 (27.7)	36(6.3)	20(3.5)	12(2.1)	6(1.0)	0.64 ± 1.01
Retching	460 (80.0)	67 (11.7)	24(4.2)	14(2.4)	9(1.6)	1(0.2)	0.34 ± 0.82
Vomiting	511 (88.9)	37 (6.4)	20(3.5)	2(0.3)	4(0.7)	1(0.2)	0.18 ± 0.59

Table 5.10 describes the rate of antiemetic medication used by pregnant women among severity groups for each time period. Severe NVP was significantly associated with the decision to use antiemetic medication both at Time 1 and in later pregnancy.

Table 5.10. Comparison of NVP Severity and Antiemetic Medication Use

		n	%	χ^2	*p*-value
	None/Mild NVP				
Time 1	(Tertile 1 and 0 scores)	12	15.8		
	Moderate NVP				
(17.6 ± 5.10 weeks)	(Tertile 2)	25	32.9		
	Severe NVP				
(n=76)	(Tertile 3)	39	51.3	78.50	< 0.001
	None/Mild NVP				
Time 2	(Tertile 1 and 0 scores)	6	20.7		
	Moderate NVP				
(30.7 ± 2.6 weeks)	(Tertile 2)	1	3.4		
	Severe NVP				
(n=29)	(Tertile 3)	22	75.9	95.73	< 0.001

5.3 Determinants of Moderate and Severe NVP at Time 1

The sociodemographic determinants of age, ethnicity, employment, and income ($p<0.25$) were entered into the logistic regression model. The final model, Table 5.11, shows that pregnant women who are not working were twice as likely to have moderate NVP symptoms, and about 1.8 times more likely to have severe NVP compared to none or mild NVP.

Table 5.11. Final Model of Sociodemographic Determinants of Moderate and Severe NVP at Time 1 (17.6 ± 5.10 weeks) (n=551)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Employment Working			
No	2.01	1.23, 3.30	0.006
Severe NVP (Tertile 3)			
Employment Working			
No	1.79	1.03, 3.09	<0.001

All obstetrical/biological variables $p \leq 0.25$ were entered into the model using Backward Stepwise Logistic Regression. This included: gestation, number of pregnancies, and number of live-born children. In the final model for the biological/obstetrical determinants (Table 5.12), time in weeks was protective in this sample as women were less likely to have both moderate and severe NVP compared to none or mild symptoms for every additional week in their pregnancy.

Table 5.12. Final Model of Obstetrical/Biological Determinants of Moderate and Severe NVP at Time 1 (17.6 ± 5.10 weeks) (n=551)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Gestation	0.89	0.85, 0.93	<0.001
Severe NVP (Tertile 3)			
Gestation	0.85	0.85, 0.93	<0.001

The variables that measure the psychological determinants $p \leq 0.25$ were entered into the model for logistic regression using backward stepwise regression. Stressors, worry, support, moods up and down, history of depression, anxiety, and depression were entered in the model. There were no interactions between the terms and no confounding between variables in the final model. As the final model for the psychological determinants shows, Table 5.13, women who had high levels of worry about their health were almost 1.9 times as likely to have moderate NVP. Both groups of women with medium and high worry about their health were over 2 times and 3 times more likely to have severe NVP. Also, women with symptoms of major depression were 2.18 times as likely to have severe NVP symptoms compared to none and mild symptoms.

Table 5.13. Final Model of Psychological Determinants of Moderate and Severe NVP at Time 1 (17.6 ± 5.10 weeks) (n=551)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Worry own health			
Low	1.00		
Medium	1.87	0.77, 2.25	0.401
High	1.28	1.17, 2.98	0.009
Severe NVP (Tertile 3)			
Worry own health			
Low	1.00		
Medium	2.04	1.11, 3.70	0.021
High	3.30	1.79, 6.10	<0.001
Major Depression (EPDS≥13)			
Yes	2.18	1.13, 4.20	0.020

To derive a model of behavioural determinants, the variables smoking and substance use had p-values less than or equal to 0.25 and as such were entered into the analysis. Employing a 0.05 criterion of statistical significance, no behavioural determinants were significant in the final model.

5.4. Final Model for Determinants of Moderate and Severe NVP at Time 1

All determinants that had a reported *p*-value ≤ 0.10 at Time 1 were included in the final model to predict the probability that a pregnant women would have moderate or severe NVP symptoms compared to mild or less than mild NVP, adjusting for confounding factors. The model as a whole explained between 22.2% (Cox and Snell R squared) and 26.2% (Nagelkerke R squared) of variance, and correctly classified 62.0% of cases. The Hosmer-Lemeshow (H-L) test yielded a χ^2 (364) of 493.85 and was not significant ($p > 0.05$), suggesting that the model was fit to the data well.

The final logistic regression model at Time 1, as depicted in Table 5.14, shows pregnant women taking antiemetic medication were more than 6.2 times as likely to report moderate symptoms and 12.5 times more likely to report severe NVP. Women who were not working reported both moderate and severe symptoms almost twice as often. Women who reported high levels of worry about their health were 1.5 times as likely to have moderate NVP and over twice as likely to report severe symptoms. Pregnant women with symptoms of major depression were 2.4 times more likely to report moderate NVP and 2.5 times more likely to report severe NVP, compared to mild or less than mild symptoms. In this sample, time in weeks was protective as women were less likely to have both moderate and severe NVP for each additional week in pregnancy.

Table 5.14. Final Model for Determinants of Moderate and Severe NVP at Time 1 (17.6 ± 5.10 weeks) (n=551)

None/Mild NVP vs. (Tertile 1 and 0 scores)	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Gestation	0.88	0.84, 0.92	<0.001
Antiemetic Medication			
Yes	6.21	2.90, 13.33	<0.001
Worry own health			
Low	1.00		
High	1.45	1.18, 3.42	0.009
Employment Working			
No	2.14	1.27, 3,62	0.005
Major Depression (EPDS≥13)			
Yes	2.36	1.53, 5.43	0.043
Severe NVP (Tertile 3)			
Gestation	0.84	0.79, 0.90	<0.001
Antiemetic Medication			
Yes	12.50	9.68, 27.78	<0.001
Major Depression (EPDS≥13)			
Yes	2.54	1.76, 5.15	0.009
Worry own health			
Low	1.00		
High	2.17	1.19, 3.95	0.012
Employment Working			
No	2.11	1.11, 4.04	0.023

5.5 Determinants of Moderate and Severe NVP at Time 2

The sociodemographic determinants of age, ethnicity, employment, and income ($p \leq 0.25$) were entered into the logistic regression model. Employing a *p* value of 0.05, no behavioural determinants were significant in the final model.

All obstetrical/biological variables $p \leq 0.25$ were entered into the model using Backward Stepwise Logistic Regression. This included: gestation, number of pregnancies, and number of live-born children as well as moderate and severe NVP symptoms during Time 1 for the purposes of exploring the possible intercorrelation between NVP at Time 1 and Time 2. In the final model for the biological/obstetrical determinants (Table 5.15),

pregnant women who experienced moderate NVP at Time 1 were 3.2 and 5.5 times as likely to report moderate and severe NVP symptoms. Pregnant women who experienced severe NVP at Time 1 were 2.9 and 7.2 times as likely to report moderate and severe NVP symptoms.

Table 5.15. Final Model of Obstetrical/Biological Determinants of Moderate and Severe NVP at Time 2 (30.7 ± 2.6 weeks) (n=575)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Moderate NVP at Time 1			
Yes	3.21	1.56, 6.62	0.002
Severe NVP at Time 1			
Yes	2.92	1.33, 6.41	0.008
Severe NVP (Tertile 3)			
Moderate NVP at Time 1			
Yes	5.49	2.59, 11.63	<0.001
Severe NVP at Time 1			
Yes	7.19	3.47, 14.93	<0.001

The variables that measure the psychological determinants $p \leq 0.25$ were entered into the model for logistic regression using backward stepwise regression. Stressors, worry, support, history of depression and depression were entered in the model. There were no interactions between the terms and no confounding between variables in the final model. As the final model for the psychological determinants shows, Table 5.16, women who had high worry about their health were 2.5 times more likely to have moderate NVP and 3.4 times more likely to have severe NVP, compared to none and mild symptoms. Women with symptoms of major depression were 3.3 times more likely to have severe NVP symptoms. The presence of high support was protective for severe NVP symptoms in this sample.

Table 5.16. Final Model of Psychosocial Determinants of Moderate and Severe NVP at Time 2 (30.7 ± 2.6 weeks) (n=575)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Worry own health			
Low	1.00		
High	2.45	1.22, 4.93	0.011
Severe NVP (Tertile 3)			
Worry own health			
Low	1.00		
High	3.37	1.86, 6.09	<0.001
Support			
Low	1.00		
High	0.31	0.17, 0.56	<0.001
Major Depression (EPDS≥13)			
Yes	3.34	1.34, 8.40	0.010

To derive a model of behavioural determinants, the variables smoking, substance use, and pregnancy planning had p-values ≤ 0.25 and as such were entered into the analysis. Table 5.17 shows the final model from the analysis at Time 2. The behaviour of currently smoking was protective for severe nausea and vomiting symptoms in this sample of pregnant women. No behavioural determinants were significantly associated with moderate NVP.

Table 5.17. Final Model of Behavioural Determinants of Severe NVP at Time 2 (30.7 ± 2.6 weeks) (n=575)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Severe NVP (Tertile 3)			
Smoking			
Yes	0.44	0.23, 0.86	0.016

5.6. Final Model for Determinants of Moderate and Severe NVP at Time 2

All determinants that had a reported *p*-value ≤ 0.10 at Time 2 were included in the final model to predict the probability that a pregnant women would have moderate or severe NVP symptoms compared to mild or less than mild NVP, adjusting for confounding factors. The model as a whole explained between 28.0% (Cox and Snell R squared) and 42.3% (Nagelkerke R squared) of variance, and correctly classified 82.0% of cases. The Hosmer-Lemeshow (H-L) test yielded a χ^2 (242) of 267.57 and was not significant ($p > 0.05$), suggesting that the model was fit to the data well.

The final logistic regression model at Time 2, as depicted in Table 5.18, shows that pregnant women in this sample with severe NVP at Time 1 were over 3 times more likely to report moderate NVP and about 5.5 times more likely to report severe NVP symptoms. Women who reported high levels of worry about their health were 2.3 times more likely to report moderate NVP and 3.4 times more likely to report severe NVP, compared to mild or less than mild symptoms. Taking antiemetic medication was not protective enough in this sample as these women were 26 times more likely to severe NVP compared to mild or less than mild symptoms. Women who reported symptoms of major depression were almost 4.1 times more likely to also report symptoms of severe NVP. Both smoking and high support in pregnancy were protective for severe nausea and vomiting in this sample.

Table 5.18. Final Model for Determinants of Moderate and Severe NVP at Time 2 (30.7 ± 2.6 weeks) (n=575)

None/Mild NVP (Tertile 1 and 0 scores) vs.	Adjusted Odds Ratio	95% Confidence Interval	*p*-value
Moderate NVP (Tertile 2)			
Severe NVP at Time 1			
Yes	3.22	1.31, 7.87	0.011
Worry own health			
Low	1.00		
High	2.26	1.14, 4.59	0.024
Severe NVP (Tertile 3)			
Antiemetic Medication			
Yes	26.32	7.04, 47.62	<0.001
Severe NVP at Time 1			
Yes	5.52	2.54, 12.05	<0.001
Worry own health			
Low	1.00		
High	3.40	2.74, 6.62	<0.001
Support			
Low	1.00		
High	0.32	0.17, 0.62	0.002
Smoking			
Yes	0.34	0.22, 0.92	0.005
Major Depression (EPDS≥13)			
Yes	4.07	1.43, 11.43	0.010

5.7 Nature of the Relationship between NVP and Psychological Determinants

The association between antiemetic medication use and symptoms of major depression (EPDS≥13) is presented in Table 5.19. No statistically significant differences were found between antiemetic medication use and major depression at either time point (*p*=0.105, 0.159). However, of women taking antiemetic medication during pregnancy about 84-85% did not have symptoms of major depression at either time period.

Table 5.19. Comparison of Antiemetic Medication Use and Symptoms of Major Depression

Major Depression (EPDS≥13)	*n*	%	χ^2	*p*-value
Time 1 (17.6 ± 5.10 weeks)				
No	56	83.6		
Yes	11	16.4	2.63	0.105
Time 2 (30.7 ± 2.6 weeks)				
No	17	85.0		
Yes	3	15.0	1.98	0.159

The association between psychotropic medication use and NVP severity is presented in Table 5.20. No statistically significant differences (p=0.13) was found between NVP severity at time 1 and women who were administered medication for anxiety or depression in pregnancy. Psychotropic medications used in pregnancy were significantly associated with severe nausea and vomiting in later pregnancy (p=<0.001).

Table 5.20. Comparison of Psychotropic Medication Use and NVP Severity

		n	%	χ^2	*p*-value
Time 1	None/Mild NVP	11	47.8		
(17.6 ± 5.10 weeks)	Moderate NVP	4	17.4		
(n=23)	Severe NVP	8	34.8	4.02	0.134
Time 2	None/Mild NVP	7	36.8		
(30.7 ± 2.6 weeks)	Moderate NVP	1	5.3		
(n=19)	Severe NVP	11	57.9	30.96	< 0.001

Women who completed the NVPI at both time periods (n=511) were assessed for differences in NVP severity and depression. Fifty-two women (10.2%) had symptoms of major depression at time 1. Of these women, 37 (71.2%) ceased to have major depressive symptoms in later pregnancy. The severity of NVP among these women (n=37) was compared and are presented in Table 5.21. Women with severe NVP were significantly associated with symptoms of major depression at Time 1 (p=0.04). No statistically significant differences in NVP severity (p=0.91) were noted with women who no longer had symptoms of major of depression. However, it is notable that among these women severe

NVP decreased from 45.9% at Time 1 to 16.2% at Time 2, and percentages of none or mild NVP symptoms increased from 43.2% at Time 1 to 75.7% in later pregnancy.

Table 5.21. Comparison of NVP Severity Among Women with Major Depression (EPDS≥13) at Time 1 but not at Time 2 (n=37)

		n	%	χ^2	*p*-value
Time 1	None/Mild NVP	16	43.2		
(17.6 ± 5.10 weeks)	Moderate NVP	4	10.8		
	Severe NVP	17	45.9	6.39	0.041
Time 2	None/Mild NVP	28	75.7		
(30.7 ± 2.6 weeks)	Moderate NVP	3	8.1		
	Severe NVP	6	16.2	0.18	0.912

Chapter 6

Discussion

The discussion of nausea and vomiting in pregnancy and its determinants, as outlined in Chapter 3, provides a detailed response to the findings of the study in relation to the literature. Implications and future directions based on this research are also proposed.

This study examined nausea and vomiting in the same group of pregnant women at two gestational time points, thus it is one of the few studies using an objective measure to explore the condition beyond 20 weeks in pregnancy and during multiple time points (Chou, Kuo, & Wang, 2008; Lindseth & Vari, 2005).

6.1 Prevalence of Nausea and Vomiting in Pregnancy

In this study women were examined with respect to nausea and vomiting in pregnancy at two gestational time points. On average, women at Time 1 were in the second trimester of pregnancy (17.6 ± 5.1 weeks) and women at Time 2 were in the third trimester of pregnancy (30.7 ± 2.6 weeks).

At trimester 2, the women in this study showed levels of NVP similar to the rates (50%-90%) found in other studies of pregnant women in early pregnancy (Broussard & Richter, 1998; Miller, 2002; Woolhouse, 2006). The high prevalence of NVP supports that this is a normal physiologic occurrence in early pregnancy. However, in support of previous studies that showed approximately 10-32% of pregnant women experiencing late NVP (Jewell, 2003; Lindseth & Vari, 2005; Miller, 2002), this study demonstrates an even greater amount of women (45%) experience NVP symptoms beyond 20 weeks gestation.

The sociodemographic characteristics of our study mirror that of an American prospective study of 414 predominantly white, upper-middle-class women (Tierson, Olsen, & Hook, 1986). Of these women, 55% reported vomiting and 89.4% reported nausea or both nausea and vomiting symptoms throughout pregnancy. The results of our study revealed that most women did not vomit in the second or third trimesters of pregnancy, although the feeling of nausea was more consistent. Comparative analysis is difficult as our study examined the condition at two specific one-week intervals, whereas Tierson et al. (1986) considered the occurrence of symptoms throughout pregnancy.

In this sample, the intensity of NVP symptoms in the second trimester were similar to other reports in early pregnancy (Jarnefelt-Samsioe, Samsioe, & Velinder, 1983). Jarnefelt-Samsioe et al. (1983) reviewed 948 pregnancies among 244 women who all had at least three children in Sweden. The authors reported that 91% of women experienced nausea in the first trimester, with moderate symptoms reported in 33% of women and severe symptoms reported in 17% of women. In our study, 63.3% of women had NVP, with reports of moderate and severe symptoms found in 24% and 19% of women, respectively. However, comparative analysis of findings is difficult since Jarnfelt-Samsioe and colleagues used self-report instead of a scale measure for nausea and vomiting.

In our study, levels of nausea and vomiting in the third trimester were significantly lower than reports during the second trimester. In contrast to these findings, Chou et al. (2008) conducted a prospective and longitudinal study of 91 pregnant women using the Index of Nausea, Vomiting, and Retching measure (INVR). They reported the second and third trimesters to be associated with significantly lower levels of nausea and vomiting than in the first trimester, even though mean INVR scores for the second trimester did not significantly differ from the third trimester. However, differences between our findings and those of Chou et al. might be explained by the inclusion of both first and second trimester women at Time 1 in our sample (n=551).

6.2 Determinants of Nausea and Vomiting in Pregnancy

6.2.1 Sociodemographic determinants. In our study, women who were employed were more likely to have mild or less than mild NVP compared to women with moderate and severe symptoms. Two other studies confirm our finding (Källén, Lundberg, & Åberg, 2003; Lacroix et al., 2000); however, the meaning of these correlations cannot be determined without knowing how many women took a leave from work or quit work because of the nausea and vomiting, or because of decisions related to multiparity. A study of 3675 Swedish women found a lower rate of nausea and vomiting among pregnant women working outside the home (Källén et al., 2003). Similarly, Lacroix et al. (2000) reported that NVP was significantly associated with low educational level, low level of income, and part-time employment. One study found no significant associations between employment status

and NVP (Chou et al., 2003). However, differences between our findings and those of Chou et al. might be explained by the small sample size of their population (n=113).

6.2.2 Obstetrical and biological determinants. NVP severity decreased significantly with gestational age among women in the first and second trimester of pregnancy (Time 1). This is reasonable since the natural history of NVP is for gradual improvement as pregnancy progresses; corresponding with the onset, peak and decline of maternal hCG levels. In addition, maternal strategies to cope with NVP may increase over time. However, more advanced gestational age was not protective against moderate and more severe nausea and vomiting symptoms in the third trimester of pregnancy.

6.2.3 Psychological determinants. Pregnant women commonly report concerns about the health of their baby and the possibility of miscarriage in early pregnancy (Georgsson Öhman, Grunewald, & Waldenström, 2003; Statham, Green, & Katesios, 1997). Echoing these concerns, our study revealed that pregnant women with moderate and severe nausea and vomiting experience high levels of worry regarding their health, at a time that should be filled with anticipation and assumption of the mothering role. However, unlike women without nausea and vomiting symptoms, these concerns extend beyond the first trimester of pregnancy.

An association between worry and NVP has been reported elsewhere in the literature. A retrospective study of 3201 Canadian and American women reported that pregnant women with both mild and severe nausea and vomiting perceived their symptoms could adversely affect their baby (Mazzotta, Stewart, Atanackovic, Koren, & Magee, 2000), although a scale measure of NVP was not used in this study. Canadian women (72%) were more often concerned about the consequences of nausea and vomiting to their unborn child than the potential risks of drug therapy for treatment than American women (24.7%). High levels of worry in pregnancy are a concern considering that the negative impact of perceived stress in pregnancy on maternal and fetal outcomes is well documented (Austin, 2005; O'Keane & Scott, 2005; Teixeira, 1999).

A new finding of our study is that pregnant women with more sources of social support are less likely to experience severe nausea and vomiting in the third trimester of pregnancy. Chou et al. (2003) reported a negative relationship between social support and

NVP using Part II of the Personal Resources Questionnaire (Weinert, 1987) to measure perceived social support among 113 women between 6 to 10 weeks gestation. A lack of social support has also been reported among women with the most severe form of NVP, hyperemesis gravidarum (Katon, Ries, Bokan, & Kleinman, 1980). Research has also revealed that prenatal social support is negatively associated with stress (Chou, Avant, Kuo, & Fetzer, 2008) and other studies have positively associated stress with NVP (Kuo, Wang, Tseng, Jian, & Chou, 2007; O'Brien, Evans, & White-McDonald, 2002). Therefore, our finding that the support in pregnancy may reduce the risk of more severe NVP in the third trimester is consistent with the literature related to stress and support in pregnancy.

The findings of depression and nausea and vomiting in pregnancy in this study confirm the coexistence of these disorders reported by others (Anderson et al., 2004; Chou, 2003; Kitamura et al., 1996; Mazzotta et al., 2000; Swallow et al., 2004). However, like others, our findings do not reveal the causal relationship between NVP and depression in pregnancy.

6.2.4 Behavioural determinants. Our findings support the hypothesis that smokers in pregnancy experience less nausea than nonsmokers do (Jarnfelt-Samsioe et al., 1983; O'Brien & Zhou, 1995; Weigel, 1988). In our study, smokers (10.5%) were less likely to have severe NVP in the third trimester than non-smokers, a rate that is 4.5% less than estimates of smoking among this population (Statistics Canada, 2006). Two theories may explain the protective effect of maternal smoking on NVP. First of all, mothers who smoke cigarettes have lower levels of circulating maternal estrogen (Weigel & Weigel, 1988) and thus may have a decreased risk in having more severe nausea and vomiting, although evidence at this point implicating estrogen as a cause for NVP is mostly circumstantial. Secondly, both senses of odour (O'Brien, Relyea, & Lidstone 1997; Swallow, Lindow, Masson, & Hay 2005) and taste (O'Brien & Naber, 1992) have been associated with NVP, and the effects of maternal smoking may blunt these senses.

6.2.5 Antiemetic medication in pregnancy. The hypotheses that women who used medication to relieve nausea would report less severe NVP at both time periods were rejected. In this study, the use of antiemetic medications to ease NVP at both time periods was associated with more severe nausea and vomiting compared to women who did not

use antiemetic medications. It may be postulated that the decision to use antiemetic medications to alleviate symptoms may be a consequence of more severe nausea and vomiting. Mazzotta et al. (2000) reported the severity of NVP to be the factor most closely related to women's decisions to take antiemetic medication. In that study, other significant and independently related factors related to women's decisions to take antiemetic medication included an adverse effect of NVP on their partner's daily life and feelings of depression due to NVP. In this study, we do not know the reasons behind the woman's decision to use antiemetic medication.

6.3 Nature of the Relationship between NVP and Psychological Determinants

Women in our study reported a significant decrease in the degree of nausea and vomiting, stress, anxiety and depression significantly between the second and third trimesters of pregnancy. This trend would seem to coincide with normal patterns of circulating pregnancy hormones. Surprisingly, the use of antiemetic medication in pregnancy (14% at Time 1 and less than 5% at Time 2) was significantly associated with the occurrence of more severe nausea and vomiting symptoms in the second and third trimester of pregnancy. Therefore, the finding that antiemetic use did not reduce symptoms of major depression in pregnancy seems logical since these women still suffered severe NVP. Only a small percentage of women reported psychotropic medication use, but there was a significant association between these women and severe nausea and vomiting in the third trimester of pregnancy. This finding may confirm the theory that psychological responses to physiological stimuli may interact to exacerbate existing symptoms of anxiety and depression (Buckwalter & Simpson, 2002).

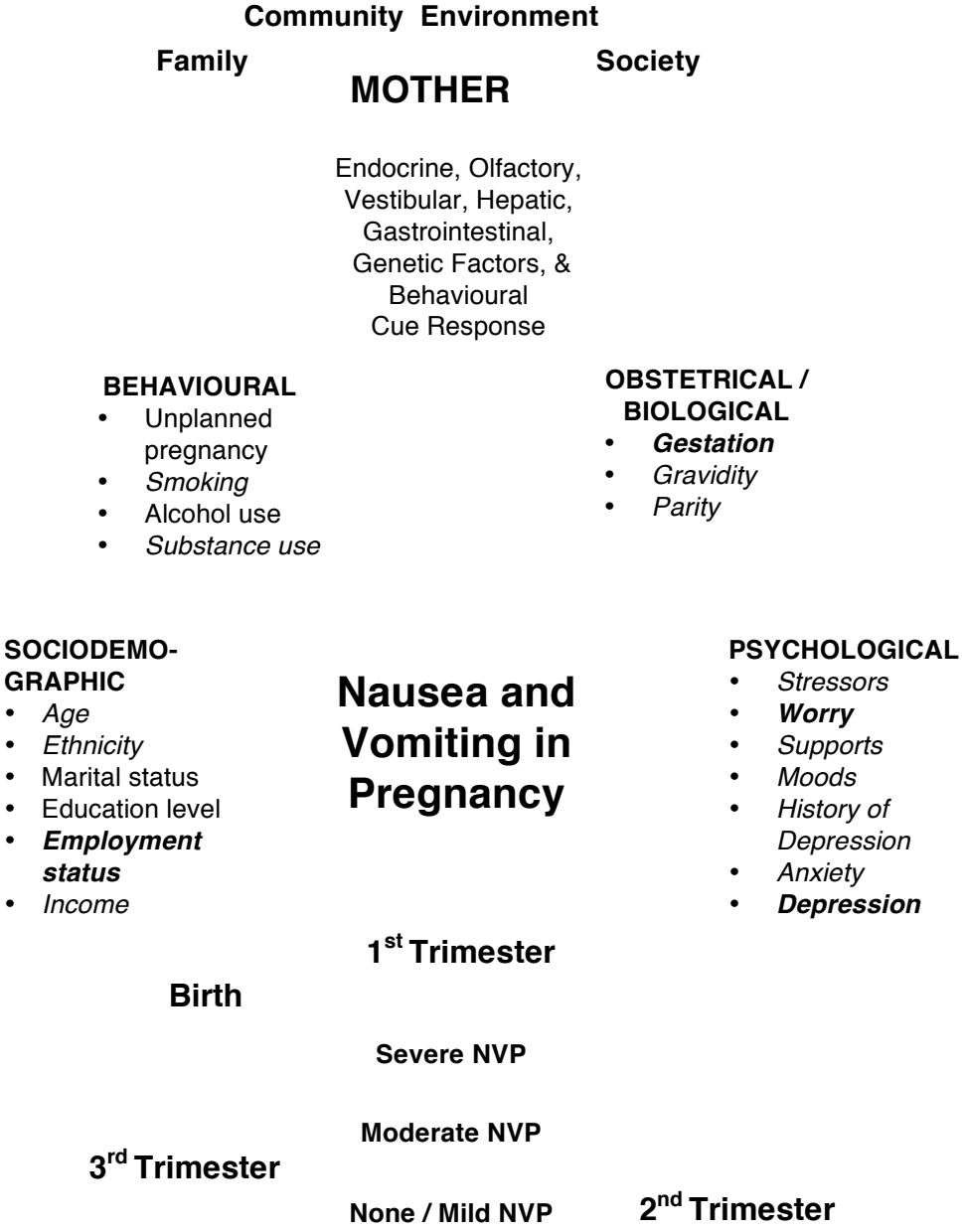
On the other hand, symptoms of major depression may be the direct result of nausea and vomiting in pregnancy. One study reported disturbances in the areas of depression, anxiety, psychotism, and obsessive-compulsive characteristics in pregnant women with hyperemesis gravidarum but no significant differences in the same women when tested after they gave birth (Simpson et al. 2001). In our study, of those women who reported symptoms of major depression at Time 1 but not at Time 2 (n=37), women with severe NVP (n=17) were significantly associated with symptoms of major depression during Time 1. However, no significant differences were found in NVP severity at Time 2, although the

number of women with severe NVP decreased to 9 cases. While we are unable to ascertain the nature of the relationship between NVP and symptoms of major depression, a review of the impact of NVP (section 2.2) certainly reinforces the idea that nausea and vomiting could subject any normal expectant mother to stress sufficient to trigger adjustment disorders, generalized anxiety or even depressive episodes (Bogen, 1994).

Figure 6.1 summarizes the determinants of moderate and severe and vomiting in pregnancy in this sample at Time 1. Likewise, Figure 6.2 summarizes the determinants of moderate and severe symptoms at Time 2. The determinants of NVP proposed in the study but were not significantly associated are in plain font. The determinants that were found to be significant in the bivariate analysis are in italics. Finally, those determinants that were significant in the final model are presented in bold font.

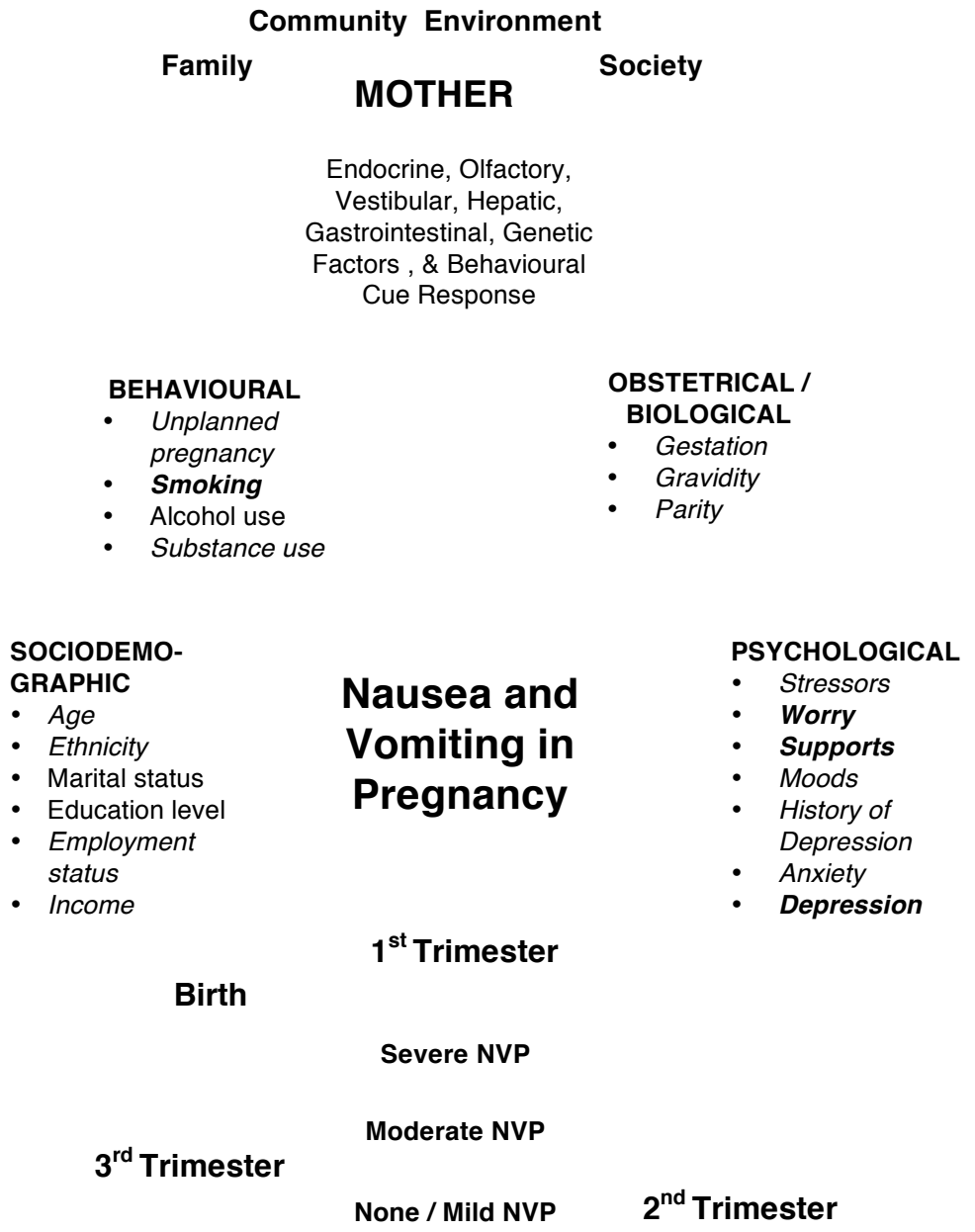
It appears from the final regression model at Time 1 that more severe nausea and vomiting in this sample of pregnant women was related to a combination of sociodemographic, obstetrical/biological, and psychological factors rather than to the other determinants analyzed in this study. The final regression model at Time 2 clearly indicates that psychological determinants are associated with more severe nausea and vomiting in the third trimester of pregnancy.

Figure 6.1 The Population Health Approach Illustrating the Interrelated Determinants of NVP at Time 1



Legend: **Bold font = Significant in final model**
Italic font = Significant bivariate analysis
Normal font = No statistically significant association

Figure 6.2 The Population Health Approach Illustrating the Interrelated Determinants of NVP at Time 2



Legend: **Bold font = Significant in final model**
Italic font = Significant bivariate analysis
Normal font = No statistically significant association

6.4 Implications for Care Providers

Nausea and vomiting prior to 20 weeks gestation are common symptoms known by health care providers, pregnant women and their families, and the general public; however, NVP in later pregnancy is a lesser known phenomenon. Since the etiology remains unknown, assessment of the condition focuses on severity, and management is largely supportive. Because of the higher than previously reported prevalence of nausea and vomiting in the third trimester recorded in this study, health care providers should be aware of determinants of women experiencing symptoms both prior to and beyond 20 weeks in pregnancy so that a more holistic approach is used to manage symptoms.

Being aware of women at risk may be important in developing helpful strategies to deal with women's suffering and promote the quality of women's lives. In this study, women in both the second and third trimester experienced high levels of worry and support reduced the severity of nausea and vomiting in later pregnancy. While women may feel that NVP is a sign of early pregnancy and is transitory, women experiencing symptoms into the second and third trimesters may have a sense that their symptoms are not considered normal in pregnancy (Lindseth & Vari, 2005). Women experiencing NVP beyond 20 weeks gestation should be informed that 20% to 45% of pregnant women do have late NVP. The media portrays NVP as a common occurrence to be endured (Deuchar, 1995), thus validation of symptoms beyond the first trimester may assert in women that their suffering is not normal and they can and should seek assistance and support from care providers. Since women require 'permission' to rest and avoid excessive sensory stimulation (O'Brien & Naber, 1992), education should be directed at partners and family of the suffering women regarding dietary and lifestyle recommendations (e.g., help with cooking, take over household duties, and encourage the mother to rest often). Support, understanding, and information regarding symptoms and measures for relief may relieve their worry of having continued nausea and vomiting during pregnancy.

Despite the protective effects of smoking cigarettes found in this study, health care providers should continue to encourage and support smoking cessation among pregnant women. This poses a challenge, as withdrawal symptoms associated with addiction would increase the level of stressors facing the pregnant woman. Nonetheless, cigarette smoking

is a known reproductive toxin that affects fetal birth weight, incidence of pre-term births, and poor future health of children (Statistics Canada, 2006). In addition, the risk of miscarriage is increased among smokers compared to nonsmokers (Barkai, Reichman, & Reis, 1994) and increasing number of prior miscarriages has been linked nausea and vomiting in pregnancy (Louik, Hernandez-Diaz, Werler, & Mitchell, 2006).

Antiemetic medication was not significantly associated with a reduction in the degree of nausea and vomiting in pregnancy. The meaning of this result is unclear; however, it is possible that concerns over adverse fetal affects resulted in the women not taking the medication as prescribed. In addition to the distress caused by NVP, the ingestion of antiemetic medications may cause distress and fears over the effects of such medications on the unborn baby (Mazzotta, Stewart, Atanackovic, Koren, & Magee, 2000). Women with more severe symptoms need to be reassured of the safety and efficacy of antiemetic medications prescribed in pregnancy. It is also possible that the prescribed dosage or the timing of medication administration was not sufficient to bring relief to women suffering more severe NVP.

The present study found a significant association between symptoms of major depression and nausea and vomiting in the second and third trimester of pregnancy. Acute major depressive episodes in pregnancy are often not treated or undertreated (Flynn et al., 2006; Marcus & Flynn, 1997). Untreated mood disorders in pregnancy increase the risk for preterm delivery, poor nutrition, inadequate weight gain, poor prenatal care, inability to care for oneself, substance use, consideration of pregnancy termination, and postpartum depression (Wisner et al., 2009; Wilsner et al., 2000). Therefore, women with NVP represent both a physical and psychological crisis that can be detrimental to both the mother and the baby, and pregnant women should be screened and treated for nausea and vomiting as well as their depression. Combined efforts may minimize the physical and psychological suffering of pregnant women, as well as the potential negative consequences of untreated maternal depression on infant development and family functioning (Wisner et al., 2009). Furthermore, depression in pregnancy may increase in severity if left untreated and can increase risk for future depressions. Treatment strategies that address only the

physical symptom of vomiting but disregard the subjective and pervasive nature of nausea, the need for support and associated depression are not likely to be as effective.

6.5 Future research

Additional research is needed to determine causation of nausea and vomiting in both early and late pregnancy, the temporal relation between psychosocial determinants and NVP, and then to test interventions addressing pregnant women with more severe nausea and vomiting symptoms and depression during different trimesters in pregnancy.

While our study adds to the literature about the psychosocial factors of NVP we particularly need to know more about all the health determinants associated with varying levels of nausea and vomiting in pregnancy. In addition, the finding that more severe NVP was highly associated with antiemetic therapy needs to be explored, as well as the doses of medications prescribed, timing of medication administration, compliance, and other treatment modalities used.

Finally, in cases with severe and extended duration of symptoms, the burden of more severe NVP on the developing fetus and long-term consequences to both the mother and child warrant further investigation. In addition, the long-term maternal and fetal effects of having both nausea and vomiting and depression in pregnancy needs to be examined. The additional knowledge gained will enable health care providers to identity women at risk for NVP earlier and to advise women early on about the recourse to the symptoms, particularly in later pregnancy, thus helping to improve their quality of life throughout pregnancy and to ameliorate the potential deleterious consequences to the fetus, baby, and mother herself.

6.6 Conclusions

Sixty-three percent of women experienced NVP during the second trimester of pregnancy, with 24% reporting moderate and 19% reporting more severe symptoms. Forty-five percent of women experienced NVP in the third trimester of pregnancy, with 8% reporting moderate and 14% reporting more severe symptoms. To further understand this phenomenon, this study examined the differences between those women with moderate and more severe nausea and vomiting symptoms on sociodemographic, obstetrical/biological, psychological, and behavioural determinants at two gestational time points, during the second and third trimesters.

Women experiencing more severe nausea and vomiting in the second trimester of pregnancy were not working, were prescribed antiemetic medication, had higher worry levels, and symptoms of major depression. Gestation mediated symptom severity in these women. Women experiencing more severe NVP during the third trimester were non-smokers, were prescribed antiemetic medication, had high levels of worry, and had symptoms of major depression. Higher levels of social support were protective against severe nausea and vomiting in the third trimester of pregnancy. Such findings can provide health care providers with information needed to identify women at risk and provide them with support to avoid increased psychological distress. Until further understanding of the causality of such symptoms is available, health care providers should use a holistic approach to maximize the quality of life for women experiencing nausea and vomiting in pregnancy.

References

Adouard, F., Glangeaud-Freudenthal, N., & Golse, B. (2005). Validation of the Edinburgh Postnatal Depression Scale (EPDS) in a sample of women with high-risk pregnancies in France. *Archive of Women's Mental Health*, 8, 89-95.

Agresti, A. (2002.) *Categorical Data Analysis* (2nd ed). NY: Wiley.

Akerman, F.M., Zhenmin, L., Rao, C.V., & Nakajim, S.T. (2000). A case of spontaneous ovarian hyperstimulation syndrome with a potential mutation in the hCG/LH receptor gene. *Fertility and Sterility*, 74, 3-4.

Allen, K., & Feeney, E. (1997). Alcohol and other drug use, abuse, and dependence. In K. Allen & J. Phillips (Eds.), *Women's health across the lifespan: a comprehensive perspective (pp.311-332)*. Philadelphia, PA: Lippincott.

American College of Obstetrics and Gynecology Practice Bulletin (ACOG). (2004). Nausea and Vomiting in Pregnancy. *Obstetrics and Gynaecology*, 103, 803-814.

Andersson, L., Sundstrom-Poromaa, I., Wulff, M., Astrom, M., & Bixo, M. (2004). Implications of antenatal depression and anxiety for obstetric outcome. *Obstetrics and Gynecology*, 104, 467-476.

Apfel, R., Kelly, S., & Frankel, Fl. (1986). The role of hypnotizability in the pathogenesis and treatment of nausea and vomiting of pregnancy. *Journal of Psychosomatic Obstetrics and Gynecology*, 5, 179-186.

Appleby, L. (1991). Suicide during pregnancy and in the first postnatal year. *British Journal of Medicine*, 301, 137-140.

Arsenault, M.Y., & Lane, C.A. (2002). The management of nausea and vomiting of pregnancy. *Journal of Obstetrics and Gynaecology of Canada*, 24(10), 817-823.

Askling, J., Erlandsson, G., Kaijser, M., Akre, O., & Ekbom, A. (1999). Sickness in pregnancy and sex of child. *Lancet*, 354, 2053.

Atanackovic, G., Wolpin, J., & Koren, G. (2001). Determinants of the need for hospital care among women with N.V.P. *Clinical Investigative Medicine*, 24, 90-93.

Attard, C., Kohli, M., Coleman, S., Bradley, C., Atanackovic, G., & Torrance, G. (2002). The burden of illness of severe nausea and vomiting of pregnancy in the United States. *American Journal of Obstetrics and Gynecology*, 186(5 Suppl.), 220-227.

Austin , M.P., Leader, L.R., & Reilly, N. (2005). Prenatal stress, the hypothalamic-pituitary-adrenal axis, and fetal and infant neurobehavior. *Early Human Development*, 81, 917-926.

Beatie, W., Buckley, D., & Forrest, J. (1991). The incidence of postoperative nausea and vomiting in women undergoing laparoscopy is influenced by the day of menstrual cycle. *Canadian Journal of Anesthesia*, 38, 298-302.

Black, F.O. (2002). Maternal susceptibility to nausea and vomiting of pregnancy: is the vestibular system involved? *American Journal of Obstetrics and Gynecology*, 186, S204-S209.

Bogen, J. (1994). Neurosis: A mis-diagnosis. *Perspectives in Biology and Medicine*, 37, 263-274.

Borgeat, A., Fathi, M., & Valiton, A. (1997). Hyperemesis gravidarum: is serotonin implicated? *American Journal of Obstetrics and Gynecology*, 176(2), 476-477.

Bowen, A. (2007). *Antenatal Depression: prevalence and determinants in a high-risk sample of women in Saskatoon* (Unpublished doctoral thesis). University of Saskatchewan, Saskatoon, Saskatchewan.

Bowen, R., Clark, M., & Baetz, M. (2004). Mood swings in patients with anxiety disorders compared with normal controls. *Journal of Affective Disorders*, 78(3), 185-192.

Brandes, J.M. (1967). First-trimester nausea and vomiting as related to outcome of pregnancy. *Obstetrics and Gynecology*, 30, 427-431.

Brent, R. (2002). Medical, social, and legal implications of treating nausea and vomiting of pregnancy. *American Journal of Obstetrics and Gynecology*, 186(5 Supplement), S262-S266.

Broussard, C.N., & Richter, J.E. (1998). Nausea and vomiting of pregnancy. *Pregnancy and Gastrointestinal Disorders*, 27(1), 123-151.

Brown, S. S., & Eisenberg, L., (Eds.) (1995). *The best intentions: unintended pregnancy and the well-being of children and families*. Washington DC: National Academy Press.

Buckwalter, J., & Simpson, S. (2002). Psychological factors in the etiology and treatment of severe nausea and vomiting in pregnancy*, American Journal of Obstetrics and Gynecology*, 186, 210-214.

Chandra, K., Magee, L., Einarson, A., & Koren, G. (2003). Nausea and vomiting in pregnancy: results of a survey that identified interventions used by women to alleviate their symptoms. *Journal of Psychosomatic Obstetrics and Gynecology*, 24, 71-5.

Chin, R.K.H., & Lao, T.T. (1988). Low birth weight and hyperemesis gravidarum. *European Journal of Obstetrics and Gynecology*, 28, 179-183.

Chou, F., Avant, K., Kuo, S., & Fetzer, S. (2008). Relationships between nausea and vomiting, perceived stress, social support, pregnancy planning, and psychosocial adaptation in a sample of mothers: A questionnaire survey. *International Journal of Nursing Studies*, 45, 1185-1191.

Chou, F.H., Chen, C.H., Kuo, S.H., & Tseng, Y.L. (2006). Experience of Taiwanese women living with nausea and vomiting during pregnancy. *Journal of Midwifery and Women's Health*, 51(5), 370-375.

Chou, F., Kuo, S., & Wang, R. (2008). A longitudinal study of nausea and vomiting, fatigue and perceived stress in, and social support for, pregnant women through the three trimesters. *The American Journal of Medical Sciences*, 24(6), 306-313.

Chou, F., Lin, L., Cooney, A., Walker, L., & Riggs, M. (2003). Psychosocial factors related to nausea, vomiting, and fatigue in early pregnancy. *Journal of Nursing Scholarship*, 35, 119-125.

Chung, T.K.H., Lau, K., Yip, A.S.K., Chiu, H.F.K., & Lee, D.T.S. (2001). Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. *Psychosomatic Medicine*, 63(5), 830-834.

Corey, L., Berg, K., Solaas, M., & Nance, W. (1992). The epidemiology of pregnancy complications and outcome in a Norwegian twin population. *Obstetrics and Gynecology*, 80, 989-994.

Cox, J., Holden, J., & Sagovsky, R. (1987). Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry*, 150, 782-786.

Crystal, S.R., Bowen, D.J., & Bernstein, I.L. (1999). Morning sickness and salt intake, food cravings, and food aversions. *Physiology and Behaviour*, 67, 181-187.

Czeizel, A.E. (1996). Prevention of hyperemesis gravidarum is better than treatment. *American Journal of Obstetrics and Gynecology*, 174(5), 1667.

Czeizel, A.E., & Puho, E. (2004). Association between severe nausea and vomiting in pregnancy and lower rate of preterm births. *Paediatric and Perinatal Epidemiology*, 18(4), 253-259.

Danzer, H., Braunstein, G.D., Rasor, J., Forsythe, A., & Wade, M.E. (1980). Maternal serum hCG concentrations and fetal sex prediction. *Fertility and Sterility*, 34, 336-340.

Davis, M. (2004). Nausea and vomiting of pregnancy: an evidence-based review. *Journal of Perinatal & Neonatal Nursing*, 18(4), 312-328.

Deuchar, N. (1995). Nausea and vomiting in pregnancy: a review of the problem with particular regard to psychological and social aspects. *British Journal of Obstetrics and Gynaecology*, 102(1), 6-8.

Deupe, R.H., Bernstein, L., Ross, R.K., Judd, H.L., & Henderson, B.E. (1987). Hyperemesis gravidarum in relation to estradiol levels, pregnancy outcome, and other maternal factors: A seroepidemilogic study. *American Journal of Obstetrics and Gynecology*, 156, 1137-1141.

Draper, N., Guttman, I., & Lapczak, L. (1979). Actual rejection levels in a certain stepwise test. *Communications in Statistics*, A8, 99-105.

Einarson, T.R., Navioz, Y., Maltepe, C., Einarson, A., & Koren, G. (2007). Existence and severity of nausea and vomiting in pregnancy (NVP) with different partners. *Journal of Obstetrics and Gynaecololgy*, 27(4), 360-362.

El Younis, C.M., Abulafia, O., & Sherer, D.M. (1998). Rapid marked response of severe hyperemesis gravidarum to oral erythromycin. A*merican Journal of Perinatology*, 15, 533–534.

Emelianova, S., Mazoota, P., Einarson, A. & Koren, B. (1999). Prevalence and severity of nausea and vomiting of pregnancy and effect of vitamin supplementation. *Clinical Investigative Medicine*, 22, 106-110.

Fairweather, D.V. (1968). Nausea and vomiting in pregnancy. *American Journal of Obstetrics & Gynecology*, 102, 135.

Fejzo, M.S., Poursharif, B., Korst, L.M., Munch, S., MacGibbon, K.W., Romero, R., & Goodwin, T.M. (2009). Symptoms and pregnancy outcomes associated with extreme weight loss among women with hyperemesis gravidarum. *Journal of Women's Health*, 18(12), 1981-1987.

Fisher-Rasmussen, W., Kjær, S.K., Dahl, C., & Asping, U. (1990). Ginger treatment of hyperemesis gravidarum. *European Journal of Obstetrics and Gynecologic Reproductive Biology*, 38:19–24.

Fitzgerald, C. (1984). Nausea and vomiting in pregnancy. *Journal of Medical Psychology*, 57(Pt.2), 159-165.

Flaxman, S., & Sherman, P. (2000). Morning sickness: a mechanism for protecting mother and embryo. The *Quarterly Review of Biology*, 75, 113-48.

Fox, J. (1991). *Regression diagnostics: Quantitative applications in the social sciences series* (No. 79). Thousand Oaks, California: Sage.

Gadsby, R., Barnie-Adshead, A., & Jagger, C. (1993). A prospective study of nausea and vomiting during pregnancy. *British Journal of General Practitioners*, 43, 245-248.

Gadsby, R., Barnie-Adshead, A., & Jagger, C. (1997). Pregnancy nausea related to women's obstetric and personal histories. *Gynecologic and Obstetrics Investigations*, 43, 108-111.

Gaynes, B., Gavin, N., Melzer-Brody, S., et al. (2005). Perinatal depression: Prevalence, screening accuracy, and screening outcomes, *Evidence of Reproductive Technology Assessment (Summ)*, 119, 1-8.

Gazmararian, J.A., Petersen, R. Jamieson, D.J., Schild, L., Adams, M.M., Deshpande, A.D., & Franks, A.L. (2002). Hospitalizations during pregnancy among managed care enrollees. *Obstetrics and Gynecology*, 100, 94-100.

Georgsson Öhman, S., Grunewald, C., & Waldenström, U. (2003). Women's worries during pregnancy: testing the Cambridge Worry Scale on 200 Swedish women. *Scandinavian Journal of Caring Science*, 17, 148-152.

Gertraud, E.M., Strunz-Lehner, C., Egen-Lappe, V., Lack, N., & Hasford, J. (2007). The association of psychosocial factors with nausea and vomiting during pregnancy. *Journal of Psychosomatic Obstetrics & Gynecology*, 29(1), 17-22.

Godet, P.F., & Marie-Cardine, M., (1991). Neuroleptics, schizophrenia and pregnancy. Epidemiological and teratologic study. *Encephaly*, 17, 543-547.

Goodwin, T. (2000). Human chorionic gonadotropin and hyperemesis gravidarum. In G. Koren & R. Bishai (Eds.), *Nausea and vomiting of pregnancy. State of the art* (pp. 15-22). Toronto: Transcontinental Inc.

Goodwin, T.M. (2002). Nausea and vomiting of pregnancy: an obstetric syndrome. *American Journal of Obstetrics and Gynecology*, 186(Supplement), S184-S189.

Goodwin, T.M., Montoro, M., Mestman, J.H., Pekary, A.E., & Hershman, J.M. (1992). The role of chorionic gonadotropic in transient hyperthyroidism of hyperemesis gravidarum. *Journal of Clinical Endorinology and Metabolism*, 75, 1333-1337.

Goodwin, T.M., Poursharif, B., Korst, L.M., MacGibbon, Romero, R., & Fejzo, M.S. (2008). Secular trends in the treatment of hyperemesis gravidarum. *American Journal of Perinatology*, 25(3), 141-147.

Green, J., Kafetsios, K., Statham, H., & Snowdon, C. (2003). Factor structure, validity and reliability of the Cambridge Worry Scale in a pregnant population. *Journal of Health Psychology*, 8, 753-764.

Gross, S., Librach, C., & Cecutti, A. (1989). Maternal weight loss associated with hyperemesis gravidarum: a predictor of fetal outcome. *American Journal of Obstetrics and Gynecology*, 160, 906-909.

Health Canada. (2003). *Women's Health Surveillance Report: A Multi-dimensional Look at the Health of Canadian Women*. Ottawa: Canadian Population Health Initiative, Canadian Institute for Health Information.

Heinrichs, L. (2002). Linking olfaction with nausea and vomiting of pregnancy, recurrent abortion, hyperemesis gravidarum, and migraine headache. *American Journal of Obstetrics and Gynecology*, 186, S215-S219.

Hellerstedt,W.L., Pirie, P.L., Lando, H.A., Curry, S.J., McBride, C.M., Grothaus, L.C., & Nelson, J.C. (1998). Differences in preconceptional and prenatal behaviors in women with inended and unintended pregnancies. *American Journal of Public Health*, 88(4), 663-666.

Hod, M., Orvieto, R., Kaplan, B., Friedman, S., & Ovadia, J. (1994). Hyperemesis gravidarum: a review. *Journal of Reproductive Medicine*, 39(8), 605-612.

Hosmer, D.W., Hosmer, T., le Cessie, S., & Lemeshow, S. (1997). A comparison of goodness-of-fit tests for the logistic regression model. *Statistics in Medicine*, 16, 695-980.

Hosmer, D.W., & Lemeshow, S. (2000). *Applied Logistic Regression* (2nd ed). New York: John Wiley & Sons, Inc.

Hsu, C.D., & Witter, F.R. (1993). Fetal sex and severe hyperemesis gravidarum. *International Journal of Gynecology and Obstetrics*, 40, 63-67.

Huxley, R. (2000). Nausea and vomiting in early pregnancy: its role in placental development. *Obstetrics and Gynecology*, 95, 779-782.

Iancu, I., Kotler, M., Spivak, B., Radwan, M., & Weizman, A. (1994). Psychiatric aspects of hyperemesis gravidarum. *Psychotherapy and Psychosomatics*, 61, 143-9.

Iatrakis, G., Sakellaropoulos, G., Kourkoubas, A., & Kabounia, S. (1998). Vomiting and nausea in the first 12 weeks of pregnancy. *Psychotherapy and Psychosomatics*, 49, 22-24.

Jacoby, E.B., & Porter, K.B. (1999). *Helicobacter pylori* infection and persistent hyperemesis gravidarum. *American Journal of Perinatology*, 16, 85-88.

Jarnfelt-Samsioe, A., Bremme, K., & Eneroth, P. (1986). Steroid hormones in emetic and non-emetic pregnancy. *European Journal of Obstetrics and Gynecologic Reproductive Biology*, 21, 87-99.

Jarnfelt-Samsioe, A., Samsioe, G., & Velinder, G.M. (1983). Nausea and vomiting in pregnancy: a contribution to its epidemiology. *Gynecologic and Obstetric Investigation*, 16, 221-229.

Jesse, E., Walcott-McQuigg, J., Mariella, A., & Swanson, M. (2005). Risk and protective factors associated with symptoms of depression in low-income African American and Caucasian women during pregnancy. *Journal of Midwifery and Women's Health*, 50, 405-410.

Jewell, D., & Young, G. (2000). *Interventions for nausea and vomiting in early pregnancy* (Cochrane Review). In The Cochrane Library, Issue 4. Oxford: Update Software.

Jewell, D., & Young, G. (2003). *Interventions for nausea and vomiting in early pregnancy* (Cochrane Review). In The Cochrane Library, *Issue 4*. Oxford: Update Software.

Jordan, V., Grebe, S.K.G., Cooke, R.R., Ford, H.C., Larsen, P.D., Stone, P.R., & Salmond, C.E. (1999). Acidic isoforms of chorionic gonadotrophin in European and Samoan women are associated with hyperemesis gravidarum and may be thyrotrophic. *Clinical Endocrinology*, 50, 619-627.

Kallen, B. (1987). Hyperemesis during pregnancy and delivery outcome: a registry study. *European Journal of Obstetrics, Gynecology and Reproductive Biology*, 26, 291-302.

Kallen, B., Lundberg, G., & Aberg, A. (2003). Relationship between vitamin use, smoking, and nausea and vomiting of pregnancy. *Acta Obstetricia et Gynecologica Scandinavica*, 82, 916-920.

Katon, W.J., Ries, R.K., Bokan, J.A., & Kleinman, A. (1980). Hyperemesis gravidarum: a biopsychosocial perspective. *International Journal of Psychiatric Medicine*, 10, 151-162.

Kindig D., & Stoddart G. (2003). What Is Population Health? *American Journal of Public Health*, 93(3), 380-383.

Kitamura, T., Sugawara, M., Sugawara, K., Toda, M., & Shima, S. (1996). Psychosocial study of depression in early pregnancy. *British Journal of Psychiatry*, 168, 732-738.

Klebanoff, M.A., Koslowe, P.A., Kaslow, R., & Rhoads, G.G. (1985). Epidemiology of vomiting in early pregnancy. *Obstetrics and Gynecology*, 66(5), 612-616.

Klebanoff, M., & Mills, J. (1986). Is vomiting during pregnancy teratogenic? *British Journal of Medicine*, 292, 724-726.

Koch, K.L. (2002). Gastrointentinal factors in nausea and vomiting of pregnancy. *American Journal of Obstetrics and Gynecology*, 186(5 Suppl), S198-S203.

Koch, K.L., & Frissora, C.L. (2003). Nausea and vomiting during pregnancy. *Gastroenterology Clinics of North America*, 32, 201-234.

Koren, G., & Levichek, Z. (2002). The teratogenicity of drugs for nausea and vomiting of pregnancy: perceived versus true risk. *American Journal of Obstetrics and Gynecology*, 186(5 Supplement), S248-S252.

Kuo, S.H., Wang, R.H., Tseng, H.C., Jian, S.Y., & Chou, F.H. (2007). A comparison of different severities of nausea and vomiting during pregnancy relative to stress, social support, and maternal adaption. *Journal of Midwifery and Women's Health*, 52(1), 1-7.

Lacasse, Rey, Ferreira, E., Morin, C., & Berard, A. (2008). Nausea and vomiting of pregnancy: what about quality of life? *British Journal of Obstetrics and Gynecology*, 115, 1484-1493.

Lacasse, A., Rey, E., Ferreira, E., Morin, C., & Berard, A. (2008). Validity of a modified Pregnancy-Unique Quantification of Emesis and Nausea (PUQUE) scoring index to assess severity of nausea and vomiting of pregnancy. *American Journal of Obstetrics and Gynecology*, 198(1), 71.

Lacroix, R., Eason, E., & Melzack, R. (2000). Nausea and vomiting during pregnancy: a prospective study of its frequency, intensity and patterns of change. *American Journal of Obstetrics and Gynecology*, 183, 931-937.

Lagiou, P., Tamimi, R., Mucci, L.A., Trichopoulos, D., Adami, H.O., & Hsieh, C.C. (2003). Nausea and vomiting in pregnancy in relation to prolactin, estrogens, and progesterone: A prospective study. *Obstetrics and Gynecology*, 101, 639-644.

Lederman Placzek, R. (1990). Anxiety and stress in pregnancy: Significance and nursing assessment. *Perinatal Womens Health Nursing*, 2, 279-288.

Lindenberg, C.S., Alexander, E.M., Gendrop, S.C., Nencioli, M., & Williams, D.G. (1991). A review of the literature on cocaine abuse in pregnancy. *Nursing Research*, 40(2), 69-75.

Lindseth, G., & Vari, P. (2005). Nausea and vomiting in late pregnancy. *Health Care for Women International*, 26, 372-386.

Little, R., & Hook, E. (1979). Maternal alcohol and tobacco consumption and their association with nausea and vomiting during pregnancy. *Acta Obstetricia et Gynecologica Scandinavica*, 58, 15-17.

Locock, L. Alexander, J., & Rozmovits, L. (2008). Women's responses to nausea and vomiting in pregnancy. *Midwifery*, 24, 143-152.

Louik, C., Hernandez-Diaz, S., Werler, M.M., & Mitchell, A.A. (2006). Nausea and vomiting in pregnancy: maternal characteristics and risk factors. *Paedicatric and Perinatal Epidemiology*, 20(4), 270-278.

Maggioni, C., Margola, D., & Fillippi, F. (2006). PTST, risk factors, and expectations among women having a baby: a two-wave longitudinal study. *Journal of Psychosomatic Obstetrics and Gynecology*, 27, 81-90.

Marcus, S.M., Barry, K.L., Flynn, H.A., Tandon, R., & Greden, J.F. (2001). Treatment guidelines for depression in pregnancy (review). *International Journal of Gynecology and Obstetrics*, 72, 61-70.

Marcus, S., Flynn, H., Blow, F., & Barry, K. (2003). Depressive symptoms among pregnant women screened in obstetric settings. *Journal of Women's Health*, 12, 373-80.

Martin, H. (1987). The temptations of the consulting psychiatrist. *Psychosomatics*, 28, 275-278.

Martin, R., Wisenbaker, J., & Huttunen, M. (1999). Nausea during pregnancy: relation to early childhood temperament behavioral problems at 12 years. *Journal of Abnormal Child Psychology*, 27, 323-9.

Marzuk, P.M., Tardiff, K., Leon, A.C., Hirsch, C.S., Portera, L., Hartwell, N., & Iqbal, M.I. (1997). Lower risk of suicide during pregnancy. *American Journal of Psychiatry*, 154(1), 122-123.

Masson, G.M., Anthony, F., & Chau, E. (1985). Serum chorionic gonadotropin (hCG), schwanerschaftsprotein 1 (SP1), progesterone and oestradiol levels in patients with nausea and vomiting in early pregnancy. *British Journal of Obstetrics and Gynecology*, 92, 211-215.

Mazzotta, P., & Magee, L.A. (2000). A risk-benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. *Drugs*, 59, 781-800.

Mazzota, P., Magee, L., & Koren G. (1997). Therapeutic abortions due to severe morning sickness. Unacceptable combination. *Canadian Family Physician*, 43,1055-1057.

Mazzotta, P., Maltepe, C., Navioz, Y., Magee, L., & Koren, G. (2000). Attitudes, management and consequences of nausea and vomiting of pregnancy in the United States and Canada. *International Journal of Gynaecology and Obstetrics*, 70, 359-65.

Mazzotta, P., Stewart, D., Atanackovic, G., Koren, G., & Magee, L. (2000). Psychosocial morbidity among women with nausea and vomiting of pregnancy: prevalence and association with anti-emetic therapy. *Journal of Psychosomatic Obstetrics and Gynaecology*, 21, 129-136.

Mazzotta, R., Stewart, D., Koren, G., & Magee, L. (2001). Factors associated with elective termination of pregnancy among Canadian and American women with nausea and vomiting of pregnancy. *Journal of Psychosomatic Obstetrics and Gynaecology*, 22, 7-12.

McCredie, J. (1973). Thalidomide and congenital charcot's joints. *Lancet*, 2, 1058-1060.

Medalie, J.H. (1957). Relationship between nausea and/or vomiting in early pregnancy and abortion. *Lancet*, 273(6986), 117-119.

Meighan, M., & Wood, A.F. (2005). The impact of hyperemesis gravidarum on maternal role assumption. *Journal of Obstetric, Gynecologic, & Neonatal Nursing*, 34, 172-9.

Menard, S. (1995). *Applied logistic regression analysis.* Sage university paper series on quantitative applications in the social sciences. Thousand Oaks, CA: Sage.

Milkovich, L., & Van Den Berg, B.J. (1976). An evaluation of the teratogenicity of certain antinauseant drugs. *American Journal of Obstetrics and Gynecology*, 125, 244-248.

Miller, F. (2002). Nausea and vomiting in pregnancy: the problem of perception-is it really a disease? *American Journal of Obstetrics and Gynecology*, 186(Supp. 5), 182-193.

Minturn, L., & Weiher, A. (1984). The influence of diet on morning sickness: A cross-culture study. *Medical Anthropology*, 8, 71-75.

Morgan, H. (1985). Functional vomiting. *Journal of Psychosomatic Research*, 29, 341-352.

Myers, R. (1990). *Classical and modern regression with applications* (2nd ed.). Boston, MA: Duxbury.

Naimi, T.S., Lipscomb, L.E., Brewer, R.D., & Gilbert, B.C. (2003). Binge drinking in the preconception period and the risk of unintended pregnancy: Implications for women and their children. *Pediatrics*, 111, 1136-1141.

Nelson-Piercy, C. (1997). Hyperemesies gravidarum. *Current Obstetrics and Gynaecology*, 7, 98-103.

Niebyl, J.R., & Goodwin, T.M. (2002). Overview of nausea and vomiting with an emphasis on vitamins and ginger. *American Journal of Obstetrics and Gynecology*, 186(Supp. 1), S253-S255.

Nulman, I., Rovet, J., Stewart, D.E., Wolpin, J., Gardner, H.A., Theis, J.G., Kulin, N., & Koren, G. Neurodevelopment of children exposed in utero to antidepressant drugs. *New England Journal of Medicine*, 336(4), 258-262.

O'Brien, B., Evans, M., & White-McDonald, E. (2002). Isolation from "being alive": coping with severe nausea and vomiting of pregnancy. *Nursing Research*, 51, 302-308.

O'Brien, B., & Naber, S. (1992). Nausea and vomiting during pregnancy: Effects on the quality of women's lives. *Birth*, 19, 138-143.

O'Brien, B., Relyea, J., & Lidstone, T. (1997). Diary reports of nausea and vomiting during pregnancy. *Clinical Nurse Researcher*, 6, 239-252.

O'Brien, B., Relyea, J., & Taerum, T. (1996). Efficacy of P6 acupressure in the treatment of nausea and vomiting during pregnancy. *American Journal of Obstetrics and Gynecology*, 174(2), 708-715.

O'Brien, B., & Zhou, Q. (1995). Variables related to nausea and vomiting during pregnancy. *Birth*, 22, 93-100.

O'Keane, V., & Scott, J. (2005). From 'obstetric complications' to a maternal-foetal origin hypothesis of mood disorder. *The British Journal of Psychiatry*, 186, 367-368.

Ornstein, M., Einarson, A., & Koren, G. (1995). Benedictin/Diclectin for morning sickness: a Canadian follow-up of an American tragedy. *Reproductive Toxicology*, 1, 1-6.

Pastuszak, A. (1995). Doxylamine/pyridoxine for nausea and vomiting of pregnancy. *Canadian Pharmaceutical Journal*, 128, 39-42.

Pigott, T. (2003). Anxiety disorders in women. The *Psychiatric Clinics of North America*, 26, 621-672.

Pines, D. (1990). Pregnancy, miscarriage, and abortion: a psychoanalytic perspective. *International Journal of Psychoanalysis*, 71, 301-07.

Poursharif, B., Korst, L.M., Fejzo, M.S., MacGibbon, K.W., Romero, R., & Goodwin, T.M. (2008). The psychosocial burden of hyperemesis gravidarum. *Journal of Perinatology*, 28, 176-181.

Poursharif, B., Korst, L.M., MacGibon, K.W., Fejzo, M.X., Romero, R., & Goodwin, T.M. (2007). Elective pregnancy termination in a large cohort of women with hyperemesis gravidarum. *Contraception*, 76, 451-455.

Profet, M. (1988). The evolution of pregnancy sickness as protection to the embryo against Pleistocene teratogens. *Evolutionary Theory*, 8, 177-190.

Public Health Agency of Canada. (2005). What Is the Population Health Approach. http://www.phac-aspc.gc.ca/ph-sp/phdd/approach/approach.html 1. The Public Health Agency of Canada.

Rhodes, V.A. (1990). Nausea, vomiting, and retching. *Nursing Clinics of North America*, 25, 885-900.

Robins, L.M., & Mills, J.L. (1993). Effect of in utero exposure to street drugs. *American Journal of Public Health*, 83 (Suppl.), 1–32.

Rodien, P., Bremont, C., Raffin Sanson, M., Parma, J., Van Sande, J., Costagliola, S., Luton, J.P., Vassart, G., & Duprez, L. (1998). Familial gestational hyperthyroidism caused by a mutant thyrotropin receptor hypersensitive to human chorionic gonadotropin. *New England Journal of Medicine*, 339, 1823-1826.

Rodriguez, A., Bohlin, G., & Lindmark, G. (2001). Symptoms across pregnancy in relation to psychosocial and biomedical factors. *Acta Obstetricia et Gynecologica Scandinavica*, 80, 213-223.

Rotman, P., Hassin, D., Mouallem, M., Barkai, G., & Farfel, Z. (1994). Wernicke's encephalopathy in hyperemesis gravidarum: association with abnormal liver function. *Israeli Journal of Medical Science*, 30(3), 225-228.

Samsioe, G., Crona, N., Enk, L., & Järnfelt-Samsioe, A. (1986). Does position and size of corpus luteum have any effect on nausea of pregnancy? *Acta Obstetricia et Gynecologica Scandinavica*, 65(5), 427-429.

Santiago, J.R., Nolledo, M.S., Kinzler, W., & Santiago, T.V. (2001). Sleep and sleep disorders in pregnancy. *Annals of Internal Medicine*, 134(5), 396–408.

Schiff, M., Reed, S., & Daling, J. (2004). The sex ratio of pregnancies complicated by hospitalization for hyperemesis gravidarum. *British Journal of Obstetrics and Gynecology*, 111(1), 27-30.

Semmenes, J.P. (1971). Female sexuality and life situations: an etiologic psycho-socio-sexual profile of weight gain and nausea and vomiting in pregnancy. *Obstetrics and Gynecology*, 38(4), 555-563.

Sen, G., & Östilin, P. (2008). Gender inequity in health: why it exists and how we can change it. *Global Public Health*, 3(S1), 1-12.

Seto, A., Einarson, T., & Koren, G. (1997). Pregnancy outcome following first trimester exposure to antihistamines: meta analysis. *American Journal of Perinatology*, 14, 119-124.

Shah, C.P. (2003). *Public health and preventative medicine in Canada* (5th ed.). Toronto: Elsevier Canada.

Sherman, P., & Flaxman, S.M. (2002). Nausea and vomiting of pregnancy in an evolutionary perspective. *American Journal of Obstetrics and Gynaecology*, 186, S190-197.

Sipiora, M.L., Murtaugh, M.A., Gregoire, M.D., & Duffy, V.B. (2000). Bitter taste perception and severe vomiting in pregnancy. *Physiology and Behavior*, 69, 259-267.

Smith, C., Crowther, C. Beilby, J., & Dandeaux, J. (2000). The impact of nausea and vomiting on women: a burden of early pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynecology*, 4, 397-401.

Sonkusare, S. (2008). Hyperemesis gravidarum: a review. *Medical Journal of Malaysia*, 63(3), 272-276.

Statham, H., Green, J., & Katesios, K. (1997). Who worries that something might be wrong with the baby? A prospective study of 1072 women. *Birth*, 24(4), 223-233.

Statham, H., Green, J., & Snowdon, C. (1993). Psychological and social aspects of screening for fetal abnormality during routine antenatal care. In *Proceedings of the 1992 Research and the Midwife Conference* (Robinson, S., & Tickner, V., eds). School of Nursing, Universtiy of Manchester, Manchester, 44-62.

Swallow, L., Lindow, S., Masson, E., & Hay, D. (2002). Development of an instrument to measure nausea and vomiting in pregnancy. *Journal of Obstetrics and Gynaecology*, 22(5), 481-485.

Swallow, L., Lindow, S., Masson, E., & Hay, D. (2004). Psychological health in early pregnancy: Relationship with nausea and vomiting. *Journal of Obstetrics and Gynaecology*, 24(1), 28-32.

Swallow, L., Lindow, S., Masson, E., & Hay, D. (2005). Women with nausea and vomiting in pregnancy demonstrate worse health and are adversely affected by odours. *Journal of Obstetrics and Gynaecology*, 25(6), 544-549.

Stewart, D.E., & Steiner, D. (1994). Alcohol drinking in pregnancy. *General Hospital Psychiatry*, 16, 406-412.

Strong, T.H. Jr. (2001). Alternative therapies of morning sickness. *Clinical Obstetrics and Gynecology*, 44, 653-660.

Tierson, F.D., Olsen, C.L., & Hook, E.B. (1986). Nausea and vomiting of pregnancy and association with pregnancy outcome. *American Journal of Obstetrics and Gynecology*, 155(5), 1017-1022.

Teixeira, J.M., Fisk, N.M. & Glover, V. (1999). Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. *The British Journal of Medicine*, 318, 153-157.

U.S. Department of Health and Human Services. (1990). *The health benefits of smoking cessation: report of the Surgeon General*. Washington, DC: U.S. Department of Health and Human Services.

Vallacott, I., Cooke, E., & James, C. (1988). Nausea and vomiting in early pregnancy. *International Journal of Gynecology and Obstetrics*, 27, 7-62.

Verberg, M.F., Gillot, D.J., Al-Fardan, N., & Grudzinskas, J.G. (2005). Hyperemesis gravidarum, a literature review. *Human Reproductive Update*, 11, 527-539.

Vilming, B., & Nesheim, B. (2000). Hyperemesis gravidarum in a contemporary population in Oslo. *Acta Obstetricia et Gynecologica Scandinavica*, 79, 640-643.

Vutyavanich, t., Kraisarin, T., & Ruangsri, R. (2001). Ginger for nausea and vomiting in pregnancy: randomized, double masked, placebo controlled trial. *Obstetrics and Gynecology*, 97, 577-582.

Walker, A., Walker, B., Jones, J., Vervardi, M., & Walker, C. (1985). Nausea and vomiting and dietary cravings and aversions during pregnancy in South African Women. *British Journal of Obsterics and Gynecology*, 5, 484-489.

Walsh, J., Hasler, W., Nugent, C., & Owyang, C. (1996). Progesterone and estrogen are potential mediators of gastric slow-wave dysrhythmia in nausea of pregnancy. *American Journal of Physiology*, 270, 506-514.

Weigel, M.M., & Weigel, R.M. (1988). The association of reproductive history, demographic factors, and alcohol and tobacco consumption with the risk of developing nausea and vomiting in early pregnancy. *American Journal of Epidemiology*, 127, 562-570.

Weigel, R.M., & Weigel, M.M. (1989). Nausea and vomiting of early pregnancy and pregnancy outcome: a meta-analytical review. *British journal of Obstetrics and Gynecology*, 96, 1312-1318.

Weinert, C. (1987). A social support measure: PRQ85. *Nursing Research*, 36, 273-277.

Whitehed, S.A., Andrews, P.L.R., & Chamberlain, G.V.P. (1992). Characterization of nausea and vomiting in early pregnancy: a survey of 1000 women. *Journal of Obstetrics and Gynecology*, 12, 364-369.

Wisner, K.L, Sit, D.K., Hanusa, B.H., Moses-Kolko, E.L., Bogen, D.L., Hunker, D.F., Perel, J.M., Jones-Ivy, S., Bodnar, L.M., & Singer, L.T. (2009). Major depression and antidepressant treatment: impact on pregnancy and neonatal outcomes. *American Journal of Psychiatry*, 166(5), 557-566.

Wilsner, K.L., Zarin, D.A., Holmboe, E.S., Appelbaum, P.S., Gelenberg, A.J., Leonard, H.L., & Franke, E. (2000). Risk-benefit decision making for treatment of depression during pregnancy. *American Journal of Psychiatry*, 157(12), 1933-1940.

Wilkinson, J.M. (2000). What do we know about herbal morning sickness treatments? A literature survey. *Midwifery*, 16, 224-228.

Wolkind, S., & Zajicek, E. (1978). Psycho-social correlation of nausea and vomiting of pregnancy. *Journal of Psychosomatic Research*, 22(1), 1-5.

Wood, P., Murray, A. Sinha, B., Godley, M., & Goldsmith, H.J. (1983). Wernicke's encephalopathy induced by hyperemesis gravidarum. Case reports. *British Journal of Obstetrics and Gynecology*, 90, 583-586.

Woolhouse, M. (2006). Complementary medicine for pregnancy complications. *Australian Family Physician*, 35(9), 695.

Yoneyama, Y., Kobayashi, H., Kato, M., Chihara, H., Yamada, T., Ostubo, Y., & Araki, T. (2002). Plasma 5'-nucleotidase activities increase in women with hyperemesis gravidarum. *Clinical Biochemistry*, 35, 561-564.

Zhang, J., & Cai, W.W. (1991). Severe vomiting during pregnancy: antenatal correlates and fetal outcomes. *Epidemiology*, 2, 454-457.

Zhou, Q., O'Brien, B., & Relyea, J. (1999). Severity of nausea and vomiting during pregnancy: what does it predict? *Birth*, 26, 108-114.

Zhou, Q., O'Brien, B., & Soeken, K. (2001). Rhodes Index of Nausea and Vomiting: form 2 in pregnant women. A confirmatory factor analysis. *Nursing Research*, 50(4), 251-257.

Zuckerman, B.S., Amaro, H., Bauchner, H., & Cabral, H. (1989). Depression symptoms during pregnancy: relationship to poor health behaviors. *American Journal of Obstetrics and Gynecology*, 160(5), 1107-1111.

Appendix A

University of Saskatchewan-Ethics Approval

UNIVERSITY OF SASKATCHEWAN

Research Ethics Office

Box 5000 RPO University
1607 – 110 Gymnasium Place
NRC/PBI Building
Saskatoon SK S7N 4J8 Canada
Telephone: (306) 966-2975
Facsimile: (306) 966-2069

To: Angela Bowen, Nursing
Nazeem Muhajarine, Community Health and Epidemiology
Jennifer Kramer, Nursing (Masters Student)

Date: August 12, 2009

Re: Nausea and Vomiting in Early Pregnancy: Relationship with Stress, Worry, Social Support, Mood Swings, Anxiety and Depression (Beh 09-183)

The study entitled, "Nausea and Vomiting in Early Pregnancy: Relationship with Stress, Worry, Social Support, Mood Swings, Anxiety and Depression" is exempt from the Research Ethics Board review process. This decision is based on the information provided to the Research Ethics Office on August 7th, 2009.

Article 3.3 of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (1998) specifies that REB review and approval is not required to conduct a secondary analysis of data that cannot be linked to individuals, and for which there is no possibility that individuals can be identified in any published reports.

It should be noted that though your project is exempt of ethics review, your project should be conducted in an ethical manner (i.e. in accordance with the information that you submitted). It should also be noted that any deviation from the original methodology and/or research question should be brought to the attention of the Behavioural Research Ethics Board for further review. Please ensure that a full application is submitted to the Research Ethics Office prior to starting part II of this study.

Sincerely,

John Rigby

Dr. John Rigby, Chair
Behavioural Research Ethics Board
University of Saskatchewan

Appendix B

The Nausea and Vomiting in Pregnancy Instrument (NVPI) (Swallow et al., 2002)

Circle the response that fits closest to your experience during the <u>past 7 days</u>.

1. How often have you felt like being sick (nauseated) in the past week?

All the time | More than once a day | Daily | 3-6 days during the week | Occasionally | Not at all

2. How often have you retched/dry heaved (but without actually being sick) in the past week?

All the time | More than once a day | Daily | 3-6 days during the week | Occasionally | Not at all

3. How of ten have you been physically sick (vomited) during the past week?

All the time | More than once a day | Daily | 3-6 days during the week | Occasionally | Not at all

Appendix C

The Cambridge Worry Scale (CWS) (Statham et al., 1993)

Please circle a number for each one to show how much of a worry it is to you now, from 1 if it is not a worry to 5 if it is something that you are extremely worried about:

	Not a worry				**Major**
Worry					
Your housing	1	2	3	4	5
Money problems	1	2	3	4	5
Problems with the law	1	2	3	4	5
Your relationship with your partner/husband	1	2	3	4	5
Your relationship with your family and friends	1	2	3	4	5
Your own health	1	2	3	4	5
The health of someone close to you	1	2	3	4	5
Employment problems	1	2	3	4	5
The possibility of something being wrong with baby	1	2	3	4	5
Going to hospital	1	2	3	4	5
Internal examinations	1	2	3	4	5
Giving birth	1	2	3	4	5
Coping with the new baby	1	2	3	4	5
Giving up work (if applicable)	1	2	3	4	5
Whether your partner will be with you for the birth	1	2	3	4	5
Possibility of miscarriage	1	2	3	4	5

If there is anything else that is worrying you or you would like to say anything more about any of the above,
please use this space to tell us about it:

Appendix D

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987)

Please underline the answer, which comes closest to how you have felt in the <u>past 7 days</u>, not just how you feel today:

I have felt happy:

Yes, most of the time
<u>Yes, some of the time</u>
No, not very often
No, not at all

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 no 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

Appendix E

Summary of Studies of NVP and Psychosocial Determinants of Health

Author	Site	Sam-ple size	Gesta-tion (weeks)	Tool*	% NVP	Psycho-metrics	Sample characteristics	Determinants of NVP	Comments
Chou et al. (2008)	Taiwan	91	T1 6-10 T2 16-18 T3 28-32	INVR (0-32 range)	Not reported T1 mean 8 T2 mean 2.5 T3 mean 2	States tool valid & reliable in English perinatal studies	Age 30 ± 4.2 Employed 79% Parity-1 59% college level 43% planned pregnancies 59%	Stress Support Fatigue 1st & 2nd tri: fatigue affected by NV, stress correlated with fatigue & not NV, stress negatively correlated with support	Longitudinal NV pattern: 1st trimester had significantly higher levels than trimesters 2 & 3. Stress & Support levels remained same throughout trimesters.
Shih-Hsien et al. (2007)	Taiwan	150	6-16 Mean 11.3	INVR	NV occurred between week 3-15 gest-ation 3 groups: Mild Moderate Severe	States tool valid & reliable in English perinatal studies	Age 28 ± 4.4 Employed 65% Parity-1 52% college level 51% unplanned pregnancies 52%	Stress Support Maternal-Psychosocial-Adaptation Mild NV: sig lower stress levels, more accepting of pregnancy Moderate NV: less accepting of pregnancy Severe NVP: sig. higher stress levels, less accepting of pregnancy, feared more helplessness & loss of control in labor than mod/mild NV groups.	Support & Psychosocial adaptation not different among 3 severity groups. Causal relation b/w stress, lack of pregnancy acceptance & NV not determined. Mild & Mod NV had better adaptive responses to pregnancy acceptance and labor fears.

Chou et al. (2007)	Taiwan	243	6-16 week	INVR	77.4% prevalence Mild 25% Mod 36.2% Severe 12.3	States tool valid & reliable in English perinatal studies. Pilot study conducted prior to this research to ensure language accuracy & cultural appropriateness.	Age 28 ± 4.3 Married 100% Employed 70% Parity-1 50% college level 50% unplanned pregnancies 50%	Stress Support Pregnancy Planning Psychosocial-Adaptation Severe NV associated with high stress may be mediated by support. Women at risk for poor adaptation have severe NV.	…
Lacasse et al. (2008)	Montreal, Canada	367	≤ 16 Mean 11±1.8	PUQE (range 3-15),	78.5% prevalence in 1st trimester Mean Nausea intensity 4.7 ± 2.5	States tool valid & reliable in previous 1st trimester studies.	Age 31.7 ± 4.7 Living with partner/others 97.8% Employed 76% Parity-1 53% University completed 62% Income>$80 000 43%	NVP presence associated with both lower physical & mental scales. Intensity of nausea symptoms, more severe NVP & nonpharmacological methods to ease symptoms associated with poorer NVPQOL. Higher gestational age & having private insurance plan associated with superior NVPQOL. Women with more severe NVP had mental QOL scores similar to women with postpartum depression.	Primary outcome: NVP specific QOL First NVPQOL study to account for confounding factors with multivariate analysis. Caucasians had worse QOL than Asians & Hispanics, however small minority groups in sample. Controlled for multiple psychosocial variables.

Swallow et al. (2004)	Northern England	273	Range 8-18 Mean 12.8 ± 2.8	NVPI	Prevalence not reported. Mean NVPI 4.3 ± 3.9	These authors created the tool & validated it for use in 2002.	Caucasian 98%, no other demographic data reported	50.5% found to have potential psychiatric problems. NVP associated with somatic symptoms (r=0.35), social dysfunction (r=0.25), anxiety/insomnia (r=0.16) & severe depression (r-0.17). p=<0.001 for all correlates.	Casual relationship undetermined. The internal validity of the GHQ may be questionable for pregnant women. More NVP = more ill-health perception. However, mood perception not affected by NVP severity.
Mazzotta et al. (2000)	Canada	3201	Retro-spective	All telephone respon-dents had reported previous or current NVP.	Not applicable	States tool valid & reliable in previous 1st trimester studies.	Age 28.3 ± 5.0 Parity-1 48% Planned pregnancy 75% Elective termination 3.4% Most pregnancies resulted in term infants with average birthweight.	1st trimester: more severe symptoms & more nausea compared to vomiting. 60.5% took anti-emetic therapy. More likely to have taken antiemetic therapy if vomiting severely. Severe NV associated with depression, consideration of pregnancy termination, adverse affect on relationship with partner & partner's daily life, & fear of NVP harming the baby.	Interviewees may report severity of symptoms to be higher than actuality as study retrospective in design.

Munch et al. (2010)	Califor-nia, U.S.	93	Mean 11.9 ± 3.5	NVPQOL, SF36 PUQUE	NVP 51.6% Hyper-emesis gravidar-um 31.2% QOL is low for HG or NVP women in the 1st trimester compared to asympto-matic U.S. women in 1st trimester.	States although NVPQOL validated, it does not have published normative values.	Age 27.6 ± 6.1 Partnered 72% <College level 61.3% Hispanic 73% Multiparous 52.7%	HG women 3-6 times more likely than NVP women to have low QOL scores. For both NVPQOL & SF36 tests, perceived symptoms severity & marital status, depression, age seemed to be equally or more important contributor to low QOL than having HG diagnosis.	Controlled for psychosocial variables & compared HG with NVP. Psychosocial interactions also explored. Having HG alone didn't fully explain hypothesis of lower QOL, the presence of some NVP symptoms with psychosocial factors put these women equally or more at risk.
Gerraud et al. (2008)	Bavaria, Germany	422	1st trimester	anti-emetic pre-scrip-tion (A04)	Antiem-etic use for NVP 7.5%	Not applicable	Median 32, Working 52.3%, European 95.7% German 91.5% Partnered 92.5% Parity-1 36.5% Current smokers 4.2%	NVP risk 2x higher for non-smokers (OR 2.03, CI 1.02-4.05) and dropped 3% /year in age (OR 0.97, CI 0.94-0.99). Single increased risk by 50% (OR 1.49, CI 1.24-1.79) & for these women working lowered risk by 2/3 (OR 0.4, CI 0.24-0.49).	Interactions among correlates explored.

Bozzo et al. (2006)	Toronto, Canada	2 x 179	1st trimester	Self-identified NVP	Depressed with NVP 61% Non-depressed with NVP 68%	Self-identified as having NVP or not.	Depressed: Age 32.5 ± 4.2 Gravidity 2 Parity 1 Nondepresed: Age 32.4 ± 5.8 Gravidity 2 Parity 0	Depression, Age Gravidity, Parity Logistic regression did not identify any correlates as significantly explaining NVP. No difference in NVP incidence between the 2 groups.	Comparison between depressed women Tx with antidepressants & nondepressed women. Respondents called "hotline" to partake in original study.
Louk et al. (2006)	Boston, U.S.	22487	Duration & onset recorded. Long duration group (>4months NVP) Late onset group (after 1st trimester)	Self identified NVP	NVP 66.7%	Self-identified as having NVP or not.	NVP decreased with age NVP increased with increasing: gravidity, prior miscarriages. NVP higher in twins than singletons.	NVP began between week 5-8 & lasted for <4months. Longer duration NVP more common with lower income & younger age, multigravida, unplanned pregnancy. No smoking effect observed. No changes between normal and malformed infants. Earlier onset: less-well educated, lower income, black ethnicity	Very large sample Women with late onset might have also presented late to 1st prenatal visit.

Lacroix et al. (2000)	Montreal, Canada	160	14 & 22 weeks	McGill Naus-ea ques-tionn-aire	Nausea74%	Validated in samples for cancer therapy.	Nausea lasted mean 34.6 days. "Morning sickness" 1.8% whereas 80% reported nausea lasting all day. 50% relieved by week 14, 90% no NVP by 22 weeks	Results indicate that nausea experienced by pregnant women is similar in character & intensity to the nausea experienced by caner chemotherapy clients.	
Kuo et al. (2007)	Taiwan	150	1st trimester	INVR	Mild or <Mild, Mod, Severe	States validated in both English and Taiwan popula-tions.		Stress Social Support Maternal Adaptation Stress different among 3 severity groups, support & adaptation not different. Mild NVP had significantly lower stress & severe NVP had significantly higher stress levels. Severity significantly associated with subscales of "acceptance of pregnancy" & fear of helplessness & loss of control during labor."	Cross-sectional & comparative design.