School of Population Health

Antenatal and postnatal depression in Vietnam:

A prospective cohort study

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made. This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Human Ethics (For projects involving human participants/tissue, etc.) The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The proposed research study received human research ethics approvals from the Curtin University Human Research Ethics Committee (EC00262), Approval Number HR32/2015 and from the Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee, Approval number 05/PHUMPRB.

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ABSTRACT

Background

Antenatal depression is common among women during pregnancy. Globally, the rate of antenatal depression ranges from 15% to 65%. Its incidence and prevalence are generally higher in women with low social support and socioeconomic status, younger age and lower education. The condition has adverse effects on both maternal and infant health, including a greater risk of obstetric complications and development of postnatal depressive symptoms. For postnatal depression from delivery to 12 months postpartum, it is a mental and behavioural disorder with prevalence of 4% to over 64% worldwide. Postnatal depression is known to have serious consequences, not only for the women but also for their infants and families, and is linked to a wide range of influencing factors. In Vietnam, although previous studies have been conducted to estimate the rate of perinatal depression, associated risk factors and effects, these studies mostly focused on postnatal depression and were based on either a small sample size or within a particular area or city in Vietnam, without accounting for the plausible relationship between antenatal depression and postnatal depression.

Aim and objectives

This study aimed to investigate antenatal and postnatal depression, and their association with maternal characteristics and birth outcomes in Vietnam. The objectives were: (1) to review the epidemiology of perinatal depression in Asia; (2) to determine the prevalence of antenatal depression in Vietnam and its associated maternal and risk factors; (3) to ascertain the association between antenatal depressive

symptoms and birth outcomes; (4) to determine the prevalence of postnatal depression at one month postpartum and its associated factors; (5) to determine the prevalence of postnatal depression at three months postpartum and its associated factors; (6) to examine the prospective association between postnatal depressive symptoms at three months postpartum and infant health problems at six months in Vietnam.

Methods

Literature review

A narrative review was conducted to summarise previous epidemiological studies of the prevalence and factors associated with perinatal depression, as well as its consequences on pregnancy and infant health outcomes, with an emphasis on Asia. Using PubMed and Google Scholar, an initial search for review articles pertinent to the aforementioned study objectives was undertaken, followed by an examination of their reference lists to identify primary reports. Individual articles without available reviews were also retrieved from these two databases. Keywords (e.g., depression, antenatal, antepartum, pregnancy, postnatal, postpartum, perinatal, after childbirth, perinatal depression, determinants, birth outcomes and Asia) were used to search relevant articles with three common Boolean operators “AND”, “OR” and “NOT”.

Study design and participants

This study was part of a large multi-centre prospective cohort study conducted at six hospitals in three cities across northern and southern Vietnam, namely Ha Noi, Hai Phong and Ho Chi Minh City. Dong Anh district hospital (in Ha Noi), Vinh Bao district hospital (in Hai Phong) and three district hospitals (Tan Phu District, Hoc Mon

District, District 2 hospitals) and one obstetrics hospital in Ho Chi Minh City (Hung Vuong obstetrics hospital) were chosen to be the participant recruitment sites. Data were collected from August 2015 to December 2016. Ethics approvals were obtained from Curtin University (HR32/2015) and Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number 05/HPUM RB/2015). Agreements for data collection were obtained from all hospitals involved.

Participants were recruited early in their pregnancy during prenatal care visit. Eligibility criteria were permanent residency in the recruitment areas; ≥18 years of age; at 24-28 weeks of gestation; had a singleton pregnancy; planned to deliver at the recruitment hospital; without any serious pre-existing health condition; and ability to read the information sheet and sign the consent form. Participants were excluded if they became pregnant after infertility treatment such as in-vitro fertilization or intrauterine insemination; reported illness or pre-existing health conditions following advice from their medical doctors; termination of pregnancy, experienced a subsequent still birth or infant death during the follow up period.

Data collection procedure

Pregnant women were screened by trained data enumerators when they came to the local community health centers for their routine antenatal health check. Eligible participants who satisfied the above selection criteria were consecutively recruited until the desired sampling quota of about n=2000 was achieved. The study consisted of five surveys administered at baseline, hospital discharge, and at one month, three months, and six months postpartum. Each survey took approximately 30 minutes to complete. After enrolment, participants were interviewed face-to-face using a

structured questionnaire to obtain detailed information on socio-economic, demographic, family relationship and personal characteristics, as well as lifestyle habits including cigarette smoking and alcohol drinking (using selected questions from the WHO STEPS instrument). Anthropometric (weight, height, waist and hip circumferences) and blood pressure measurements were also taken by trained personnel using standard instruments during the baseline survey. The follow-up surveys were conducted during routine examination of infants at hospital or local community health centres for vaccination.

Measuring instrument

The presence of depressive symptoms was measured using the self-administered validated Vietnamese version of the Edinburgh Postnatal Depression Scale (EPDS), which explored the women's feeling within the last seven days during the antenatal or postnatal period. The instrument consisted of 10 items rated on a 4-point Likert scale (from 0 to 3), reflecting the degree of agreement, with the total score ranging from 0 to 30.

All pregnant women at 24 to 28 weeks of gestation were required to undergo 75-gram oral glucose tolerance test to determine their glucose-metabolic status, by collecting three blood samples at fasting, one hour and two hours. The World Health Organisation's 2013 diagnostic criteria was used to confirm gestational diabetes mellitus (GDM) status.

The Pregnancy Physical Activity Questionnaire, validated for Vietnamese pregnant women, was administered to assess habitual physical activity levels and sedentary

behavior at baseline. It recorded the duration, frequency, and intensity of physical activity in 32 activities across four domains namely household/caregiving, occupation, exercise/sport, and transportation for the past three months. Energy expenditure was reported in terms of metabolic equivalent task (MET) by multiplying each activity's duration and its intensity. The total physical activity level was then calculated by summing up the energy expenditures across all activities.

After giving birth, details of obstetrical and birth outcomes, including maternal disorders and complications during pregnancy, were extracted from medical records. Both mothers and newborns were assessed before discharge from hospital. Detailed information on health problems of both mothers and infants was sought at subsequent follow ups of the cohort at one, three and six months postpartum.

Statistical analysis

Data were entered using Epi-data 3.1, and statistical analyses were performed using the Stata package version 15. Summary and descriptive statistics were first applied to summarise the response rates and participant characteristics, and to describe the cohort profile, exposure and outcome variables. Group comparisons were undertaken using chi-square test or Fisher's exact test for categorical variables, and independent samples t-test/ANOVA or Mann-Whitney U-test and Kruskal–Wallis test for continuous variables.

Multiple linear regression models were fitted to determine the associations between the EPDS depressive symptom scores, exposure variables and other outcome variables of interest such as birth outcomes and infant health problems. Plausible confounding

factors used in the regression models were chosen based on univariate analyses and findings from the literature review. Results were presented in terms of regression coefficients and their corresponding 95% confidence intervals and p values.

Results

Literature review

The literature review revealed that the global estimate of antenatal depression lied within the range 15%-64%, with an average around 21%. The prevalence of antenatal depression was greater in low-income countries and in studies using self-reported measures of depression, with South-East Asia being the region with the highest prevalence (~30%). Major risk factors for antenatal depression were socio-demographic characteristics, lifestyle factors (such as active/passive smoking, low level of physical activity), psychological factors (including history of depression, lack of social support, violence experience) and obstetric parameters (primiparity, unplanned pregnancy, past pregnancy loss). Past research also suggested some association with gestational diabetes, though the relationship appeared to be bi-directional. However, there was a lack of consistency regarding maternal pre-pregnancy body mass index, while little evidence has been obtained with respect to mode of delivery. Most studies investigating antenatal depression in relation to birth outcomes were largely confined to preterm birth and low birthweight. Although the adverse effects of prenatal depression on preterm delivery had been documented, its impact on low birthweight remains inconclusive.

Worldwide, the prevalence of postnatal depression was estimated to be between zero and 60%, with an overall pooled prevalence of about 17%. In Asian countries, the

prevalence ranged from 3.5% to 63.3%, with a mean prevalence around 16%. The most widely adopted screening tool was EPDS, with cut-point scores of above 9 or 12 being commonly applied. Commonly reported determinants of postnatal depression included physical/biological factors (e.g., poor maternal health, gestational diabetes, overweight/obesity before and during pregnancy, reduced physical activity level during the perinatal period), psychological triggers (prenatal depression or anxiety, stressful life events, lack of family and social support), obstetric/paediatric parameters (pregnancy complications, foetal anomalies, history of abnormal pregnancies), and socio-demographic and cultural characteristics (young maternal age, financial difficulties, partner's unemployment or poor education, long confinement period after giving birth). Postnatal depression can have detrimental effects on infant growth and development. Indeed, infants born to depressed mothers were more likely to incur health problems (e.g., hospitalisation, diarrhoea, respiratory infections) in the first year of life.

Cohort profile

From the initial 2030 eligible participants enrolled at the baseline survey, 1906 participants were interviewed at hospital discharge (response rate 93.9%), after exclusion of 124 mothers due to loss of contact, HIV infection, adverse pregnancy outcomes or perinatal deaths. The response rates at one month, three months and six months follow up were about 90%, mainly due to loss of contact or relocation of the participants to another city.

At baseline, nearly two-thirds of the participants were aged between 25 and 35 years. Almost all women were married (99.3%). Worker accounted for the most common

occupation (40.30%). About 17% of the participants were not employed formally and characterised themselves as housewives. Nearly two-thirds of the women achieved high school or higher education level, and less than 10% did not attain secondary school education. Sixty percent of participants were passive smokers, while two-thirds had less than two children. Most of the women had a pre-pregnancy body mass index (BMI) within the normal range for Asian women (18.5-23.0 kg/m^2). Their average physical activity level was 123.2 (SD 56.9) MET-hour/week. Light physical activities accounted for the largest proportion of total physical activity (57.5 MET-hour/week), when participants spent their highest energy expenditure on household chores and/or care giving activities (59.3 MET-hour/week). According to the WHO's 2013 diagnostic criteria, 21% of the participants had GDM.

Antenatal depression

The depressive symptoms scores followed a right skewed distribution (mean 5.1, median 4.0, range 0-27). The observed prevalence of antenatal depression was 7.04% (n=143) if adopting a cut-off score of 13 for EPDS. According to regression analysis, age was weakly and negatively associated with EPDS, whereas a positive association was found for total physical activity level. Women with GDM appeared to experience significantly less depressive symptoms during pregnancy when compared to their non-GDM counterparts. More educated women reported significantly higher EPDS scores. Body mass index was significantly and inversely associated with EPDS, while passive smoking and alcohol drinking during pregnancy showed significant positive associations with EPDS. However, there were no association between EPDS and birth outcomes such as caesarean section, low birthweight and admission to neonatal intensive care unit (NICU).

Postnatal depression at one month postpartum

The EPDS scores were skewed to the right (mean 3.5, median 2.0, range 0-24). The prevalence of postnatal depression was low at 2.8% (n=52) based on the cut-off score of 13 for EPDS. Mothers with adverse birth outcomes (caesarean section, maternal complications, low birthweight, NICU admission or jaundice) reported significantly higher mean EPDS scores than those without such experience. After adjusting for antenatal EPDS, regression analysis showed that passive smoking, caesarean section, maternal complications, jaundice, birthweight, NICU admission and total physical activity level were significantly and positively associated with EPDS at one month postpartum, which elevated the risk for postnatal depression. However, both older mothers and more educated women appeared to be less susceptible to postnatal depressive symptoms.

Postnatal depression at three months postpartum

The EPDS distribution was again right skewed (mean 3.50, median 3.0, range 0-29). The observed prevalence of postnatal depression would be 3.2% (n=59) using a cut-off score of 13. Some positive association was evident between EPDS and infant health problems (hospitalisation, diarrhoea or lower respiratory tract infection) within the first six months. In terms of risk factors, regression analysis found that EPDS at one month and physical activity level during pregnancy were significantly and positively associated with the three months postpartum EPDS. In particular, mothers who reported a high depressive symptom score at one month were more susceptible to postnatal depression later at three months.

Conclusions

This thesis reported findings from the first multi-center prospective cohort study of perinatal depression in Vietnam. In conjunction with the literature review, the study provided updated knowledge about perinatal depression in Vietnam and helped to understand factors influencing antenatal depression and postnatal depression. The results confirmed that the prevalence of perinatal depression remained low in Vietnam. However, the results indicated that younger women and those experiencing adverse birth outcomes were more susceptible to depressive symptoms, while education and physical activity during pregnancy also played a role affecting the mental condition of the mothers.

The findings could contribute to the effective identification of those women at inflated risk of developing depressive symptoms during pregnancy and after childbirth. It also provided evidence-based recommendations for formulating health promotion strategies and intervention programs to deal with perinatal depression, in order to improve the health status of Vietnamese mothers and their offspring. Therefore, the study has important implications on maternal and child health policies, particularly in terms of appropriate education, screening, and early detection of the problem for Vietnamese women

STATEMENT OF CONTRIBUTION

Curtin's School of Public Health provided the environment which supported the PhD candidate to undertake this research. The candidate was the investigator of the project which involved designing methodology, undertaking recruitment, processing data and. writing all parts of the thesis. Details are provided below:

Dr Ngoc Minh Pham was the PhD main supervisor who contributed and supported the study, as well as suggested improvements and revised the thesis.

Professor Andy Lee was the PhD co-supervisor who participated in study design, data analysis, drafting, and suggested improvements for thesis.

Professor Colin Binns was the PhD co-supervisor who provided his expertise on methodology as well as drafting and suggested improvements for the thesis.

ABBREVIATIONS

AKUADS	Aga Khan University Anxiety Depression Scale
BDI	Beck Depression Inventory
CES-D	Centre for Epidemiologic Studies Depression Scale
CI	Confidence Interval
CIDI	Composite International Diagnostic Interview
CIS-R	Clinical Interview Schedule-Revised
DASS	Depression Anxiety Stress Scale
DSM-IV	Diagnostic and Statistical Manual of Mental Disorder 4th edition
DSM-V	Diagnostic and Statistical Manual of Mental Disorder 5th edition
EPDS	Edinburgh Postpartum Depression Scale
EPDS-V	Edinburgh Postpartum Depression Scale – Vietnamese version
GDM	Gestational Diabetes Mellitus
GHQ-12	The 12-item General Health Questionnaire
GWG	Gestational Weight Gain
HADS	Hospital Anxiety Depression Scale
HAM-D	Hamilton Depression Rating Scale
HIV	Human Immunodeficiency Virus
IQR	Inter Quarter Range
K-10	Kessler Psychological Distress Scale
MADRS	Montgomery Asberg Depression Rating Scale
MET	Metabolic Equivalent of Task
NICU	Neonatal Intensive Care Unit
PDS	Pregnancy Depression Scale (the seven items)

PDSS	Postpartum Depression Screening Scale
PHQ-9	Patient Health Questionnaire - 9
PPAQ	Pregnancy Physical Activity Questionnaire
PRQ	The Pregnancy Risk Questionnaire
Rho	Spearman Rank Correlation
SCAN	Schedules or Clinical Assessment in Neuropsychiatry
SCID	Structured Clinical Interview for Depression
SD	Standard Deviation
SCL-90	The Symptom Checklist
SMD	Standardized Mean Difference
SPI	Goldberg's Standardized Psychiatric Interview
UNICEF	United Nations Children's Fund
ZSAS	Zung Self-Rating Anxiety Scale
ZSRD	Zung Self-Rating Depression Scale
WHO	World Health Organisation

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MAIN TERMS

Antenatal depression: is perinatal depression during the pregnancy period (Gavin, Gaynes et al. 2005).

Caesarean birth/caesarean section: is a surgical procedure to deliver a baby through a cut in the mother's abdomen (tummy) and uterus (womb) (Department of Health 2017).

Diarrhoea: is defined as "the passage of three or more loose or liquid stools per day, or more frequently than is normal for the individual (World Health Organization 2019)

Gestational diabetes mellitus (GDM): is carbohydrate intolerance resulting in hyperglycaemia of variable severity with onset or first recognition during pregnancy (World Health Organization 2013).

Gestational weight gain (GWG): pre-delivery weight minus pre-pregnancy weight (Institute of Medicine and National Research Council Committee 2009)

Hospitalisation: refers to any inpatient admission of the infant due to illness or medical problems.

Low respiratory infection: symptoms for a lower respiratory tract infection were "at least specific lower respiratory track sign (fast or difficulty breathing, chest wall

indrawing) and/or abnormal auscultatory findings (crackles/ crepitations or bronchial breath sounds) (Roth, Caulfield et al. 2008).

Perinatal depression: is a common mental problem among women occurring in pregnancy, after childbirth or within the first-year postpartum (Ross, Falhammar et al. 2016).

Physical activity: is any bodily movement produced by skeletal muscles that requires energy expenditure, including activities undertaken while working, playing, carrying out household chores, travelling, and engaging in recreational pursuits (World Health Organization 2017).

Postnatal depression: is perinatal depression within one year postpartum (Gavin, Gaynes et al. 2005).

Pre-pregnancy body mass index (BMI): is calculated by diving pre-pregnancy weight by square height, and categorised according to the WHO Expert Committee on Physical Status (1995)

CHAPTER 1: INTRODUCTION

This chapter provides a snapshot and overview of the study. It includes the background of the study; description of study sites and setting; the significance, aim and objectives; scope and outline; and definitions of main terms used in this chapter.

1.1. Antenatal and postnatal depression

Perinatal depression includes minor and major depressive episodes that occur either during pregnancy or within the first twelve months postpartum (Gavin, Gaynes et al. 2005). During pregnancy, women are at greater risk of antenatal depression. It is estimated that the rate of antenatal depression ranges from 15% to 65% globally (Dadi, Miller et al. 2020). The incidence and prevalence of antenatal depression are higher in women with low social support and socioeconomic status, younger age and lower education (Austin and Lumley 2003, Field 2017). Antenatal depression has adverse effects on both maternal and infant health (Field, Diego et al. 2010, Field 2011). Women with antenatal depression are found to have higher anxiety, poor health and greater risk of obstetric complications (Field, Diego et al. 2010, Accortt, Cheadle et al. 2015). Furthermore, antenatal depression is associated with postnatal depression (Austin and Lumley 2003).

After delivery to twelve months postpartum, new mothers may suffer from postnatal depression. It is a debilitating mental and behavioural disorder with prevalence ranges from zero to more than 64% worldwide (Austin and Lumley 2003, Williamson and McCutcheon 2004, Halbreich and Karkun 2006, Klainin and Arthur 2009, Jones and

Coast 2013, Arifin, Cheyne et al. 2018, Shorey, Chee et al. 2018). Higher rates have been reported from Chile, Italy and Taiwan, and lower rates in Denmark, Singapore and Malaysia (Williamson and McCutcheon 2004, Yusuff, Tang et al. 2016). The difference in postnatal depression rates may be explained by the differences in socio-economic status, cultural factors and postpartum support (Boyce 2003, Williamson and McCutcheon 2004, Underwood, Waldie et al. 2016).

Postnatal depression may have serious consequences, not only for the women but also for their infants and families (Avan, Richter et al. 2010, Mohamad Yusuff, Tang et al. 2015, Shrivastava, Shrivastava et al. 2015). It has been reported that perinatal depression is associated with poor support from husband and relatives, lower quality interactions between mothers and their children, child insecurity, attached relationships, and early termination of breastfeeding (Williamson and McCutcheon 2004).

In Vietnam, several studies have been conducted to assess the prevalence, incidence of perinatal depression, its risk factors and consequences as well. However, these studies mostly focused on postnatal depression and based on a small group of participants in a particular area. In addition, data is lacking with respect to relationship between antenatal and postnatal depression, which has been investigated in other countries (Underwood, Waldie et al. 2016). Moreover, few studies have address perinatal depression in relation to birth outcomes and infant health problems.

1.2. Background information

Vietnam is a developing country in South-eastern Asia bordering China, Laos, Cambodia and the Eastern Sea. Its land is more than three hundred thousand square kilometres, of which about 75% is highlands and mountainous areas, 25% is river deltas and lowlands (General Statistics Office of Vietnam 2017, Ministry of Foreign and Affairs 2019). Two main agriculture areas are Mekong delta in the South and Red river delta in the North (Ministry of Foreign and Affairs 2019). The Vietnam administration system is divided into four levels: central, city/province, district and community. The country comprises of 63 provinces, 713 districts and 11,162 communes, wards and town districts. About 65.5% of the population live in rural areas and 34.5% live in urban areas (General Statistics Office of Vietnam 2017). Figure 1.1. shows the map of Vietnam (Vietnam Government Portal 2017).

The population of Vietnam was approximately 96.2 million in 2017 and ranked the 15th most populous country in the world (General Statistics Office of Vietnam 2017, United Nations 2017). The urban population was nearly 34.7%. Vietnam has 54 ethnic groups. Almost all ethnic minority groups are scattered in the highlands and mountainous areas. Kinh is the predominant group accounting for about 85% of the Vietnamese population. They mainly live in delta regions and lowland areas (United Nations 2017).

Vietnam has recognised more than 37 religions in which Buddhism is the most popular. It is followed by Catholicism (about 6.5 million), Protestantism (about 1.5 million) and Muslim (about 80 thousands) (Ministry of Foreign and Affairs 2019). In 2017, the literacy rate of the population aged 15 and older was 93.5%. This rate was

slightly higher in urban than rural areas (97% versus 92%) and in males than females (95.8% versus 92%) (General Statistics Office of Vietnam 2017).

Figure 1. 1. Map of Vietnam

Source: (Vietnam Government Portal 2017)

Two decades ago, Vietnam was one of the poorest countries. Thanks to the extensive economic and political reforms (called Doi Moi), Vietnam has become a middle-income country, with gross domestic income (GDP) per capita being US$2015 (United Nations 2017). It has attained five of the ten Millennium Development Goals, and

likely achieved two more in 2015 (World Bank 2017). Vietnam has a comprehensive health care network from the central down to the grass root level in private and public health sectors. The World Health Organisation recognised Vietnam in providing an excellent health care service based on its spending. Nevertheless, the health situation of Vietnamese people has not improved as much as expected. They have been coping with communicable diseases, poor sanitation, lack of safe drinking water and inadequate nutrition (Matsuda 1997). Vietnam is now facing new challenges such as mental health problems, ageing population and non-communicable diseases (Pham, Au et al. 2009, Van Minh, Do et al. 2014). Table 1.1 summaries information about population, economy and health issues of Vietnam.

Table 1. 1. Basic information on Vietnam

Category	Value
Surface area (land, square km)	330,967
Population (million)	96.408
Less than 35 years of age (%)	55.5
Human Capital Index	0.69
GDP per capital (USD)	2015
Health expenditure (% of GDP)	5.7
Gross domestic product growth rate (annual %)	7.0
Poverty rate (US$3.2/day PPP, %)	<6
Access Electricity (%)	99
Access cleaning water (%)	70
Life expectancy at birth (years)	76
Infant mortality rate (per 1000 live birth	16.7

Source: (United Nations 2017, United Nations 2021, World Bank 2021)

1.3. Study design and data collection

A hospital-based prospective cohort study was conducted in Ho Chi Minh City, Hai Phong and Ha Noi since August 2015 and December 2016. Ho Chi Minh City is in the South Vietnam. It is the most industrialised and populated city with nearly 8.3 million people. Ha Noi is the capital of Vietnam. It is in the north with 7.3 million people living in an area of 3.4 thousand square kilometres. Hai Phong is a coastal city in the northern region with approximately two million residents (General Statistics Office of Vietnam 2017). Data were retrieved from medical records and collected from face-to-face interviews. Interviewers were female medical workers and well trained. Questionnaires used in this study have been validated.

1.4. Aim and objectives

Aim: To investigate antenatal and postnatal depression, and their association with maternal characteristics and birth outcomes in Vietnam.

Objectives:

1. To review the epidemiology of perinatal depression in Asia.
2. To determine the prevalence of antenatal depression in Vietnam and its associated maternal and risk factors including demographic and lifestyle characteristics, physical activity during pregnancy, maternal body mass index before pregnancy and gestational diabetes mellitus.
3. To ascertain the association between antenatal depression and birth outcomes in Vietnam.
4. To determine the prevalence of postnatal depression at one month postpartum and its associated factors in Vietnam.

5. To determine the prevalence of postnatal depression at three months postpartum and its associated factors in Vietnam.

6. To examine the prospective association between postnatal depression at three months postpartum and infant health problems at six months in Vietnam.

1.5. Significance

This study is important for the following reasons. It provides updated knowledge about antenatal and postnatal depression in Vietnam, helping to understand factors influencing maternal depression in terms of demographic, physical, psychological, obstetric and cultural contexts. Moreover, the prospective cohort study ascertains the apparent relationship between antenatal depression and postnatal depression, which has the potential for the effective assessment of women at inflated risk of depression after childbirth. Finally, the study provides evidence-based recommendations for developing health promotion strategies and intervention programs to deal with maternal depression, to improve the health status of Vietnamese mothers and their offspring. Vietnam is a developing country with a fast-growing economy. In view of the rapid socio-economic and lifestyle changes of the Vietnamese population, the findings are timely and have important implications on maternal and child health policies. In particular, the epidemiological information obtained would enable appropriate screening and early detection of the problem for Vietnamese women.

1.6. Scope and outline

This thesis reported the findings from a prospective cohort study of antenatal and postnatal depression in Vietnam. The participants consisted of 2030 pregnant women recruited from three cities, namely Ho Chi Minh City, Ha Noi, Hai Phong, which are

in the south (Ho Chi Minh City) and the north (Ha Noi and Hai Phong) of Vietnam. They were recruited from six hospitals at their 24-28 weeks of gestation; and followed up until six months postpartum with five times data collections at baseline, hospital discharge, one, three and six months postpartum.

The mothers were interviewed face-to-face by well-trained interviewers using structured questionnaires to collect information on demographic characteristics, depressive symptoms and other outcomes. Data were analysed and presented in the form of descriptive statistics using univariate analysis. Multivariable regression analyses were then performed to determine the association between the exposure variables and the outcome variables of interest.

The thesis is presented as follows:

Chapter 1. Introduction: Provides a brief introduction about antenatal and postnatal depression. It also states the aim, objectives, significance, and locations of the study.

Chapter 2. Literature review: Reviews the literature on antenatal and postnatal depression, their risk factors and effects, such as physical activity, GDM, obstetric complications, adverse birth outcomes, maternal morbidity, etc.

Chapter 3. Methodology: Describes the study methodology including the study design, data collection procedure, research instruments, data management, statistical analysis and ethical considerations.

Chapter 4. Results: Presents the results of the study from univariate and multivariable regression analyses.

Chapter 5. Discussion: Discusses the research findings in relation to the literature and previous reports, together with the strength and limitations of the study.

Chapter 6. Conclusion: Summarises the main findings, gives conclusion; and provides recommendations.

Appendices include Ethics approval letters, information sheet, consent form, instruments and survey questionnaires, and other relevant documents.

CHAPTER 2: LITERATURE REVIEW

In this chapter, an in-depth review of the literature on the epidemiology of perinatal depression is presented. In the first part, maternal depression and its pathophysiology are described. Perinatal depression and associated factors in Asian countries in general and in Vietnam particularly are also reviewed, followed by factors associated with antenatal and postpartum depression. This chapter also provides a detailed review of antenatal and postpartum depression in relation to demographic and lifestyle characteristics (e.g., physical activity during pregnancy, smoking), gestational weight gain (GWG) and gestational diabetes mellitus (GDM).

2.1. Definition

The perinatal period represents a critical time of transition for the mothers and their families. It may be influenced by many factors, including environmental, social, psychological, behavioural, and biological forces (Misra, Guyer et al. 2003). Depressive disorders during pregnancy and after giving birth are common medical illnesses manifested by the feelings of emptiness, sadness, or irritability together with cognitive and somatic changes (American Psychiatric Association 2013). Perinatal depression implies the experience of minor or major depressive episodes during pregnancy or within one year after childbirth (National Institute of Mental Health , Seth, Lewis et al. 2016). Perinatally depressed mothers commonly express feelings of extreme sadness, frequent crying or weepiness, anxiety, trouble sleeping, fatigue or low energy, decreased appetite and lack of enjoyment. These manifestations can prevent the mother from undertaking daily tasks, including caring for themselves or

others (Belmaker and Agam 2008). Perinatal depression lasts more than 14 days and impairs a woman's quality of life (Van Niel and Payne 2020).

2.2. Pathophysiology

Biologic mechanisms of perinatal depression are not well understood; however, it has been suggested that hormonal factors, genetics, immune function and environmental influencers are possible culprits (Belmaker and Agam 2008, Stewart and Vigod 2019). Human and animal studies concerning perinatal depression provide valuable insights into the understanding of potential mechanisms, therefore can help early identify women at increased risks of perinatal depression.

2.2.1. Hormonal factors

Pregnant and postpartum mothers experience rapid changes in reproductive steroid hormones, progesterone and oestrogen (Mastorakos and Ilias 2003, Kuijper, Ket et al. 2013), which are derived from cholesterol as the major precursor. These hormones have been suggested to play important roles in emotional and cognitive functioning as well as motivation (Rubinow 2005, Albert, Pruessner et al. 2015), and thus may contribute to the aetiology of perinatal depression. They are also known to control different biological systems involving major depression, such as lactogenic hormones, the immune system, thyroid function, the hypothalamic–pituitary–adrenal (HPA) axis, and genetic expression (Schiller, Meltzer-Brody et al. 2015). In addition, brain scanning has indicated that reproductive hormones regulate the neurocircuitry that can influence affective states (Berman, Schmidt et al. 1997, Goldstein, Jerram et al. 2005, Protopopescu, Pan et al. 2005). Evidence suggested that perinatal changes in allopregnanolone, a major progesterone metabolite, may be involved in perinatal

depression (Epperson, Gueorguieva et al. 2006, Deligiannidis, Sikoglu et al. 2013, Schiller, Meltzer-Brody et al. 2015). Allopregnanolone, a modulator of γ-aminobutyric acid (GABA) receptors, is demonstrated to trigger both anxiety and depression through GABA receptors (Schiller, Meltzer-Brody et al. 2015).

There is growing evidence that abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis activity play a key role in the aetiology of both major depressive symptoms and postpartum depression (Magiakou, Mastorakos et al. 1996, Bloch, Daly et al. 2003, Bloch, Rubinow et al. 2005). Progesterone and oestrogen have profound interactions with the HPA axis (Oyola and Handa 2017) and may therefore induce the HPA axis abnormalities in vulnerable women. The HPA has been acknowledged as an important inducer of perinatal mental illnesses (Seth, Lewis et al. 2016) and has been implicated in the pathogenesis of perinatal depression (Dickens and Pawluski 2018).

2.2.2. Genetic factors

Accumulating evidence has suggested that perinatal depression may have a genetic predisposition (Payne and Maguire 2019, Stewart and Vigod 2019). For instance, postpartum depression has been associated with genetic polymorphisms based on twin and family studies (Forty, Jones et al. 2006). Genetic studies of postpartum depression have found some similar polymorphisms identified in non-perinatal depression, like Val66Met polymorphism of brain-derived neurotrophic factor (Figueira, Malloy-Diniz et al. 2010). Genetic variations on chromosome 1q21.3–q32.1 and 9p24.3–p22.3 as well as in Hemicentin-1, which contain several oestrogen-binding sites, have been found in genome-wide linkage studies of over 1200 women (Mahon, Payne et al.

2009). A recent large-scale epidemiological study also found that antenatal depression is heritable (Viktorin, Meltzer-Brody et al. 2016).

2.2.3. Immune factors

During pregnancy, several anti-inflammatory cytokines (e.g., adiponectin, interleukin [IL]-1 receptor antagonist, IL-4, IL-6, IL-10, IL-11, and IL-13) are elevated to boost women's immune system to protect the foetus. After giving birth, the immune system soon becomes proinflammatory and exists for a period of time. Compared with women who are not depressed, those with postnatal depression appear to have different gene expression related to immunity (Segman, Goltser-Dubner et al. 2010). Findings of prenatal and postnatal immune markers in relation to perinatal depression remain contradictory or unclear (Krause, Jobst et al. 2014, Schiller, Meltzer-Brody et al. 2015) and thus further research is required.

2.2.4. Environmental factors

Past life adverse events, history of anxiety disorders and depression, sociocultural factors, psychological attributes and coping skills have been found to increase the risk for postpartum depression (Payne and Maguire 2019). There was a myriad of factors associated with antenatal depression included high perceived stress, personal history of mental illness, being from the culturally and linguistically diverse population and low socioeconomic status, history of intimate partner violence, lack of partner support, unplanned or unwanted pregnancy, pregnancy loss and pregnancy complications (Zauderer and Galea 2010, Ogbo, Eastwood et al. 2018). Potential causal factors for perinatal depression will further be reviewed in the epidemiology section.

2.3. Search strategy

The PubMed database was used to identify articles relevant to the study objectives using the Medical Subject Heading (MeSH) search terms. The Google Scholar was also employed to complement the search. The Boolean operators "AND", "OR", and "NOT" were utilised to narrow or broaden searched results. The word "Asia" and/or "Asian" was added to the search when research information in this region was focused. Review papers (i.e., systematic review and meta-analysis, narrative review and umbrella review) was attempted for an initial search. The reference lists of retrieved review articles were examined to create a further batch of primary papers. As with review papers, individual studies were identified using the following keywords.

To review data on perinatal depression prevalence the following keywords were used: *perinatal depression, prenatal/antenatal depression, depression during pregnancy, postnatal depression, maternal depression after delivery AND prevalence OR distribution. Similar words such as depressive symptoms, peripartum, antepartum, postpartum AND prevalence OR distribution were used to maximise the result of search.*

To summarise major determinants of perinatal depression, the MeSH terms for depression as presented above together with the followings were used: *risk factors, predictors, causes, determinants, correlates, associated factors, triggers, harbingers, contributors, inducers, influencers.*

Regarding the consequences of perinatal depression, the following additional terms were used together with keywords for depression: *effects, consequences, complications*

To search for available measuring tools for perinatal depression, the following terms were used: *Measuring, screening, diagnosis, assessing, ascertaining, identifying*

To review interventions for perinatal depression, the following keywords were used: *consulting, home-based intervention, work-based intervention, psycho-educational intervention, psychosocial intervention, psychotherapy, paraprofessional intervention, women's groups intervention, community-based intervention, treatment, prevention.*

2.4. Assessment of perinatal depression

Depression is characterised by a combination of symptoms rather than a single entity, and there are many measurement scales in use. Individuals often present with widely differing symptoms, and it is not possible to diagnose depression based on a single manifestation. Depressive symptoms are frequently classified into affective (sadness, crying, apathy), cognitive (thoughts of worthlessness, hopelessness, helplessness, guilt, suicide,), and somatic (change in energy level, sleep disturbance, sleep, elimination, appetite) (Friedman and Anderson 2014). However, not all manifestations are present in each person. Depression measurements are divided into two major groups: diagnostic tools and non-diagnostic screening instruments, with the former commonly used in clinical practice and the latter for epidemiological studies. Diagnostic tools are considered as the "gold standard" for assessing depression and

other psychiatric disorders. Commonly used diagnostic tools are the seven-item Pregnancy Depression Scale (PDS) (Altshuler, Cohen et al. 2008), Schedules for Clinical Assessments in Neuropsychiatry (SCAN) (World Health Organization. Division of Mental Health 1994), Structured Clinical Interview for Depression –SCID (Spitzer, Williams et al. 1992), Composite International Diagnostic Interview (CIDI) (Robins, Wing et al. 1988), Goldberg's Standardized Psychiatric Interview (SPI) (Goldberg 1972), the Raskin Depression Rating Scale (Raskin, Schulterbrandt et al. 1969), the Montgomery-Asberg Depression Rating Scale (MADRS) (Montgomery and Asberg 1979), and the Hamilton Depression Rating Scale (HAM-D) (Hamilton 1960). However, these methods remain questionable regarding their feasibility and practicability in large-scale epidemiological studies (Baggaley, Ganaba et al. 2007, Spies, Stein et al. 2009). A formal diagnosis of depression needs to exclude other symptoms like depression, and this normally requires a clinical examination. The DSM-V (American Psychiatric Association 2013), for example, should rule out alternative explanations such as the physiological effects of drugs or medications and medical conditions such as hypothyroidism or schizophrenia. Accordingly, non-diagnostic screening tools are widely utilized to identify people at risk of depression in the general population.

Screening tools have speed, economy and objectivity, but generally have a lower level of accuracy compared to the lengthier and more complex clinical diagnostic instruments. A large number of screening tools have been developed and used to detect perinatal depression (Ukatu, Clare et al. 2018). They include the Beck Depression Inventory (BDI), the Center for Epidemiologic Studies Depression Scale (CES-D), the Edinburgh Postnatal Depression Scale (EPDS), the General Health Questionnaire-

12(GHQ-12), the Patient Health Questionnaire 9 (PHQ-9), the Postpartum Depression Screening Scale (PDSS), the Pregnancy Risk Questionnaire (PRQ), and Zung Self-Rating Depression Scale (ZSDS) (Sit and Wisner 2009, American College of Obstetricians and Gynecologists 2018, Ukatu, Clare et al. 2018). These tools have various levels of sensitivity and specificity, and the choice of each instrument depends on the goal of assessment and available resources. Because EPDS is the most widely used to screen perinatal depression (Gibson, McKenzie-McHarg et al. 2009, Kozinszky and Dudas 2015, Levis, Negeri et al. 2020), its details are described below.

The EPDS was originally developed in the UK by Cox et al. in 1987(Cox, Holden et al. 1987). It assesses emotional experiences over the past week using ten Likert-scale items (10-item self-report questionnaire). Each question is scored 0–3 (resulting range 0–30), with a higher score indicating the presence of depression, and completion takes around five minutes. It was initially designed to ascertain postnatal depression for the purposes of clinical practice and research. Subsequent studies showed that it is also valid for assessing antenatal depression (Murray and Cox 1990, Gibson, McKenzie-McHarg et al. 2009, Kozinszky and Dudas 2015, Levis, Negeri et al. 2020). Choosing a suitable cut-off score using the EPDS tool to define perinatal depression is of interest to researchers and clinical psychiatrists. In their original work, Cox and his colleagues reported that the sensitivity, specificity and positive predictive value of EPDS was 86%, 78% and 73%, respectively, when a cut-off score 13 was used (Cox, Holden et al. 1987). They also showed that a more conservative cut-off-point of 10 or more could reduce the failure to identify postpartum depression by less than 10%. A meta-analysis of eleven EPDS validation studies found that optimal cut-off-point for prenatal major depression was in the range of 5.5 and 14.5, and the corresponding data for perinatal

depression varied from 4.5 to 13.5 (Kozinszky and Dudas 2015). The estimates of sensitivity for major depression and combined depression were in the range of 70%-100% and 64%-87%, respectively. The corresponding values of specificity for the two forms of depression were 74%-97% and 73%-96%, respectively. According to this meta-analysis, using a cut-off score of 10, the sensitivity across trimesters varied from 81% to 88% (major depression), 75%-87% (combined depression) and the correspondent specificity was 91%-97% and 92%-96%, respectively. An early systematic review and meta-analysis of 37 studies reported that most of the included studies used cut-off-points of 10 and 13 to define possible minor and major depression, respectively. A more recent individual participant meta-analysis obtaining data from 58 studies (15,557 participants) documented that pooled sensitivity and specificity of the EPDS to screen prenatal and postnatal depression were 85% and 84%, respectively, for the cut-off-point of 10, and the respective results for the cut-off-point of 13 were 66% and 95%. It is noted, however, that the selection of an appropriate cut-point of this tool to define perinatal depression should both be culturally and scientifically validated.

2.5. Epidemiology of perinatal depression in Asia

2.5.1. Prevalence of antenatal depression

Antenatal depression is one of the most common mental disorders occurring during pregnancy. It does not only affect the mother's mental and physical well-being but also the foetus and the child during infancy and in later life (Dadi, Miller et al. 2020). According to a recent umbrella review of ten review studies on antenatal depression prevalence, the estimated data worldwide varied from 15 to 65%, with the prevalence being greater in low- and middle-income countries than their developed counterparts

(Dadi, Miller et al. 2020). Of 244 individual studies included in the review, the common screening tools used was EPDS followed by CES-D and BDI. In fact, a more recent meta-analysis that was not included in the above umbrella review yielded an overall pooled prevalence of 11.9% (95% CI: 11.4-12.5%) (Woody, Ferrari et al. 2017). The most updated and comprehensive meta-analysis including 173 studies with 182 reports involving 197,047 subjects showed the pooled prevalence estimate of antenatal depression worldwide was approximately 21% (Yin, Sun et al. 2021). Of the depression screening tools used, EPDS was the most common measure, followed by CES-D and BDI. For EPDS, there was a variation in cut-off-point scores ranging from 9 to 13.

There were notable differences in antenatal depression prevalence among Asian countries. In South Asia, a meta-analysis of 33 studies comprising 13,087 pregnant women reported an overall pooled prevalence of prenatal depression was 24.3% (95% CI: 19.0 – 30.5%) (Mahendran, Puthussery et al. 2019). Studies included in this review were largely conducted in Pakistan, followed by India, with fewer studies being undertaken in Bangladesh, Sri Lanka, Maldives and Nepal. EPDS was also the most widely utilised to ascertain prenatal depression. Other tools were the Aga Khan University Anxiety Depression Scale (AKUADS), BDI, CES-D, Depression Anxiety Stress Scale (DASS-42), Hamilton Depression Scale (HAM-D), Hospital Anxiety Depression Scale (HADS), Kessler Psychological Distress Scale (K-10), the Montogomery and Asberg Depression Rating Scale (MADRS), and PHQ-9. According to the systematic review and meta-analysis, the estimates of antennal depression for India and Sri Lanka were 17.74% (95% CI: 11.19 - 26.96) and (12.95%, 95% CI: 8.29 - 19.68), respectively. Meanwhile, the respective data for Maldives,

Pakistan and Nepal were 24.02 (95% CI: 20.32 - 28.14), 32.0% (95% CI: 23.11 - 42.87) and 50% (95% CI: 35.64 - 64.36). High rates of antenatal depression (19%) were also found in Jordan in a sample of 353 women (Mohammad, Gamble et al. 2010).

In East Asia, the rates of antenatal depression are seemingly similar to those in Western countries, such as 18.1-20.1% in Hong Kong, 20% in Taiwan, 5.6% in Japan and 4.8% in China(Schatz, Hsiao et al. 2012). However, the estimates of antenatal prevalence are variable due to the difference in the screening tools used and cut-off-points adopted, sample sizes and pregnancy trimesters under study. A more recent systematic review and meta-analysis of 95 studies in China, for example, reported a relatively high prevalence of antenatal depression (Nisar, Yin et al. 2020). In this review, the most used scales to detect perinatal depression were the EPDS (n = 55), followed by the ZSRD (n = 18), CES-D Scale (n = 5), HADS (n = 5), GHQ-12 and others (n = 5). Only two studies used a diagnostic interview using DSM-IV or the Symptom Checklist (SCL-90). Of the 95 studies included in the review, 33 ones showed a pooled antenatal depression prevalence of 19.7% (95% CI: 15.8% - 24.2%). This result is comparable to a relatively high rate of antenatal depression (19%) reported in a sample of 353 women in Jordan, a representative country from the Middle-East (Mohammad, Gamble et al. 2010). A newly published meta-analysis including 47 studies from Asia reported that the prevalence of antenatal depression in Southeast Asia and Western Pacific Region was 29.4% (95% CI: 18.8 -40.0) and 19.2% (95% CI: 16.8-21.6), respectively (Yin, Sun et al. 2021).

2.5.2. Determinants of antenatal depression

Despite the lack of understanding about antenatal depression causation, accruing evidence has suggested protective and risk factors of depression during pregnancy. Factors putatively contributed to the occurrence of antenatal depression have largely been studied using a conceptual model of bio-psychosocial mechanisms. Accordingly, an interaction of vulnerability, precipitating and sustaining factors of perinatal depression has been reported in the literature (Leigh and Milgrom 2008). In a recent systematic review of determinants of antenatal depression, it was recommended that determinant factors of antenatal depression have been less studied in low- and middle-income countries (Woody, Ferrari et al. 2017). In the next section, determinants of antenatal depression are discussed.

2.5.2.1. Demographic and lifestyle predictors of antenatal depression

Socio-demographic determinants of prenatal depression reported consistently across the different regions are low socio-economic status or financial difficulty, marital status (separate/single), length of marital relationship, low education level, age and ethnicity (Ryan, Milis et al. 2005, Adewuya, Ola et al. 2007, Ogbo, Eastwood et al. 2018, Mahendran, Puthussery et al. 2019, Dadi, Miller et al. 2020, Nisar, Yin et al. 2020, Van Niel and Payne 2020). A systematic review of 97 papers found a large number of studies showing a significant correlation between antenatal depression and young age at birth (Biaggi, Conroy et al. 2016). Indeed, adolescents were at increased risk of being depressed during pregnancy. However, a small proportion of studies included in that review suggested a positive association between older age and antenatal depression. Other demographic factors correlated with antenatal depression reported in the literature were unemployment, ethnicity, family conflicts, housewife,

farmers, and food insecurity (Biaggi, Conroy et al. 2016, Ogbo, Eastwood et al. 2018, Nisar, Yin et al. 2020). In a newly published systematic review and meta-analysis, Yin and colleagues reported that unemployed women were 2.4 times more likely to experience depressive symptoms during pregnancy (95% CI: 1.76-3.29) (Yin, Sun et al. 2021). A similar risk of antenatal depression was also found for single status compared with married status (OR: 2.37; 95% CI: 1.80-3.13). Women with low social support had about a three-fold increased risk of antenatal depression compared to those with high level of social support.

Accumulating studies have also reported lifestyle factors in relation to antenatal depression. An umbrella review of ten reviews involving 306 primary studies and 877,246 participants indicated that smoking, alcohol drinking and illicit drug use were predictive of antenatal depression (Dadi, Miller et al. 2020). Notably, smoking before pregnancy and during pregnancy were significantly associated with antenatal depression as documented in a newly released meta-analysis, with the respective ORs (95% CI) of antenatal depression being1.97 (1.63–2.38) and 2.04 (1.41–2.95) as compared to non-smoking women (Yin, Sun et al. 2021). However, findings remain inconsistent regarding the role of diet and nutrition supplementation in antenatal depression (Sparling, Henschke et al. 2017). Another common lifestyle factor is physical activity which has been found to be related to depressive symptoms during pregnancy. A systematic review including 17 primary studies suggested that physical activity during pregnancy may reduce the onset of antenatal depression and its severity (Kolomanska, Zarawski et al. 2019). Due to the lack of studies necessary for performing meta-analysis of physical activity/exercises and antenatal depression, there is a further need for undertaking original studies on this topic to quantify the effect of

and/or association between antenatal depression and exercises/habitual physical activity during pregnancy.

In addition to socio-demographic characteristics and lifestyle behaviours, antenatal depression was reported to be related to psychological and obstetric factors. Women with a history of depression was 3.17 times more likely to incur depressive symptoms during pregnancy as reported by Yin and colleagues in a meta-analysis (Yin, Sun et al. 2021). According to their analysis, women who experienced violence in life (e.g., partner or family violence) had a significantly 2.72 times higher risk of being depressed during pregnancy. As with previous studies, Yin and colleagues' meta-analysis confirmed the positive association of primiparity and unplanned pregnancy with antenatal depression.

2.5.2.2. Maternal pre-pregnancy body mass index and gestational weight gain and gestational diabetes mellitus in relation to antenatal depression

Body mass index is commonly used to represent total body fat mass (Sommer, Teufer et al. 2020), and high BMI has considerably contributed to the global burden of chronic diseases (Lin, Xu et al. 2020). Elevated BMI has also been associated with mental health disorders in general adults and women in the perinatal period (Molyneaux, Poston et al. 2014, Amiri, Behnezhad et al. 2018). An increasing number of studies have investigated pre-pregnancy maternal BMI in relation to antenatal depression, and their results are not entirely consistent. An earlier meta-analysis of 29 antenatal depression found maternal overweight and obesity before pregnancy were significantly associated with higher depressive symptoms during pregnancy; the

respective ORs (95% CI) were 1.19 (1.09 – 1.31) and 1.43 (1.27 – 1.61). Despite pooled data suggested a positive association, there was a moderate heterogeneity among included studies (I^2 = 44.4%, p <0.05). Moreover, of 28 primary reports used to meta-analyse obesity in relation to antenatal depression, there were 19 studies showing no significant association while one study displayed an inverse association. An updated meta-analysis including 13 studies confirmed maternal obesity before pregnancy was significantly associated with antenatal depressive symptoms (overall summary OR: 1.33; 95% CI: 1.20 – 1.48) (Dachew, Ayano et al. 2021). However, pooled results showed no significant association for maternal underweight or overweight. Of 8 data points addressing the overweight-antenatal depressive symptoms association, only two supported a positive association while five displayed no significant association and one found an inverse association. In the meta-analyses, the majority of primary studies was conducted among Western populations and common depression screening tools were CES-D in the old and EPDS in the latest meta-analysis (Molyneaux, Poston et al. 2014, Dachew, Ayano et al. 2021).

Gestational diabetes defined as any glucose intolerance with first diagnosis during pregnancy (Metzger, Buchanan et al. 2007), is a crucial health concern for both the mother and infant (Koning, Hoogenberg et al. 2016). It has been linked to mental health illness during pregnancy, including antenatal depression (Riggin 2020). Evidence suggests that there is a bidirectional relationship between GDM and antenatal depression. GDM may occur due to elevated cortisol excretion and increased insulin resistance as a result of hypothalamic-pituitary-adrenal hyperactivity – a hypothesis of depression pathophysiology (Belmaker and Agam 2008). In addition, antenatal depression may lead to GDM through increased levels of inflammatory

markers (e.g., tumour necrosis factor-alpha, c-reactive protein and interleukin-6), and increased subclinical inflammation has been implicated in the pathophysiology of GDM (Plows, Stanley et al. 2018). On the other hand, GDM may increase the risk of antenatal depression through the reverse mechanism, such as inflammatory changes cause depression and hypothalamic-pituitary-adrenal dysregulation and (Azami, Badfar et al. 2019). A recent meta-analysis of 34 studies addressing GDM in relation to depression during pregnancy showed that gestational diabetic mothers were two times as likely to experience depressive symptoms during pregnancy as compared to their gestational non-diabetic counterparts (Wilson, Newham et al. 2020). Similarly, women with GDM had greater mean EPDS scores during pregnancy relative to those without pregnancy complications (Mautner, Greimel et al. 2009).

2.5.2.3. Antenatal depression and birth outcomes

Numerous studies have reported that antenatal maternal depression is associated with adverse effects upon birth outcomes, though results are not entirely consistent (Grote, Bridge et al. 2010, Grigoriadis, VonderPorten et al. 2013, Accortt, Cheadle et al. 2015, Dadi, Miller et al. 2020, Fekadu Dadi, Miller et al. 2020). In addition, antenatal depression is associated with abnormal infant and child development, as well as cognitive problems and psychopathology in the offspring. An earlier systematic review and meta-analysis of 29 original studies reported that antenatal depression, regardless of measurement (i.e., categorical or continuous), was associated with modest but statistically significant increased risks of preterm birth, low birthweight and intrauterine growth restriction (Grote, Bridge et al. 2010); pooled relative risks (95% CI) were 1.39 (1.19-1.61), 1.49 (1.25-1.77), and 1.45 (1.05-2.02), respectively, when compared antenatally depressed mothers with their prenatally non-depressed

counterparts. Similarly, a meta-analysis published in 2013 including 30 original articles concluded that there was a significantly positive association between antenatal depression and preterm delivery (OR: 1.37; 95% CI: 1.04-1.81); however, neither birthweight nor low birth weight was significantly associated with antenatal depression (Grigoriadis, VonderPorten et al. 2013). Such review found lack of significant association between antenatal depression and APGAR scores at 1 ad 5 minutes. Consistent with pooled results of the meta-analysis by Grote et al (Grote, Bridge et al. 2010), Accortt and his colleagues stated that less than a quarter of 50 published articles showing prenatal depression was significantly associated with preterm birth while slightly more than half of the 33 reports displaying a significant association between prenatal depression and low birthweight or birthweight (Accortt, Cheadle et al. 2015). A recent umbrella review comprising six reviews (39 studies with 75,451 participants) was undertaken to investigate the impact of prenatal depression on preterm birth and low birthweight (Dadi, Miller et al. 2020). Similar to prior systematic reviews and meta-analyses (Grote, Bridge et al. 2010, Grigoriadis, VonderPorten et al. 2013, Fekadu Dadi, Miller et al. 2020), preterm birth and low birthweight was each significantly associated with prenatal depression; the respective odds ratios (95% CI) were 1.49 (95%CI: 1.32-1.68) and 1.39 (95%CI: 1.22-1.58). It is noted, however, that one review found no association for low birthweight (Grigoriadis, VonderPorten et al. 2013) and the other yielded inconclusive results (Accortt, Cheadle et al. 2015). In low- and middle-income countries, women with prenatal depression are also more likely to deliver preterm and low birthweight babies, with the odds ratios of (95% CI) 2.68 (1.89-3.79) and 1.66 (1.06-2.61), respectively (Grote, Bridge et al. 2010, Grigoriadis, VonderPorten et al. 2013, Fekadu Dadi, Miller et al. 2020). In summary, most of studies to date investigating the effect of antenatal depression on

birth outcomes have largely focused on preterm birth and low birthweight. Although pooled findings from systematic reviews and meta-analyses support an adverse association between prenatal depression and preterm delivery or low birthweight, a number of primary reports showed null or inconclusive results. In addition, antenatal depression in relation to birth outcomes has been less studied among Asian women and thus requires further investigations in this region.

2.5.3. Prevalence of postnatal depression

Postpartum depression is a debilitating mental illness representing an important public health problem. It can affect the mother, the infant and their family (World Health Organization 2008). Its prevalence is highly variable among countries, with earlier reviews showing the global estimates of postnatal depression prevalence ranging from zero to 60% and from 3.5% to 63.3% in Asian countries (Halbreich and Karkun 2006, Klainin and Arthur 2009). A recent systematic review included 124 studies from over 50 countries in different continents (58 in Asia, 22 in North America, and seven in South America, 23 in Europe, nine in Australia and New Zealand, and five in Africa) (Arifin, Cheyne et al. 2018). The EPDS was the most common instrument employed to screen or define maternal postnatal depression, in addition to other self-report measures such as CES-D, PHQ, Mini-International Neuropsychiatric Interview (MINI) or International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). The cut-off points of EPDS commonly used in included studies were 10 and 13. The overall prevalence of postnatal depression varied from 4.0% to 63.9%, with the lowest and highest data reported in Japan and the US, respectively. A wide range of postnatal depression prevalence were also found within each continent. Data in Asia ranged from 4.0 to 48.3% and that in Europe were

between 4.4–22.8%. The corresponding results from America, Africa, Australia and New Zealand were in the range of 5.0–63.9%, .2–50.3%, 6.0–32.8% and 0.6–30.9%, respectively (Arifin, Cheyne et al. 2018). At the same time, a meta-analysis of 58 studies including 37,294 apparently health mothers (without antenatal depression) from different geographical regions (e.g., Asia, Europe, Middle East, North America…) reported a pooled prevalence of 17% (95% CI: 0.15–0.20) (Shorey, Chee et al. 2018). There are also some variations regarding the prevalence of postpartum depression among continents. The pooled prevalence of postpartum depression was highest in the Middle East (26.0%) and lowest in Europe (8.0%). The corresponding values in Australia, South America, Asia, North America, and Africa were 21%, 19%, 16%, 16% and 11%, respectively.

Asia is the most populated continent (60% of the world's population), with an increasing, but still varying, prevalence of postnatal depression among regional countries. A narrative review by Klainin and Arthur, which included 64 research papers conducted in 17 Asian countries, reported the prevalence of postnatal depression varied substantially from 3.5% to 63.3%, with the highest data in Pakistan and lowest in Malaysia (Klainin and Arthur 2009). In 2012, Jones and Coast undertook a systematic review of postpartum depression in relation to aspects of social relationships in South Asia. A review of nine studies from Nepal, Bangladesh and India estimated the prevalence of postnatal depression varying from 4.9% to 35.6% (Jones and Coast 2013). An updated systematic review also revealed wide variations in the rates of postnatal depression reported within Asian countries. For example, the reported prevalence of postnatal depression ranged from 15.8-46.9% in India, 9.4–27.4% in China, and 6.8–27.3% in Malaysia (Arifin, Cheyne et al. 2018). More

recently, a meta-analysis including 13 papers published in Asia of the total 58 studies meta-analysed found an overall postnatal depression of 16% (Shorey, Chee et al. 2018).

In short, the prevalence of postpartum depression varies greatly between countries. This large heterogeneity may be due to the difference in cross cultural variables, biological variability factors, sampling methods, varying stages of the postpartum period, stigma and mental health perceptions, methodologies (point or period prevalence, assessment tools and cut-off points, etc). For instance, according to the study by Buist, Austin et al. (2008), the prevalence of postnatal depression varied depending on research methodology (diagnostic or screening tools, cut-off score, etc). The problem appears to be more frequent in Asia than other regions. However, in non-Western cultures, the reported prevalence may be lower due to somatization of mental illness. Depression after delivery occurs more often in India, Pakistan, Korea and Taiwan. It is plausible that self-reported instruments underestimate the prevalence of depression because women feel reductant to endorse negative mood symptoms. Epidemiological data on postpartum depression should be interpreted with consideration of the study design, sampling method, measuring instruments and assessment time points in the postpartum period.

2.5.4. Determinants of postnatal depression

Postnatal depression can arise at any time after giving birth up to one year postpartum, although most studies limit their observation length to a shorter period, often only three months. Literature has identified biological, psychosocial, genetics and cultural factors associated with postnatal depression (Halbreich and Karkun 2006). Actually, different

bio-psycho-socio-cultural factors have been suggested to induce postnatal depression (Halbreich 2005). An increasing number of literatures has investigated protective and risk factors for postnatal depression in different countries through traditional and systematic reviewing approaches (Klainin and Arthur 2009, Jones and Coast 2013, Mehta and Mehta 2014, Ghaedrahmati, Kazemi et al. 2017, Upadhyay, Chowdhury et al. 2017, Arifin, Cheyne et al. 2018, Guintivano, Manuck et al. 2018, Nisar, Yin et al. 2020, Zhao and Zhang 2020). Postnatal depression can be categorised into five major groups: cultural, socio-demographic, psychological, physical/biological and obstetric/paediatric factors. A list of putative risk and protective factors for postpartum depression is shown in Table 2.1.

Table 2. 1: Common risk factors for postpartum depression reported in Asia

Risk Factors	Studies
Lack of social support	(Glasser, Barell et al. 2000, Chaaya, Campbell et al. 2002, Chandran, Tharyan et al. 2002, Rodrigues, Patel et al. 2003, Wang, Jiang et al. 2003, Heh, Coombes et al. 2004, Chee, Lee et al. 2005, Husain, Bevc et al. 2006, Wang and Chen 2006, Mohammad, Gamble et al. 2010)
low self-esteem	(Wang, Jiang et al. 2003)
low education attainment	(Chaaya, Campbell et al. 2002, Inandi, Elci et al. 2002, Wang, Jiang et al. 2003, Ekuklu, Tokuc et al. 2004, Chien, Tai et al. 2006)
domestic violence	(Leung, Kung et al. 2002, Patel, Rodrigues et al. 2002, Rodrigues, Patel et al. 2003, Husain, Bevc et al. 2006)

Risk Factors	Studies
poor relationship with mother in-law	(Chandran, Tharyan et al. 2002, Danaci, Dinc et al. 2002, Lee, Yip et al. 2004, Green, Broome et al. 2006, Mohammad, Gamble et al. 2010)
antenatal depression	(Glasser, Barell et al. 1998, Lee, Yip et al. 2000, Chaaya, Campbell et al. 2002, Chandran, Tharyan et al. 2002, Chen, Chan et al. 2004, Lee, Yip et al. 2004, Aydin, Inandi et al. 2005, Kitamura, Yoshida et al. 2006, Lee, Lam et al. 2007, Mohammad, Gamble et al. 2010, Hamdan and Tamim 2011)
past history of depression	(Lee, Yip et al. 2000, Lee, Yip et al. 2004, Ho-Yen, Bondevik et al. 2007)
marital status (single/divorce/separation)	(Glasser, Barell et al. 2000, Lee, Yip et al. 2004)
infant's gender	(Chandran, Tharyan et al. 2002, Patel, Rodrigues et al. 2002, Rodrigues, Patel et al. 2003, Kitamura, Yoshida et al. 2006, Ho-Yen, Bondevik et al. 2007, Mohammad, Gamble et al. 2010)
low income	(Chandran, Tharyan et al. 2002, Inandi, Elci et al. 2002, Patel, Rodrigues et al. 2002, Rodrigues, Patel et al. 2003, Andajani-Sutjahjo, Manderson et al. 2007)
unplanned pregnancy	(Iranfar, Shakeri et al. 2005, Eilat-Tsanani, Merom et al. 2006, Andajani-Sutjahjo, Manderson et al. 2007, Mohammad, Gamble et al. 2010)

Risk Factors	Studies
traditional postpartum practices	(Yoshida, Yamashita et al. 2001, Chee, Lee et al. 2005, Leung, Martinson et al. 2005, Chien, Tai et al. 2006)
multi-parity	(Hamdan and Tamim 2011)
unemployment	(Chaaya, Campbell et al. 2002, Inandi, Elci et al. 2002, Aydin, Inandi et al. 2005)
infant's illness	(Glasser, Barell et al. 2000, Danaci, Dinc et al. 2002, Aydin, Inandi et al. 2005, Andajani-Sutjahjo, Manderson et al. 2007)
poor relationship with husband	(Huang and Mathers 2001, Patel, Rodrigues et al. 2002, Chee, Lee et al. 2005, Gulseren, Erol et al. 2006, Dindar and Erdogan 2007)
not breastfeeding	(Green, Broome et al. 2006)
lack of confidants	(Fisher, Morrow et al. 2004, Rahman and Creed 2007)
stressful life events	(Chaaya, Campbell et al. 2002, Ho-Yen, Bondevik et al. 2007)
lack of husband's support	(Rodrigues, Patel et al. 2003, Sagami, Kayama et al. 2004, Aydin, Inandi et al. 2005)

Physical/biological factors

Many studies have reported the following risk factors for postnatal depression: poor physical health, premenstrual symptoms, difficulties in carrying out daily activities, diet with high glycaemic index (Klainin and Arthur 2009). It is reported that glucose metabolism disorders during pregnancy disposed postnatal depression (Ghaedrahmati, Kazemi et al. 2017). A recent meta-analysis of ten cohort studies comprising 2,000,002

participants found mothers with GDM had 1.32 times of developing postnatal depression compared with those without GDM (Arafa and Dong 2019). Individuals with less physical activity during pregnancy are more likely to experience postnatal depression compared with more physically active mothers. In an updated meta-analysis, intervention studies found a significant inverse association between physical activity during pregnancy and postpartum depression (SMD=−0.58 [95% CI −1.09 to −0.08]. Observational studies also suggested an inverse association, despite the lack of statistical significance (SMD=−0.58 [95% CI −1.09 to −0.08] (Nakamura, van der Waerden et al. 2019). In view of rapid socioeconomic change, overweight and obesity have become a significant public health issue. Several studies have revealed an association between overweight/obesity and postnatal depression. A recent systematic review reported that pre-pregnancy obesity associated with postnatal depression, two of the four included studies found a positive association while one found none (Steinig, Nagl et al. 2017). To examine the association between the obesity and postnatal depression, Molyneaux and colleagues undertaken a meta-analysis of 16 studies, reporting that obese pregnant women had a statistically significant 30% higher odds of postnatal depression than normal-weight women (Molyneaux, Poston et al. 2014). With increasing research being undertaken into obesity and overweight, the body image has also been studied. Indeed, it has been observed that body dissatisfaction was consistently, but weakly, associated with the onset of postnatal depression (Silveira, Ertel et al. 2015).

Studies also reported that postpartum depressive symptoms were reduced by the following protective factors included Vitamin D, calcium, zinc, multivitamin supplementation, higher concentrations of Docosahexaenoic acid (DHA) in mothers'

milk, greater seafood consumption, fish and Polyunsaturated Fatty Acid (PUFA) intake, health conscious, Brazilian diet patterns, healthy dietary patterns (Sparling, Henschke et al. 2017, Silva, Cobucci et al. 2019, Zhao and Zhang 2020).

Psychological factors

Psychological effects on postnatal depression have been intensively investigated in different countries. In Asia, for example, strong predictors for postnatal depression include stressful life events, antenatal anxiety, antenatal depression, past psychiatric history, premenstrual dysphoric disorder, childcare stress, negative affect, poor self-image, low self-esteem, insecure attachment style, negative attitude at work, poor accommodation, lack of instrumental support or medical resources, cultural conflict, lack of social support, lack of confidant/friend, conflicts with relatives/being abused by in-laws (Klainin and Arthur 2009, Mehta and Mehta 2014). History of anxiety and depression are associated with a higher risk of postnatal depression. The occurrence of mental health disorders, including antenatal depression is a predicting factor of postpartum depression (Ghaedrahmati, Kazemi et al. 2017). Besides history of depression, history of sexual abuse and negative attitude toward the recent pregnancy were suggested predictors of postpartum depression. Additional contributors to postnatal depression were low self-esteem and the reluctance of the baby gender (Ghaedrahmati, Kazemi et al. 2017).

It is also noted that husband/marriage related factors can induce postpartum depression. They include psychiatric illness in husband, current alcoholism, poor educational status, uncertainty about husband's work/unemployment, husband's

polygamous relationships , lack of support from husband, marital conflict or disturbed relationships with husband, regret for marriage (Mehta and Mehta 2014).

Obstetric/paediatric factors

The role of obstetric/paediatric factors in the occurrence of postnatal depression has been examined. Accumulating studies have found major risk factors, namely past abortion, previous pregnancy loss, unintended/unplanned pregnancy, negative attitude toward pregnancy, maternal health problems during pregnancy, negative attitude toward mother roles, parity (primiparity) the lack of childcare knowledge, the absence of breastfeeding (Klainin and Arthur 2009, Mehta and Mehta 2014). Birth defects in child, short period of rest/exhaustion after childbirth, child health problems, dissatisfaction with child's gender, child's temper tantrums, child's feeding difficulties, and stress with childcare were all associated with postpartum depression (Mehta and Mehta 2014).

Socio-demographic factors

Several cultural and socio-demographic factors have been linked to postnatal depression. A review of studies in Asia showed potential risk factors including

Unemployment, hungry, economic difficulties, dissatisfaction with living conditions, being an immigrant, being a homemaker, husband having psychiatric disorder, uneducated husband, intimate partner violence and lack of emotional support (Klainin and Arthur 2009). In addition, age of mother at the time of childbirth as well as older age at marriage are risk factors. Young mother has higher risk of postnatal depression. The mothers aged from 13 to 19 year had highest level of postpartum depression, whereas

Women age from 31 to 35 years had the lowest rate (Ghaedrahmati, Kazemi et al. 2017). Race and ethnicity have been associated with postnatal depression (Guintivano, Manuck et al. 2018).

Cultural factors

It has been suggested several cultural factors can help prevent postpartum depression such as practical and emotional support from Asian family members (e.g., mother-in-law, relatives, and husband) after giving birth. Because women often experience physiological vulnerability in the postpartum period, a certain convalescence period, appropriate diets, and specific activities are promoted in most Asian countries to support recovery and bring the mother back to normal state. Low support and poor relationships with the husband and parents-in-law have been suggested to increase the risk of postpartum depression (Jones and Coast 2013). It is believed that "culture bound" plays a role in postpartum depression, and this may explain the reason why women from developed countries are prone to incurring postnatal depression due to lack of social support (Stern and Kruckman 1983). However, accumulating evidence suggests that postpartum depression has also become a concerning issue in less developed nations. In Turkey, postnatal depression ranged from 14% to 40.4% (Danaci, Dinc et al. 2002, Ekuklu, Tokuc et al. 2004, Aydin, Inandi et al. 2005, Ayvaz, Hocaoglu et al. 2006) while in India (Patel, Rodrigues et al. 2002) and Vietnam (Fisher, Morrow et al. 2004) prevalence of postnatal depression were 23% and 33% respectively. Cultural traditions can affect the incurrence of postpartum depression. A review by Grigoriadis and colleagues indicated that the welcome support may be more protective than the specific ritual (Grigoriadis, Erlick Robinson et al. 2009), and social support was regarded as the most important element of all postpartum rituals.

To sum up, there is an array of factors associated with postnatal depression including modifiable and non-modifiable ones. They may be related to the mother, pregnancy and birth outcomes. Factors inducing postpartum depression appear to be alike in the Western and non-Western countries; however, women in the non-Western cultures may experience additional risk factors such preference of infant's gender, intimate partner violence, poor relationships with mother-in law, and traditional postpartum practices. The most recent umbrella review identified several factors consistently associated with postnatal depression: psychological factors (including violence and abuse, history of depression, postpartum sleep disruption and poor postpartum sleep, lack of social support), socio-demographics(e.g., immigration status), physical/biological influencers (GDM, obese and overweight, vitamin D deficiency, traditional dietary pattern [Japanese, Indian, United Kingdom and Brazilian dietary pattern]) and obstetric/paediatric parameters (caesarean section), multiple births, preterm and low-birth-weight infants, postpartum anaemia, negative birth experience.

2.6. Epidemiology of perinatal depression in Vietnam

Vietnam has experienced a rapid socioeconomic and epidemiological transition, with fast-growing economy and social development together with an increase in the prevalence and incidence of chronic diseases (Nguyen and Trevisan 2020). These changes are thought to have an impact on physical as well as mental health and well-being, particularly among reproductive-aged women (Fisher, Tran et al. 2007). Increasing interest has been focused on the morbidity of perinatal depressive disorders and their determinants over the past 15 years (Fisher, Morrow et al. 2004, Fisher, Tran et al. 2007, Fisher, Tran et al. 2010, Tran, Tran et al. 2011, Fisher, Tran et al. 2013, Fisher, Tran et al. 2013, Niemi, Falkenberg et al. 2013, Murray, Dunne et al. 2015,

Van Vo, Hoa et al. 2017, Do, Nguyen et al. 2018, Tho Tran, Nguyen et al. 2018, Van Ngo, Gammeltoft et al. 2018, Upadhyay, Singh et al. 2019, Hue, Nguyet Van et al. 2020, Stocker, Nguyen et al. 2020, Wesselhoeft, Madsen et al. 2020, Luong-Thanh, Nguyen et al. 2021). The prevalence of and risk/protective factors for antenatal and postnatal depressive disorders in Vietnam from 17 studies are summarised in Table 2.2. Cross-sectional study designs accounted for two-thirds, and the remaining one-third is classified as prospective cohort study design. Most investigations were undertaken in the Northern region, with fewer studies in the South and Central parts of the country. The number of participants ranged from 61 to around 2000, and EPDS is the most common instrument used to measure perinatal depression/common depressive disorders. Using EPDS, the prevalence of antenatal depression varied from 4.9 to 24.5%, with the cut-off point of EPDS to define depression being 4 and 10. Studies on postnatal depression are more common, reporting the prevalence in the range of 1.9% and 33% with a cut-off of greater than 12 being the most frequent threshold for use in depression definition. The following factors were found to be associated with perinatal depression.

Physical/biological factors*:* Lack of exercise after childbirth, less than 30 days of complete rest after delivery, nutrient insufficiency during lactation period, and mother's poor health during pregnancy.

Psychological factors*:* Unintended or unwanted pregnancy, lack of confidence in the husband, coercion experience in marital relationship, family and intimate partner violence, being afraid of family members, maternal anxiety, mother's chronic diseases

during pregnancy, family conflict, limited social communication, and stressful life events (childhood abuse, loss of family relatives).

Obstetric/paediatric factors*:* primiparity*,* past pregnancy loss, preterm birth, low birthweight, and foetal abnormalities.

Socio-demographic factors*:* insecure job, crowded living condition, rural residence, poverty, older age at pregnancy, unemployment, maternal and paternal low level of education.

Cultural factors*:* Baby sex preference and family support.

Table 2. 2: Studies on perinatal depression in Vietnam (2004-2021)

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
(Fisher, Morrow et al. 2004)	To examine depressive symptomatology in women after childbirth in Ho Chi Minh City, Vietnam	2000	Cross-sectional survey	South Vietnam	506	EPDS (>12)	33%	Unwelcome pregnancy, an unsettled baby, <30 days complete rest after childbirth, not being given special foods, avoiding prescribed foods, lack of a permanent job and being unable to confide in their husbands.
(Fisher, Tran et al. 2007)	To investigate the prevalence and determinants of depression in a cohort of pregnant	2004	Cross-sectional survey	North Vietnam	61	EDS	Mean score = 5.42 ±3.8	Insecure casual work, crowed living conditions and experiencing critical coercion in the marital relationship

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	Vietnamese women							
(Fisher, Tran et al. 2010)	To establish the prevalence of common perinatal mental disorders their determinants, and their association with preventive health care use among women in one rural and one urban province in	2006 and 2007	Cross-sectional survey	North Vietnam	392	(DSM-IV)	29.9% was diagnosed with a common perinatal mental disorder	rural residence, poverty and exposure to family violence

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	northern Vietnam							
(Tran, Tran et al. 2011)	To establish the validity of three widely used psychometric screening instruments in detecting common mental disorders in women in northern Vietnam	2006 and 2007	Cross-sectional survey of a cohort study	North Vietnam	364	EPDS ZSAS GHQ12	EPDS mean score =7.6±4.3 Zung SAS mean score =41.8±7.4 GHQ12 mean score= 24. ±1.9	N/A
(Fisher, Tran et al. 2013)	To examine the associations	2009-2010	Community-based	North Vietnam	497	EPDS	CPMD (EPDS>3)	Any form of intimate partner violence

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	between different exposures to IPV and women's mental health during pregnancy and after childbirth in rural Vietnam		longitudinal study				W1=41.4%, W2=28.2% W3=13.4% W4=14.6% Mean score (no experience IPV) =3.5 (3.0-3.8) Mean score (any experience IPV) = 5.8(4.9-6.8)	
(Fisher, Tran et al. 2013)	To establish the prevalence of and	2009-2010	Community-based	North Vietnam	419	EPDS (>3)	Early pregnancy =	Non-economic and economic coincidental life adversity, intimate partner violence, past

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	psychosocial factors for clinically significant symptoms of CMD in early and late pregnancy in women in rural Vietnam		longitudinal study				22.4% (95%CI 18.4-26.4) Late pregnancy= 10.7% (95%CI 7.8-13.7)	pregnancy loss and childhood abuse Early pregnancy: older age, baby's sex preference, nulli or primiparity
(Niemi, Falkenberg et al. 2013)	To examine the association of low birthweight and prematurity with clinically significant	2008	Prospective community-based cohort study	North Vietnam	355	EDS	ACMD=37.4%	Preterm birth, low birthweight,

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	symptoms of antenatal common mental disorders during the third trimester of pregnancy in a semi-rural area in Vietnam							
(Murray, Dunne et al. 2015)	To investigate the prevalence and socio-cultural correlates of postnatal mood disturbance	2010	Cross-sectional study	Central Vietnam	431	EPDS (>12)	18.1% (95CI 14.6-22.1)	Poverty, food insecurity, being frightened of family members and intimate partner violence

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	amongst women 18-45 years old in Central Vietnam							
(Van Vo, Hoa et al. 2017)	To estimate the prevalence of Postpartum depression (PPD) To identify the social and personal factors of PPD	2013-2014	Cross-sectional study	Central Vietnam	600	EPDS (>12)	19.3% (95CI 16.2-22.5)	Not being able to rely on husband for help, husband does not spend time to discuss problems, have anxiety, ill baby, no exercise after childbirth
(Van Ngo, Gammeltoft et al. 2018)	To describe the association between	2014-2015	Prospective cohort study	North Vietnam	1337	EPDS (>9)	4.9%	Low birth weight Preterm birth

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	antenatal depressive symptoms and preterm birth, low birthweight and small for gestation age							
(Tho Tran, Nguyen et al. 2018)	To investigate the association between various types of emotional experience during life with present partner and postnatal	2014-2015	Prospective cohort study	North Vietnam	1274	EPDS (>9)	8.2%	Presence of mental disorder, depression during pregnancy, emotional violence, type of employment, lack of family support after childbirth, low level of education, husband's preference for baby's sex.

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	depressive symptoms							
(Do, Nguyen et al. 2018)	To identify the prevalence of postpartum depression and its risk factors	2020	Cross-sectional study	North Vietnam	116	EPDS (>12)	27.6%	Level of education, diseases during pregnancy, being the first-time mothers, dissatisfaction about family, limited communications and interaction with others
(Upadhyay, Singh et al. 2019)	To examine the association between birth intention and postpartum depression in Ethiopia, India,	2002-2009	Longitudinal study	Vietnam and three other countries	About 2000 each country	WHO SRQ	Vietnam 21%	Unintended birth Mother's poor health during pregnancy, stressful life events (job loss, death of family member)

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	Peru and Vietnam							
(Hue, Nguyet Van et al. 2020)	To describe the status of antenatal depression and its associated factors among pregnant women in Vietnam	2019	Cross-sectional study	Multiple centres	1260	EPDS>9	24.5%	Foetus abnormalities and higher education
(Wesselhoeft, Madsen et al. 2020)	To compare postnatal depressive symptoms between women in three	2014-2015	Cross-sectional study of a population-based cohort study	Vietnam and other two countries	Vietnam 1278	EPDS (>12)	1.9%	Low level of education

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
	countries included Denmark, Vietnam and Tanzania							
(Stocker, Nguyen et al. 2020)	To establish whether changes in the socioeconomic context were associated with changes in population-level antenatal mental health indicators in Vietnam	2006 and 2010	Cross-sectional study. Secondary data analysis	North Vietnam	Year 2006=134 Year 2010=419	EPDS-V	Mean score 2006: 2.75±4.46 2010: 3.82±4.18	Household wealth and intimate partner controlling behaviour

Author, year of publication	Study aims	Year of data collection	Design	Location	Sample size	Measures of depression	Prevalence, or mean score	Associated factors
(Luong-Thanh, Nguyen et al. 2021)	To assess the prevalence of depression and its associated factors amongst pregnant women in a central Vietnam city	2019	Cross-sectional study	Central Vietnam	150	PHQ9	Moderate to severe depression: 12.7% (95%CI 7.3-18.1)	Experiencing stress, husband's low level of education

EPDS: Edinburgh Postnatal Depression Scale

EPDS-V: Edinburgh Postnatal Depression Scale – Vietnamese version

EDS: term of EPDS for antenatal survey

DSM-IV: Diagnostic and statistical manual of mental disorder, fourth edition

PHQ9: Patient Health Questionnaire-9

WHO SRQ: World Health Organization self-reported questionnaire

ZSAS: Zung Self-rated Anxiety Scale

GHQ12: General Health Questionnaire 12 item

2.7. Consequences of perinatal depression for the mother and infant health

Substantial evidence has suggested that antenatal and postpartum depression may negatively impact on pregnancy and infant health outcomes in early infancy throughout the childhood days of the new-born (Beck 1998). To date, studies investigating consequences of perinatal depression are largely confined to the use of cohort designs. Nonetheless, due to limited sample sizes in some studies, it may be difficult to detect small differences.

2.7.1. Consequences of antenatal depression

Increasing attention has been drawn to the public health significance of antenatal depression due to its consequences on maternal and infant health. Besides the most commonly reported finding that antenatal depression is associated with postnatal depression (Underwood, Waldie et al. 2016), it is also a predictor of multiple maternal health problems, including maternal poor diet (Khan, Waqas et al. 2020), poor health, anxiety, and increased risk of obstetric complications (Byrn and Penckofer 2013). The review by Byrn and colleagues showed that pregnant women with early prenatal depression are at a higher risk of developing GDM compared to their prenatally non-depressed mothers (Byrn and Penckofer 2013). Research into the impact of antenatal depression on infant health has been on the rise. Mothers who experienced depressive symptoms during pregnancy are vulnerable to deliver low birthweight babies (Byrn and Penckofer 2013, Dadi, Miller et al. 2020) and affect children's emotional, cognitive and physical health and development (Hollins 2007, Muzik and Borovska 2010, Pearlstein 2015).

2.7.2. Consequences of postnatal depression

Maternal-infant interaction is an important relationship in the postpartum period, which has been associated with the infant's development (Rocha, Dos Santos Silva et al. 2020). A moderate to large adverse effect of postpartum depression on maternal-infant interaction during the first year after delivery was reported by Beck and colleagues in their earlier meta-analysis of nine studies (Beck 1995). Postpartum depression may negate woman's social and personal adjustment and the marital relationship. A matter of concern is that postnatal depression may exert detrimental long-term effects on behavioural, cognitive and emotional development of children (Beck 1998, Jacobsen 1999). Postpartum depression if untreated may act as the precursor of recurrent depression for the mother. Infants of depressed mothers tend to be more discontent, more fussier, and un-avoidant (Field 1995).

The effects of postnatal depression on maternal and infant health outcomes are corroborated in recent studies. A systematic review including 122 studies, of which 61 addressed maternal consequences of postnatal depression, reporting that postnatally depressed mothers had a lower score of physical health status compared to the general population of women (Slomian, Honvo et al. 2019). Women with more severe postnatal depressive symptoms tended to use health care services and experience psychological problems (e.g., anxiety, subsequent depression and decreased quality of life more often than those with mild depressive symptoms or apparently healthy women. Postnatal depression has also been associated with social and family relationships and had a negative impact on the mother's lifestyle and behaviour (such as smoking, alcohol drinking) (Slomian, Honvo et al. 2019).

Infants born to mothers experiencing depression in the postpartum period are at a higher risk of having physical and mental health problems compared to those of mothers without postnatal depression (Waqas, Elhady et al. 2018, Slomian, Honvo et al. 2019, Dadi, Miller et al. 2020). A meta-analysis of eight studies on the association between postnatal depression and infant diarrhoea found infants born to mothers with postnatal depression were 1.9 times more likely to have diarrheal illness (pooled OR: 1.90; 95% CI: 1.39-2.61). A more recent review including 58 studies in low- and middle-income countries showed that postnatal depression was significantly associated with 31% of developing adverse infant health incomes (e.g., common infant illness [diarrhoea, fever, lower respiratory tract infection], malnutrition [stunting, wasting, short stature], and non-exclusive breastfeeding) (Dadi, Miller et al. 2020). It has also been suggested that postnatal depression may affect the infant's socio- and emotional and behavioural development (Slomian, Honvo et al. 2019).

2.8. Approaches to preventing and controlling perinatal depression

Effective countermeasures for postpartum depression is not only to reduce maternal morbidity and mortality but also minimise the sustainable effects on her family (Brockington 2004). Available interventions for the treatment and/or prevention of perinatal depression have employed various pharmacologic and psychological approaches (e.g., Cognitive Behavioural Therapy, Interpersonal Psychotherapy, non-directive counselling support groups and antenatal/postnatal classes).

A growing number of studies have been carried out to evaluate the effectiveness of intervention approaches on perinatal depression. A systematic review and meta-analysis of 50 primary studies reported different intervention methods including

counselling, health system and other social and lifestyle interventions (e.g., physical activity, education [without counselling or extensive support), supportive interventions, infant sleep advice, birth-experience postpartum debriefing, expressive writing, antidepressant and supplementation usage, and yoga (O'Connor, Senger et al. 2019). The review showed that counselling-based interventions reduced the likelihood of perinatal depression by 39% in the intervention group compared to its control counterpart (pooled risk ratio: 0.61; 95% CI: 0.47-0.78). Likewise, a systematic review and meta-analysis of 40 primary reports (26 studies for treatment and 14 for prevention) concluded that cognitive behavioural interventions significantly decreased depressive symptoms compare to control conditions (Sockol 2015). Social and lifestyle intervention together with pharmacological interventions also demonstrated some effectiveness but lack of a robust evidence base and require further research (Misri and Kendrick 2007). Another systematic review including 18 studies conducted in low- and middle-income countries indicated evidence-based psychological strategies were the most effective in preventing perinatal depression (Gajaria and Ravindran 2018).

2.9. Conclusions and gaps

This chapter reviews global epidemiological studies of perinatal depression worldwide, with focus on Asia and Vietnam. In addition, some aspects of biological mechanisms and intervention approaches are reviewed. The global prevalence of antenatal depression was estimated approximately 21%, with the prevalence was up to 64% in some areas. In Asia, the prevalence of antenatal depression in Southeast Asia appears to be the highest among regional countries (~30%). Representing East Asia, an overall prevalence of antenatal depression in China is nearly 20%. Several

predictors for antenatal depression and its birth outcome effects have been reviewed. Factors associated with antenatal depression commonly reported are age, maternal education, employment, financial condition, family issues, smoking, alcohol drinking, physical activity, GDM and GWG. Major birth outcomes related to maternal antenatal depression include preterm birth and low birthweight.

Epidemiological studies of postnatal depression predominate those addressing antenatal depression. Worldwide, postnatal depression prevalence was estimated at 17%, with a wide range of the estimate from null to 63.9%. The corresponding summary data in Asia was around 16%. An array of risk and protective factors for postnatal depression has been identify, including physical and biological factors, psychological triggers, obstetric and child contributors, as well as socio-demographic and cultural influencers. Postnatal depression has also been associated with multiple infant health problems, physically and mentally.

Perinatal depression has attracted growing interest in Vietnam; however, epidemiological studies on this topic remain limited. Over the past five years, only about a half dozen of investigations have been undertaken in this country. The reported prevalence of antenatal depression is in the range of 4.9 to 24.5%, and the correspondent value in the postpartum period varied between 1.9 and 33%. Most determinants studied are related to socio-demographic/cultural and psychological factors, while very few reports examined lifestyle and/or obstetric/child factors. In addition, most reported data was derived from cross-sectional study designs and used self-administered questionnaires, making it difficult to infer causal relationships and minimise potential bias. Moreover, representativeness is a concerning issue because

many studies recruited participants from single centres or areas. It is therefore necessary to conduct further epidemiological research addressing perinatal depression in Vietnam to provide evidence for designing appropriate measures for prevention and control of maternal depression in the country.

CHAPTER 3: METHODOLOGY

This chapter describes the methods used including the study design and location, participant selection criteria, sample size calculation, recruitment and data collection procedure, measuring and survey instruments, data management, statistical analysis and ethical considerations.

3.1. Study design

A hospital-based prospective cohort study was conducted at six hospitals in three cities of Vietnam, namely Ho Chi Minh City, Ha Noi and Hai Phong, from August 2015 to December 2016. Dong Anh district hospital (from Ha Noi), Vinh Bao district hospital (from Hai Phong) and three district hospitals (Tan Phu District, Hoc Mon District, District 2 hospitals) and one obstetrics hospital in Ho Chi Minh City (Hung Vuong hospital) were chosen to be the participant recruitment sites; see Figure 3.1.

This prospective cohort study consisted of five surveys administered at baseline, hospital discharge, and at one month, three months, and six months postpartum, in order to collect information on outcome measures, exposure variables and confounding factors, especially maternal characteristics, perinatal depression scores, as well as birth and infant health outcomes.

3.2. Study location

Vietnam is a developing country located in the Southeast Asia with a long coastline of 3,260 km (General Statistics Office of Vietnam 2017). It has 63 provinces and cities,

with a population of more than 92 million people (General Statistics Office of Vietnam 2017). This study was conducted in three metropolitan cities, namely Ho Chi Minh City, Ha Noi and Hai Phong. Hanoi is the capital, the centre of politics, education and economics, located in the north of Vietnam. According to General Statistics Office of Vietnam, it has 29 districts with a population of over 7.3 million (General Statistics Office of Vietnam 2017). Ho Chi Minh City is the largest and the most important economic city in the heart of the southern region. The population in 2016 was just over eight million people living in 24 districts (General Statistics Office of Vietnam 2017). Hai Phong is one of five municipalities located in the east coastal region, with economics based on sea transport, heavy industry and agricultural sectors. It has 15 districts with a population of nearly two million (General Statistics Office of Vietnam 2017).

Within each city, certain districts were chosen based on their characteristics and advice from experts who had experience in collecting data in these areas. In Ha Noi and Hai Phong, Dong Anh and Vinh Bao districts were selected, respectively. Dong Anh is a suburban district with rapid development and extension of urbanisation. It has 23 communes and one town with a population of over 300,000 people, encompassing a mixture of agriculture and industry (Hanoi Capital 2017). Vinh Bao is a rural district of Hai Phong, located in the northeast along the coastal area. It has a population of about 180,000 people residing in 29 communes and one town. Its economy is based on agriculture, fishery and light industry (Haiphong City 2017). Due to the variety of social-economical characteristics in Ho Chi Minh City, three districts namely Hoc Mon, District No 2 and Tan Phu were selected. Hoc Mon is a typical suburban district with a population of 422,000 living in one town and eleven communes covering an

area of 109 square km (Ho Chi Minh City Statistics Office 2016). District No 2 and Tan Phu are typical urban districts. They have eleven wards each, with a population of 147,000 and 262,000, respectively (Ho Chi Minh City Statistics Office 2016).

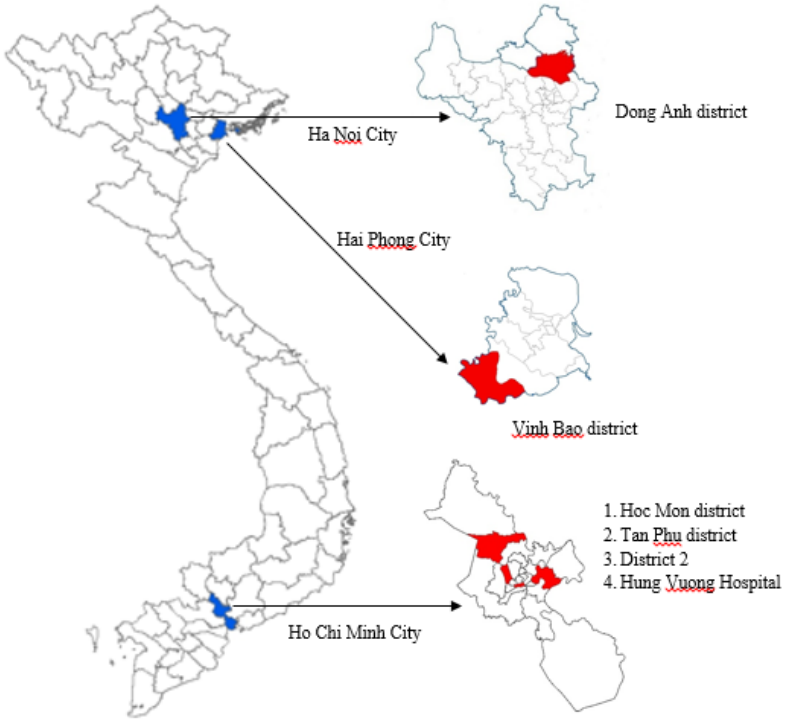

Figure 3. 1. Location of six recruitment sites

Source: Cohort Profile paper (Nguyen, Nguyen et al. 2017)

Vietnam has a large health care system covering every level from commune to central. Each district has one governmental district hospital. The district hospitals are the largest health care provider offering a variety of medical services including obstetrics. Hung Vuong Hospital is the second leading obstetric hospital in Ho Chi Minh City, located in District 5. It is accredited under the Baby Friendly Hospital Initiative. Hung Vuong Hospital provides specialised maternal and childcare. Pregnant women from surrounding districts, such as Hoc Mon, Tan Phu and District 2, may also visit Hung Vuong Hospital. This obstetrics hospital was chosen to capture women with high-risk pregnancies from different areas of Ho Chi Minh City, in order to minimise potential

selection bias. Figure 1 shows the locations of the study (Nguyen, Nguyen et al. 2017). The six hospitals chosen represented different areas and levels of maternity care in Vietnam.

3.3. Participants

Eligible participants were recruited following selection criteria:

- Vietnamese permanent resident in the recruitment area.
- had attended antenatal care at local community health centres.
- planned to deliver at the recruitment hospital.
- ≥ 18 years of age.
- at 24-28 weeks of gestation.
- with a singleton pregnancy.
- able to read the information letter and sign the consent form. *

** No selection bias was introduced due to almost universal literacy in the catchment area.*

Exclusion criteria were:

- became pregnant after infertility treatment such as in-vitro fertilization or intrauterine insemination.
- deemed ineligible due to illness or pre-existing health conditions following advice from their medical doctors.
- termination of pregnancy, experienced a subsequent still birth or infant death during the follow up periods.

3.4. Sample size calculation

It was hypothesised that pregnant women with antenatal depression were more susceptible to postnatal depression at three months postpartum. The sample size was calculated based on the cohort design with specific parameters Kelsey formula (Kelsey JL, Whittemore AS et al. 1996). Input variable was antenatal depression, and outcome variable is postnatal depression.

Two-sided significance level (*1-alpha*)	95
Power (*1-beta, % chance of detecting*)	90
Ratio of unexposed to exposed (*to antenatal depression*)	4*
Percent of postnatal depression in non-antenatal depression	10%*
Odds ratio	1.8*

(*Of postnatal depression in the antenatal depressive group divided by odds of postnatal depression in the non-antenatal depressive group*)

** Estimated values based on previous studies conducted in Vietnam and other Asian countries (Fisher, Tran et al. 2013, Murray, Dunne et al. 2015, Zhou, Ogihara et al. 2017).*

The estimated sample size (n=1485) was calculated with two-sided confident level being 95% and 90% power. With the expectation of a 10% non-response rate and a further 15% attrition during the four follow ups, the total minimum sample size required for the baseline survey was n=1857. A total of n=2030 participants were subsequently recruited, which should be sufficient to detect perinatal depression in the target population. Consequently, the sub-sample sizes assigned to Ho Chi Minh City, Ha Noi and Hai Phong were 820, 900 and 298, respectively. Participants were consecutively recruited from the five district hospitals and one obstetric hospital until the desired sampling quota was reached.

3.5. Procedure

Figure 3.2 summarises the procedure of data collection. It should be remarked that the present study was part of a larger project so that information on other outcomes of interest (e.g., maternal diet, infant feeding practices) was also collected at the surveys.

3.5.1. Screening and recruitment

Pregnant women were screened by well-trained data enumerators when they came to the local community health centres for their routine antenatal health check. A list available from these community health centres enabled the capture of community-dwelling pregnant women within their catchment area. Eligible participants who satisfied the selection criteria (Section 3.3) read through a given information letter then signed informed consent. Participants were consecutively recruited until the desired sampling quota was achieved. A logbook was used to record all approached women with their basic contact information, reasons for exclusion, refusal or withdrawal.

3.5.2. Baseline survey

After enrolment, pregnant women who consented (see Appendices C, D) to participate were interviewed face-to-face using a structured questionnaire to gather information on personal characteristics, socio-demographic, and lifestyle including alcohol drinking and cigarette smoking, and other factors related to the main outcome variables of interest (antenatal and postnatal depression), based on a literature review of these topics. Questions from established instruments were adopted. Anthropometric measurements (height and weight) were also taken during the baseline survey. A digital scale was used to measure weight to the nearest 100g. Height was recorded by

a stadiometer to the nearest 1mm. Information on weight before pregnancy, GDM status, medications usage, and obstetric complications during pregnancy such as hypertensive disorders preeclampsia were retrieved from medical records, together with history of general and reproductive health. The presence or absence of depressive symptoms during pregnancy was assessed at the last trimester using the self-administered EPDS; see Section 3.6 for more details. Participants were requested to complete this section of the questionnaire in a private room. Trained research assistants were available to provide further clarification if necessary. Although additional EPDS measurements throughout pregnancy may provide more information about the trajectory of depressive symptoms, they were not conducted due to subject burden and resource constraints. The baseline interview took approximately 30 minutes to complete (Appendix E).

3.5.3. Hospital discharge assessment

After delivery, detailed information concerning obstetrical and neonatal outcomes (e.g., problems/complications during delivery, mode of delivery, Apgar scores, admission to neonatal intensive care unit, and length of hospital stay) were taken from medical records. Both mothers and newborns were assessed before discharge from hospital. For birthweight, the newborns were weighed to the nearest 10g on an electronic scale immediately after birth. The discharge questionnaire required about 30 minutes to complete (Appendix F). An appointment was then made for a subsequent home visit one month after hospital discharge.

3.5.4. Postpartum follow ups

Detailed information on health problems of both mothers and their newborns was sought at the follow up interviews of the cohort at one, three, and six months postpartum. The follow-up surveys using questionnaires (see Appendix G) were undertaken during routine examination of infants at hospital, local community health clinics for vaccination or home visits. Medical records and structured questionnaires were used to collect the infant health problems such as hospitalization, low respiratory infection, and diarrhoea. The presence or absence of any postnatal depressive symptoms was assessed by the EPDS-V. It took 25-30 minutes to complete each follow-up survey.

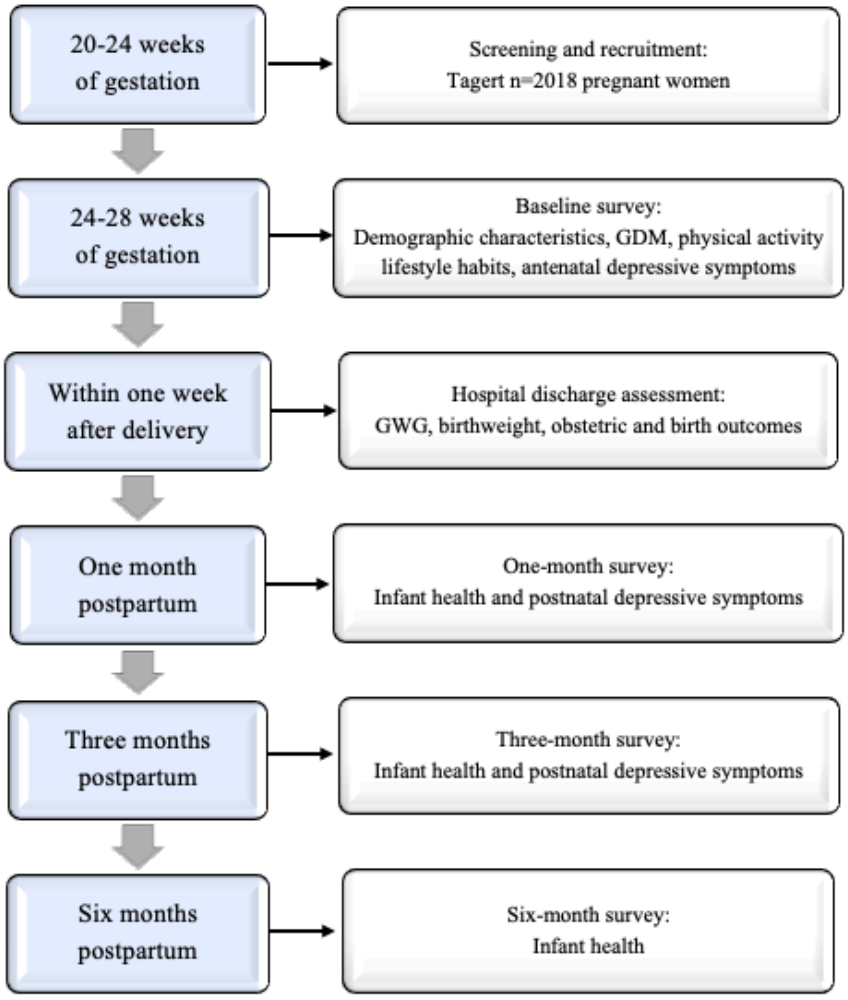

Figure 3. 2. Procedure of data collection

3.6. Variables and measurement instruments

Many potential risk factors have been considered in the literature, details of which were provided in the literature review chapter. However, not all of them are relevant to the Vietnamese culture and local context. We focused on established risk factors and included those potential factors of interest according to the study objectives but paid less attention to those without demonstrating consistent relationship with the outcome in previous studies. Information concerning the participants and their infants was extracted from medical records or obtained by using validated questionnaires and standardised instruments. Table 3.1 describes the main variables and corresponding instruments used.

Table 3. 1. Description of study variables and instruments

Variables	Instruments	Assessments
Demographic and personal characteristics		
Demographic and personal characteristics: age, marital status, occupation, education level, and parity	Structured questionnaire	Baseline
Potential factors		
Lifestyle: cigarette smoking, alcohol drinking	WHO STEPS	Baseline
Gestational diabetes status	Clinical assessment	Baseline

Anthropometrics: height, weight	Portable stadiometer, digital weight scale, tape measure	Baseline
Physical activity	PPAQ-V	Baseline
Antenatal depression	EPDS-V	Baseline
Obstetric and birth outcomes: maternal disorders and complications, preterm birth, still birth, Apgar score, mode of delivery, neonatal intensive care, length of hospital stay	Medical records, structured questionnaire	Discharge
Infant birthweight	Digital weight scale	Immediately after birth
Postnatal depression	EPDS-V	one, three and six-months postpartum
Infant hospitalisation, diarrhoea and lower respiratory tract infection	Structured questionnaire Medical records	one, three and six-months postpartum

EPDS-V: Edinburgh Postnatal Depression Scale - Vietnamese version
PPAQ-V: Pregnancy Physical Activity Questionnaire - Vietnamese version
WHO STEPS: World Health Organisation's STEP wise approach to Surveillance

Edinburgh Postnatal Depression Scale (EPDS) was utilised to ascertain maternal depressive symptoms (Cox, Holden et al. 1987). EPDS is a self-administered questionnaire widely adopted in postnatal depression studies, but also used in the antenatal period to explore the women's feeling within the past week. It comprises of 10 questions rated on a 4-point Likert scale (from 0 to 3), indicating the degree of

agreement, with the total score between 0 and 30. This study used a validated Vietnamese version of EPDS (EPDS-V) (Fisher, Morrow et al. 2004). The whole questionnaire was translated from English to Vietnamese and then back translated for verification. Two questions had been slightly modified to include appropriate Vietnamese linguistic expressions. Question 6 was modified from "*Things have been getting on top of me*" to "*Do you feel that you have too many tasks to manage*". Similarly, question 10 "*I have had thoughts of harming myself*" was modified to "*Have you had thoughts that you do not want to live any more, and if so, how often*", to avoid misinterpretation in the Vietnamese context.

Demographic and personal characteristics were collected including age, marital status, occupation, educational level, parity and contact details (address, (mobile) telephone number(s) of participant and their next-of-kin).

Alcohol drinking and cigarette smoking (active or passive) information were collected using selected questions from the WHO STEPS instrument (World Health Organization 2017).

Habitual Physical activities were assessed using the validated Vietnamese version of the Pregnancy Physical Activity Questionnaire (PPAQ-V)(Ota, Haruna et al. 2008), which is a semi-quantitative questionnaire consisting of 32 activities to measure the duration, frequency and intensity of habitual physical activity and sedentary behaviour during pregnancy. It is classified into four domains, namely, household/caregiving (13 activities), occupation (5 activities), exercise/sport (8 activities) and transportation (3 activities), and inactivity (3 sedentary activities). For each activity/inactivity,

respondents are requested to choose a category with the nearest amount of time spent per day or per week. The possible duration ranged from 0 to 6 or more hours per day. An open-ended section was added to the end to permit listing of extra activities not included in the PPAQ.

An energy expenditure was reported as metabolic equivalent task (MET-hour per week). MET was calculated by multiplying each activity's duration and its intensity. The total physical activity's energy expenditure was calculated by summing up across all activities. Intensity of physical activity was classified into four level, namely, sedentary (<1.5 MET), light (1.5-3 MET), moderate (3-6 MET) and vigorous (>6 MET) (Ota, Haruna et al. 2008).

There was moderate Pearson correlation of 0.3 ($p = 0.02$) between total physical activity and the pedometer step counts, while intra-class correlations ranged between 0.87 and 0.94 for the various intensity levels of activity (Ota, Haruna et al. 2008). Healthy pregnant women are recommended to do moderate-intensive aerobic activity at least 150 minutes per week (American College of Obstetricians and Gynecologists 2015). Therefore, participants meet this PA guideline if they did more 7.5 MET hours or more per week in exercise/sport activities of moderate intensity.

Gestational diabetes mellitus: all pregnant women between 24 to 28 weeks of gestation were required to undergo 75-gram oral glucose tolerance test to determine their glucose-metabolic status, by collecting three blood samples at fasting, one hour and two hours. The World Health Organisation diagnostic criteria 2013 was used to confirm GDM, if at least one glucose value meeting the thresholds: fasting plasma

glucose ≥5.1 mmol/L, 1-h plasma glucose ≥10.0 mmol/L, 2-h plasma glucose ≥8.5 mmol/L (World Health Organization 2013).

Anthropometric variables namely weight and height, birthweight for the new-borns, were measured by trained personnel using standard instruments. Pre-pregnancy (i.e., before pregnancy) weight was retrieved from medical records. Pre-pregnancy BMI was then computed using weight and height recorded at the baseline (kg/m^2) and classified according to (WHO Expert Consultation 2004).

Obstetric, birth outcomes and infant health including maternal disorders and complications during pregnancy, were extracted from medical records at the hospitals.

3.7. Data management

The candidate was responsible for verification of data accuracy and data management, by first screening and checking the completed questionnaires for missing or incomplete entries and typing mistakes, before transcription of information from paper records to an electronic database. The data were input into Epi-data in which legal values, logical errors values, missing information could be automatically checked. Data were then pooled and combined across the study sites and were de-identified prior to statistical analysis. Stat Transfer application was used to transfer the data sets to Stata for further cleaning and statistical analysis.

Hardcopy of the questionnaires were stored at Curtin University and locked inside a filing cabinet for seven years. After that period, they will be destroyed. Electronic data (Stata files) were stored at the Curtin University network R drive. For security

purposed, they were password-protected and accessible to the researcher and his supervisors only.

3.8. Statistical analysis

Stata version 15 (Stata Corp LP, College Station, TX, USA) was used as the data analytic platform to perform the data analyses. Firstly, summary and descriptive statistics were applied to describe the response rate and retention rate of the follow-up, cohort profile and to summarise the exposures and outcome variables. The results were reported as numbers and percentages (prevalence) for categorical variables, as mean and SD for normally distributed continuous variables, and as median and percentile/inter-quartile range for continuous variables which exhibited a skewed distribution. Univariate analysis was conducted among participants with information on antenatal depression and postnatal depression, and to summarise the sample characteristics, potential covariates and confounders. Chi-square test was reported along with Fisher exact test when appropriate for categorical variables. T-test/ANOVA test and non-parametric tests such as Mann-Whitney U/Wilcoxon rank-sum test were used to compare the outcome measures between subgroups of interest. A two-sided p value less than 0.05 was considered as statistically significant.

In view of the skewed distribution of the EPDS scores, sensitivity analyses were conducted using the logarithmic transform of the outcome variable in the regression models. However, the results were similar and thus not presented for brevity. Multiple linear regression models were fitted to determine the associations between the EPDS depressive symptom scores, exposure variables and other outcome variables of interest such as birth outcomes and infant health problems, in which predictors with $p \geq 0.2$ were removed from the full model. The criterion of $p \geq 0.2$ was adopted following the

advice from the literature (Maldonado and Greenland 1993, Latz, DeCarlo et al. 2020). Confounding factors for the multivariable regression analyses included maternal age, marital status, maternal education, occupation, smoking, alcohol drinking, pregnancy physical activity level, GDM, pre-pregnancy body mass index, parity, GWG, delivery method, Apgar score, infant birthweight, jaundice, obstetric complications, length of hospital stay, admission to neonatal intensive care, and infant health. The specific set of confounding factors corresponding to each outcome variable of interest in the multivariable analyses will be discussed in detail in Chapter 4. Results were presented in terms of regression coefficients and their 95% confidence intervals and p values.

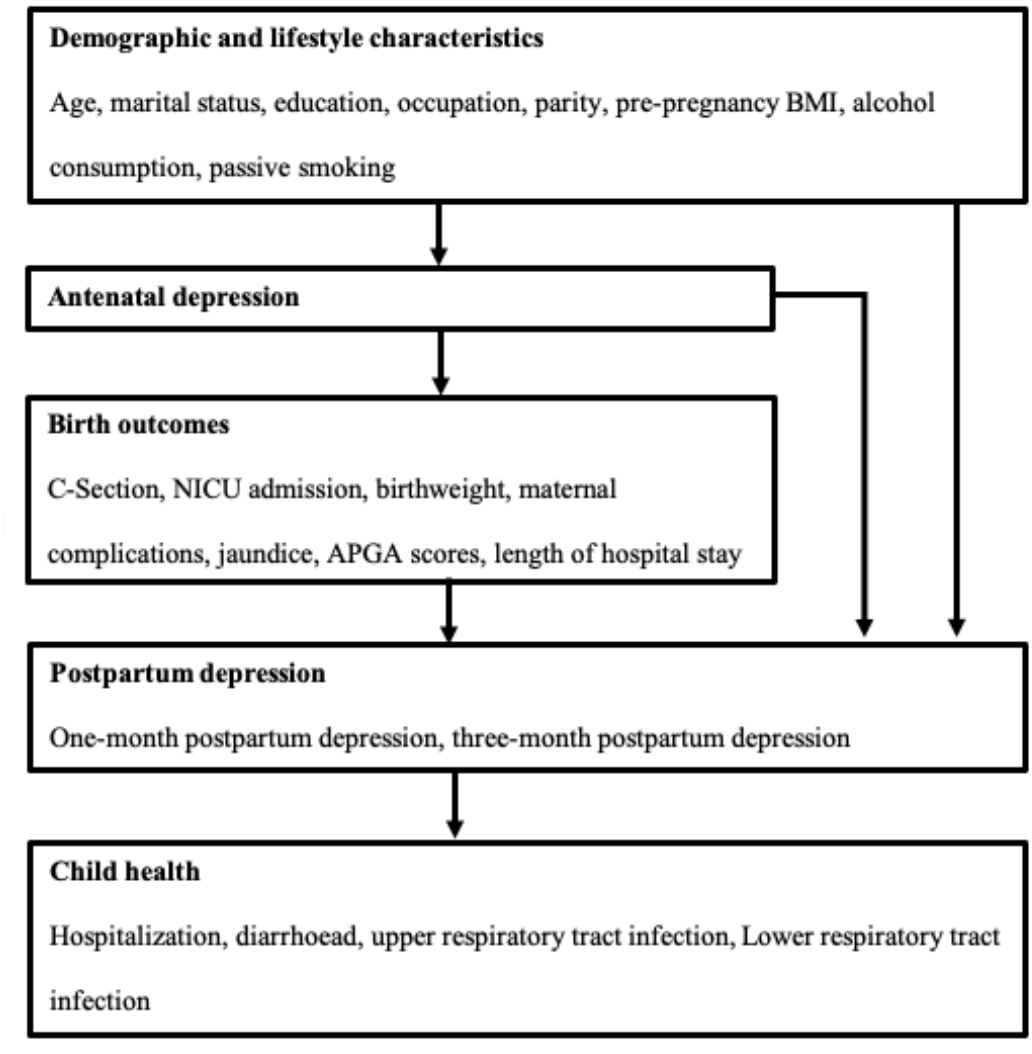

Figure 3. 3. Conceptual framework for data analysis

3.9. Ethical considerations

Taking part in this study was completely voluntary. All participants were given an information letter (written in plain Vietnamese language) and verbally explained about the purpose and nature of the study, and the assessment procedure (Appendix C). The completed consent form must be signed by the participants and witnessed by another adult before enrolment (Appendix D). Information provided was regarded as completely confidential. Participants might refuse to answer any question and had the freedom to withdraw from the study at any time they choose without prejudice. Each participant was allocated a unique identify number only known to the researchers. Their contact details such as name, address, and telephone numbers were kept in a separate electronic file. All identifiable information was kept confidentially and coded throughout the study and analysis. For statistical and publication purposes, aggregated data rather than individual data were reported. Furthermore, participants were given the contact details of the principal researchers to seek clarification if necessary. All assessments were undertaken in a private room by research assistants. Those participants who reported a high EPDS score were advised to consult their medical doctor or health professionals.

This study was part of a large project *"Maternal lifestyle and nutritional status in relation to pregnancy and child health outcomes: A multi-centre prospective cohort study in Vietnam".* The project has four main components, namely, (1) Gestational diabetes mellitus, (2) Antenatal and postnatal depression, (3) Infant feeding practice and (4) Gestational weight gain and postpartum weight retention. The candidate was solely responsible for component 2, independent of other investigations. The original protocol had been approved by Curtin Human Research Ethics Committee (approved

number HR 32/ 2015, Appendix A); and Hai Phong University of Medicine and Pharmacy Human Research Ethics Committee (approval number 05/HPUM RB/2015, Appendix B). Agreements for data collection were obtained from all hospitals involved.

CHAPTER 4: RESULTS

4.1. Overview

This chapter presents epidemiological findings from the prospective cohort study in Vietnam, using the methodology as described in Chapter 3. It comprises several sections preceded by the participation and response rate of the cohort from recruitment to the six-month follow up. General characteristics of the study participants are described, followed by the distribution of, and factors associated with, depression during pregnancy, and at one and three months postpartum. It also reports the perinatal depressive symptoms in relation to maternal physical activity during pregnancy, GDM, GWG, birth outcomes, as well as infant health problems within the first six months.

4.2. Participation and response rate

Figure 4. 1 presents the enrolment process and number of participants at each stage from the five surveys conducted throughout this study, with explanations for the dropouts or loss to follow up for the cohort. The participation rate was 90.3% due to refusal or failure to respond to the invitation (n = 218) from the initial 2248 eligible women at enrolment. As a result, 2030 participants were enrolled at the baseline survey from six hospitals of three cities at their 24-28 weeks of gestation. Among them, 1906 participants were interviewed at hospital discharge (response rate 93.9%), after exclusion of a group of 124 mothers (6.1%) because of loss of contact, HIV infection, adverse pregnancy outcomes or perinatal deaths. The response rates at one, three and six months follow up were about 90%, due to loss of contact or relocation of the participants to another city.

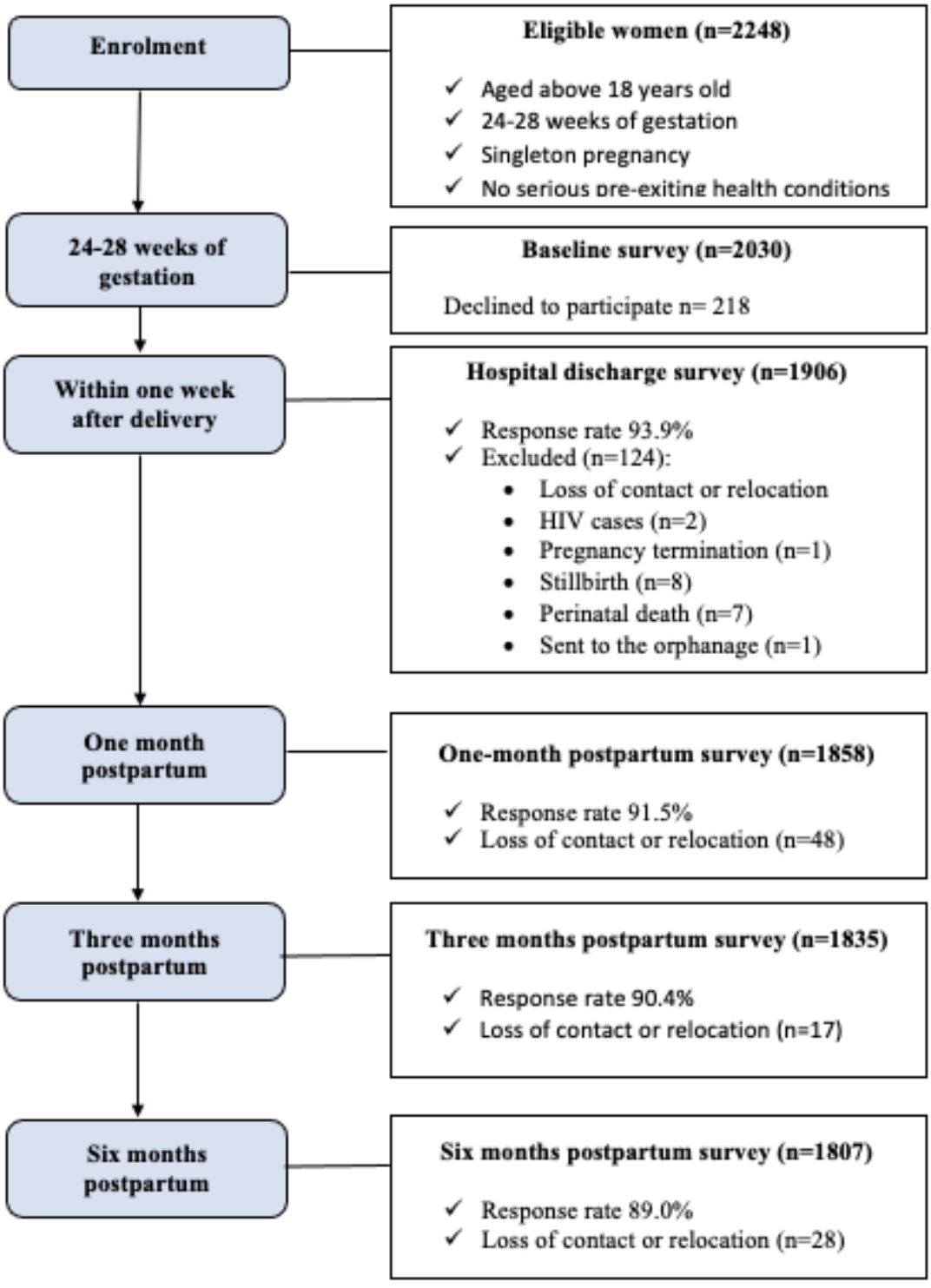

Figure 4. 1. Flow chart of participants

4.3. Characteristics of participants

Table 4.1 describes the maternal demographic profile. Nearly two-thirds of the participants were aged between 25 and 35 years, and less than 10% of the women were aged over 35 years. Almost all women were married (99.3%). Worker was the most common occupation (40.30%). They included factory workers, employees of textile and food companies, cleaners or construction workers. About 17% of the participants were not employed formally and characterized themselves as housewives. Nearly two-thirds of the women achieved high school or higher education level, and less than 10% did not attain secondary school education. Sixty percent of participants were passive smokers. Two-thirds of participants had less than two children. Most of the women had a pre-pregnancy body mass index (BMI) within the normal range for Asian women (18.5-23.0 kg/m^2) (WHO Expert Consultation 2004).

Table 4. 1. Demographic and lifestyle characteristics

Variable	Frequency (n)	Percent (%)
Age (years)		
< 25	637	31.38
25-35	1230	60.59
> 35	163	8.03
Marital status		
Single/divorced/separated/widowed	14	0.69
Married	2016	99.31
Occupation		
Farmer	296	14.57
Worker	818	40.30
Office/technical staff	456	22.46
Sales	119	5.86
Housewife/unemployed	341	16.80
Education level		

Variable	Frequency (n)	Percent (%)
Less than secondary school	171	8.42
Secondary school	551	27.14
High school graduate	525	25.86
College/university	783	38.57
Parity		
0	789	38.87
1	756	37.24
≥ 2	485	23.89
Pre-pregnancy BMI (kg/m^2) [1]		
Underweight (<18.5)	516	25.42
Normal (18.5 to <23)	1254	61.77
Overweight/obese (≥ 23)	260	12.81
Passive smoking [2]		
No	813	40.05
Yes	1217	59.95
Alcohol consumption [3]		
No	1758	86.60
Yes	272	13.40

[1] BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004)

[2]Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.

[3]Alcohol consumption: any consumption of beer or wine

Table 4.2 shows the maternal physical activity pattern during pregnancy. Physical activities were determined using the Pregnancy Physical Activity Questionnaire PPAQ-V which had been validated for pregnant women in Vietnam (Ota, Haruna et al. 2008); see Section 3.6 for details on the instrument. The average physical activity level was 123.2 (SD 56.9) MET-hour per week. Light physical activities accounted for the largest proportion of total physical activity (57.5MET-hour/week), followed by sedentary and moderate physical activity (36.8 and 26.5 MET-hour/week,

respectively). Regarding domains of physical activity, participants spent their highest energy expenditure on household chores and/or care giving activities (59.3 MET-hour/week), whereas the corresponding values for occupational and travel activities were 31.4 and 11.5 MET-hour/week, respectively. On average, only 6.1 MET-hour/week spent were devoted to sport or leisure activities.

Table 4. 2. Physical activity during pregnancy

Physical activity	Mean	SD	Minimum	Maximum
Total level (MET-hour/week)	123.2	56.9	8.4	362.8
1st tertile (8.4 to <94.3)	65.0	18.7	8.4	92.6
2nd tertile (94.3 to <144.2)	116.0	14.3	92.8	141.9
3rd tertile (144.2 to 362.8)	189.2	37.4	142.1	362.8
Intensity				
Sedentary	36.8	21.0	0	110.1
Light	57.5	32.9	0	170.1
Moderate	26.5	29.3	0	186.0
Vigorous	0.5	3.4	0	73.5
Domains				
Household/care giving	59.3	41.9	0	231.0
Occupation	31.4	29.4	0	176.2
Sport/leisure activity	6.1	9.5	0	81.4
Travel	11.5	13.1	0	170.6

SD: standard deviation; MET: metabolic equivalent task

Oral glucose tolerance test was conducted to determine the glucose-metabolic status of the participants. In addition to fasting glucose levels, each participant underwent one-hour and two-hour glucose tolerance tests to collect blood samples at around 28 weeks after administering to them 75g glucose. Table 4.3 shows the results. The mean fasting plasma glucose level was 4.47 mmol/L (SD 0.51), and the corresponding values at one and two hours were 7.62 mmol/L (SD 1.88) and 6.70 mmol/L (SD 1.88),

respectively. The blood glucose levels in fasting and postprandial states appeared to increase with age, i.e., older women generally had higher values than their younger counterparts. According to the WHO diagnostic criteria adopted in Vietnam (World Health Organization 2013), 21% of the participants had GDM. The proportion of women diagnosed with GDM based on fasting, 1-h and 2-h glucose levels were 8.23%, 10.39% and 12.86%, respectively.

Table 4. 3. Age-specific glucose levels and gestational diabetes mellitus

Glucose level		Mean (mmol/L)	SD	Minimum	Maximum
Fasting	All	4.47	0.51	2.9	7.7
	Age <25	4.43	0.51	2.9	7.6
	Age 25-35	4.48	0.51	3.1	7.7
	Age >35	4.55	0.47	3.3	6.2
1-h	All	7.62	1.88	3.4	17.1
	Age <25	7.02	1.70	3.5	14.7
	Age 25-35	7.82	1.87	3.4	17.1
	Age >35	8.49	1.95	4.0	15.4
2-h	All	6.70	1.55	2.8	16.5
	Age <25	6.19	1.35	3.2	11.7
	Age 25-35	6.86	1.53	2.8	14.6
	Age >35	7.46	1.81	3.2	16.5

GDM status		Frequency (n)	Percent (%)
By WHO criteria			
	No	1591	78.65
	Yes	432	21.35
By fasting glucose level			
	No	1863	91.77
	Yes	167	8.23
By 1-h glucose level			
	No	1819	89.61
	Yes	211	10.39

Glucose level	Mean (mmol/L)	SD	Minimum	Maximum
By 2-h glucose level				
	No	1769	87.14	
	Yes	261	12.86	

SD: standard deviation; GDM: Gestational Diabetes Mellitus (World Health Organization 2013)

Table 4.4 shows the distribution of gestational weight gain. Adequate group accounted for 42.72%, while excessive and inadequate groups were 37.93% and 19.35% respectively. Table 4.5 describes some birth outcome variables. This time, nearly forty percent of the participants had caesarean section. About three percent of infants admitted NICU and nearly four percent were low birth weight.

Table 4. 4. Gestational weight gain

Variable	Frequency (n)	Percent (%)
Gestational weight gain *		
Adequate	777	42.72
Inadequate	352	19.35
Exessive	690	37.93

**Classified according to Institute of Medicine and National Research Council Committee (Institute of Medicine and National Research Council Committee 2009)*

Table 4. 5. Birth outcomes

Variable		Frequency (n)	Percent (%)
Caesarean section			
	No	1178	61.80
	Yes	728	38.20
NICU			
	No	1851	97.11
	Yes	55	2.89
Low birth weight			
	No	1828	95.91
	Yes	78	4.09
Maternal complications [1]			

Variable			Frequency (n)	Percent (%)
		No	1817	97.84
		Yes	40	2.16
Jaundice [2]				
		No	1677	90.31
		Yes	180	9.69
	Mean	**SD**	**Minimum**	**Maximum**
Apgar 1 minute	8.2	0.72	3	10
Apgar 5 minutes	9.2	0.71	5	10
Birth weight (gram)	3143	405	900	4500
Length of hospitalization (days)	3.52	2.38	1	40

NICU: Neonatal intensive care unit, SD: Standard deviation
1 Complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain
2 Jaundice: According to medical record

Table 4.6 describes infant health issues during the first six months after giving birth. There were 14.1% of the children had to go to hospital. The percentages of children got diarrhoea and low respiratory infection were 14.98% and 25.39% respectively.

Table 4. 6. Infant health at six months postpartum

Variable		**Frequency** (n)	**Percent** (%)
Hospitalization [1]			
	No	1468	85.99
	Yes	241	14.10
Diarrhea [1]			
	No	1453	85.02
	Yes	256	14.98
Low respiratory infection [1]			
	No	1275	74.61
	Yes	434	25.39

[1] according to medical record

4.4. Antenatal depressive symptoms

This section presents the antenatal depressive symptoms scores by maternal profile and examines potential risk and protective factors for antenatal depression. The Edinburgh Postnatal Depression Scale-Vietnamese version (EPDS-V) questionnaire was used to assess antenatal depressive symptoms; see Section 3.6 for details on the instrument.

4.4.1. Distribution of antenatal EPDS scores

Figure 4. 2 displays the empirical distribution of the antenatal EPDS scores. Intuitively, the depressive symptoms scores followed a right skewed distribution, with the mean (5.1) being greater than the median (4.0). The depressive symptoms scores ranged from 0 to 27, with most participants (90.9%) having a score of less than 12.

If a cut-off-point of 13 for antenatal depression (Murray, Dunne et al. 2015) was adopted, the observed prevalence of antenatal depression would be only 7.04% (n=143). Given such a low prevalence, the antenatal EPDS was presented and analyzed as a continuous score rather than being classified as a binary variable (depressed versus not depressed) in subsequent sections, unlike some studies in the literature.

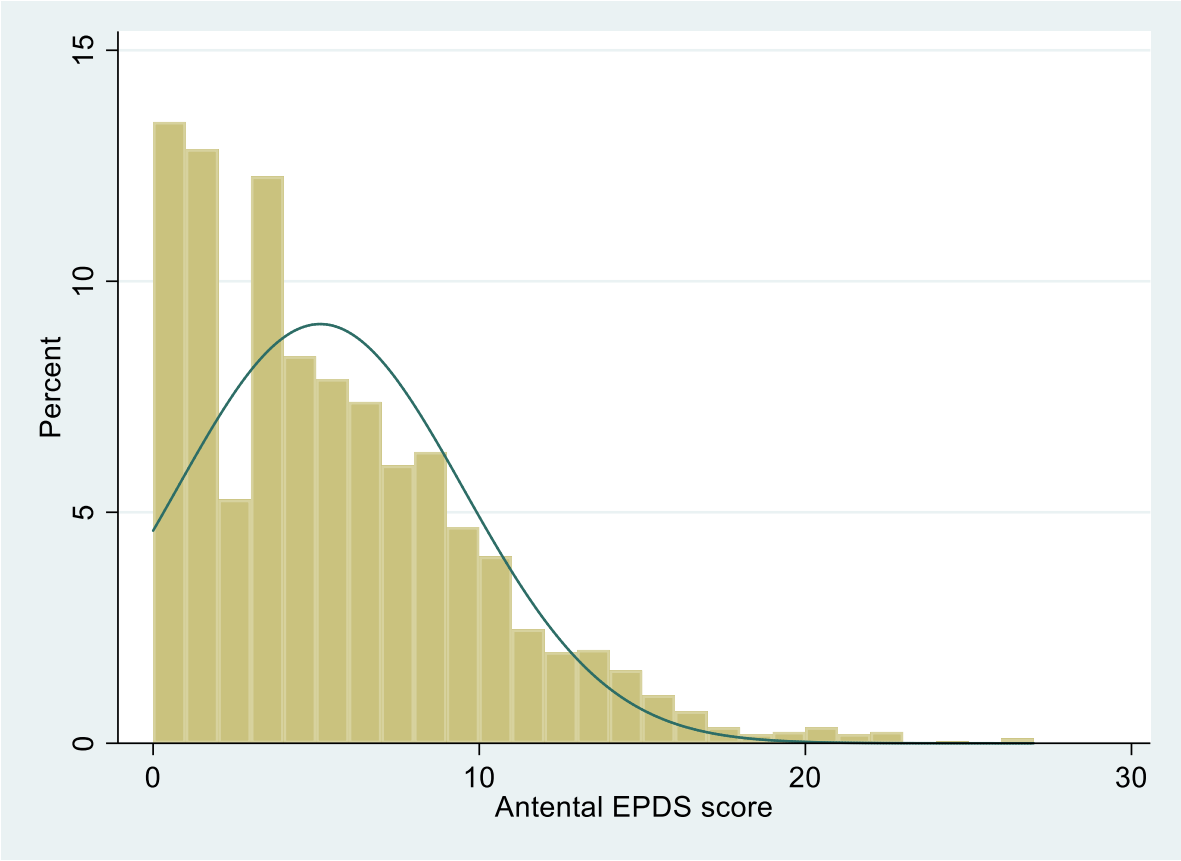

Figure 4. 2. Distribution of antenatal EPDS scores

4.4.2. Antenatal EPDS scores by participant characteristics

Table 4.7 exhibits antenatal EPDS by maternal demographic and common lifestyle characteristics. Younger pregnant women appeared to have higher mean EPDS scores than their older counterparts. The mean EPDS score in women under 25 years of age was approximately 14% and 30% greater than those women aged 25-35 and over 35 years, respectively. Married women had a lower mean EPDS score when compared to their single, divorced or separated counterparts, albeit a statistically non-significant difference. Regarding occupation, the highest depressive symptoms score was observed among women who were office or technical staff, followed by farmers, manual workers, housewives/unemployed and sales workers. Women who attained a higher education level had a significantly higher mean EPDS score, whereas those with

a higher pre-pregnancy BMI had a lower mean depressive symptoms score. There were a lack of significant difference regarding EPDS scores by parity. Depressive symptoms scores were higher in pregnant women with passive smoking than those without. Similarly, a higher mean EPDS score was found among pregnant women who drank alcohol when compared to non-drinker in early pregnancy. Blood pressures (systolic and diastolic) were weakly but negatively correlated with the antenatal EPDS scores; the Spearman rho being -0.08 and -0.22, respectively.

Table 4. 7. Antenatal EPDS scores by demographic and lifestyle characteristics

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Age (years)								
<25	637	5.63	4.45	5	6	0	26	<0.001
25-35	1230	4.96	4.39	4	6	0	27	
>35	163	4.36	4.08	3	6	0	19	
Marital status								
Married	2016	5.12	4.40	4	7	0	27	0.456
Single/divorced/ separated/widow	14	5.79	4.15	3.5	6	1	14	
Occupation								
Farmer	296	5.17	4.55	4	6.5	0	22	0.045
Worker	818	5.00	4.45	4	6	0	27	
Office/technical staff	456	5.51	4.20	5	6	0	20	
Housewife/unemployed	341	4.99	4.37	4	7	0	22	
Sales	119	4.74	4.45	3	7	0	24	
Educational level								
Less than secondary school	171	3.54	4.24	3	4	0	24	<0.001
Secondary school	551	4.44	4.36	3	6	0	27	
High school graduate	525	5.39	4.42	5	6	0	26	
College/university	783	5.78	4.29	5	5	0	21	

Variable		n	Mean	SD	Median	IQR	Min	Max	p*
Parity									
	0	789	5.04	4.31	4	7	0	22	0.82
	1	756	5.22	4.49	4	7	0	24	
	≥2	485	5.10	4.41	4	7	0	27	
Pre-pregnancy BMI (kg/m^2) [1]									
	Underweight (<18.5)	516	5.74	4.57	5	6	0	27	<0.001
	Normal (18.5 to <23.0)	1254	5.12	4.35	4	7	0	24	
	Overweight/obese (≥23.0)	260	3.93	4.02	3	5	0	20	
Passive smoking [2]									
	No	813	4.48	3.96	4	6	0	22	<0.001
	Yes	1217	5.55	4.62	5	6	0	27	
Alcohol consumption [3]									
	No	1758	4.91	4.33	4	6	0	27	<0.001
	Yes	272	6.48	4.56	6	6	0	26	

SD: standard deviation; IQR: interquartile range

**p values based on rank sum test or Kruskal Wallis test*

[1] BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004)

[2]Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.

[3]Alcohol consumption: any consumption of beer or wine

4.4.3. Antenatal EPDS scores by physical activity during pregnancy

Table 4.8 shows antenatal EPDS scores according to physical activity level during pregnancy. Pregnant women who met the physical activity recommendation (i.e., >7.5 MET-hour/week in sports/exercise activities of moderate-intensity) (American College of Obstetricians and Gynecologists 2015, Piercy, Troiano et al. 2018), appeared to have a higher mean EPDS score than those not meeting the guideline, despite the lack of statistical significance. However, women with a higher level of total physical activity recorded a significantly higher mean antenatal EPDS score, p <0.001.

As shown in Table 4.9, regarding domains of physical activity, most physical activity subtypes were weakly but significantly positively associated with antenatal EPDS scores ($p<0.001$), except for recreational physical activity. Regarding physical activity intensity, both light and moderate-intensity activities were weakly but positively associated with antenatal EPDS scores, while sitting time and vigorous-intensity activity showed no apparent association; see Table 4.9. It appears that physical activity during pregnancy has played a role in antenatal depression among Vietnamese women.

Table 4. 8. Antenatal EPDS scores by physical activity level

Physical activity		n	Mean	SD	Median	IQR	Min	Max	P*
Meeting physical activity guidelines[1]	No	1610	5.08	4.37	4	7	0	27	0.51
	Yes	420	5.28	4.50	4	6	0	22	
Total level (MET-hour/week)									
1st tertile (8.4 to <94.3)		680	4.32	4.19	3	6	0	27	<0.001
2nd tertile (94.3 to <144.2)		677	5.03	4.26	4	6	0	26	
3rd tertile (144.2 to 362.8)		673	6.04	4.58	5	6	0	24	

SD: standard deviation; IQR: interquartile range; MET: metabolic equivalent task

**p values based on rank sum tests for binary variables or Kruskal Wallis tests for categorical variables with three levels or more*

[1] >7.5 MET-hour/week in sports/exercise activities of moderate-intensity (American College of Obstetricians and Gynecologists 2015)

Table 4. 9. Antenatal EPDS scores and physical activity domain and intensity

Physical activity	n	Spearman rho	p*
Total level (MET-hour/week)	2030	0.21	<0.001
Domain			
Household/care giving	2030	0.16	<0.001
Occupation	2030	0.10	<0.001
Sport/leisure activity	2030	0.03	0.15
Travel	2030	0.15	<0.001
Intensity			
Sedentary	2030	0.04	0.10
Light	2030	0.16	<0.001
Moderate	2030	0.24	<0.001
Vigorous	2030	0.01	0.76

MET: metabolic equivalent task

**p values based on Spearman test*

4.4.4. Antenatal EPDS scores and gestational diabetes mellitus

Table 4.10 exhibits antenatal EPDS scores by GDM. Compared to non-gestational diabetic women, those with this condition reported a significantly lower mean EPDS score. In other words, the antenatal EPDS mean score of gestational diabetic women were about 20% lower than their non-gestational diabetic counterparts. The maximum EPDS score in the GDM and non-GDM group was 19 and 27, respectively, and the minimum score was zero for both groups. There were significant negative associations ($p<0.001$) between antenatal EPDS score and plasma glucose levels at one hour and two hours after drinking 75g glucose; the Spearman rho being -0.16 and -0.18, respectively. However, no association was observed for fasting glucose with Spearman rho -0.02 ($p>0.05$).

Table 4. 10. Antenatal EPDS scores by gestational diabetes mellitus

GDM	n	Mean	SD	Median	IQR	Min	Max	p*
No	1591	5.37	4.51	5	6	0	27	<0.001
Yes	432	4.25	3.83	3	5	0	19	

GDM: Gestational Diabetes Mellitus (World Health Organization 2013); SD: standard deviation; IQR: interquartile range

**p value based on rank sum test*

4.4.5. Antenatal EPDS scores and gestational weight gain

GWG is classified as *inadequate, adequate* or *excessive* according to the Institute of Medicine (Institute of Medicine and National Research Council Committee 2009) with respect to the pre-pregnancy body mass index, as shown in table 4.11:

Table 4. 11. Classification of gestational weight gain

Pre-pregnancy BMI (kg/m^2)	GWG (kg)		
	Inadequate	Adequate	Excessive
Underweight (< 18.5)	<12.5	15.5-18.0	>18.0
Normal (18.5-24.9)	<11.5	11.5-16.0	>16.0
Overweight (25-29.9)	<7.0	7.0-11.5	>11.5
Obese (≥ 30)	<5.0	5.0-9.0	>9.0

BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004); GWG: Gestational weight gain (Institute of Medicine and National Research Council Committee 2009)

Table 4.12 presents antenatal EPDS scores by GWG status. Women with adequate GWG had the highest antenatal mean EPDS score, while those with excessive GWG reported the lowest mean score. Nevertheless, no significant difference in mean EPDS was found among the three groups. The maximum EPDS scores in pregnant women with adequate, inadequate and excessive GWG were 24, 27 and 22, respectively. Also, there was no apparent association between antenatal EPDS and the continuous GWG

variable with Spearman rho -0.01 (p>0.05). Therefore, it may be concluded that GWG is not an influencing factor for antenatal depression.

Table 4. 12. Antenatal EPDS scores by gestational weight gain

GWG	n	Mean	SD	Median	IQR	Min	Max	p*
Adequate	777	5.48	4.29	5	6	0	24	0.33
Inadequate	352	5.33	4.70	4	7	0	27	
Excessive	690	4.95	4.22	4	6	0	22	

SD: standard deviation; IQR: interquartile range; GWG: Gestational weight gain (Institute of Medicine and National Research Council Committee 2009)

**p value based on rank sum test*

4.4.6. Factors affecting antenatal depression

To investigate demographic, lifestyle and other risk factors associated with antenatal depressive symptoms, a stepwise multiple linear regression model with backward selection procedure was fitted, in which predictors with $p \leq 0.2$ were removed from the full model. A total of eight independent factors were initially selected and entered into the regression model, based on the available information, the literature review of plausible confounders for antenatal depression (see Chapter 2), together with the aforementioned univariate analyses in Sections 4.4.2-4.4.5. The occupation variable was then eliminated from the model. Table 4.13 summaries results from fitting the regression model, providing estimates for the regression coefficients and their corresponding 95% confidence intervals. According to this model, age was weakly and negatively associated with EPDS, whereas a positive association was found for total physical activity level. Women with GDM appeared to experience significantly less depressive symptoms during pregnancy when compared to their non-GDM counterparts. More educated women reported significantly higher EPDS scores

(p<0.05). Body mass index was significantly and inversely associated with EPDS, while passive smoking and alcohol drinking during pregnancy showed significant positive associations with the depressive symptom scores. Overall, these seven predictors explained about nine percent of the variations in antenatal EPDS.

Table 4. 13. Factors associated with antenatal EPDS score

Variable	Coefficient*	SE	p	95% CI	
				Lower	Upper
Intercept	3.84	0.70	<0.001	2.48	5.21
Age (years)	-0.04	0.02	0.022	-0.08	-0.01
GDM					
No	reference				
Yes	-0.71	0.23	0.002	-1.17	-0.25
Maternal education					
Less than secondary school	reference				
Secondary school	0.74	0.37	0.049	0.03	1.46
High school graduate	1.32	0.38	0.001	0.57	2.07
College/university	1.68	0.36	<0.001	0.96	2.41
Pre-pregnancy BMI (kg/m^2) [1]					
Underweight (<18.5)	reference				
Normal (18.5 - <23.0)	-0.47	0.22	0.034	-0.91	-0.36
Overweight/obese (≥23.0)	-1.04	0.33	0.002	-1.69	-0.39
Passive smoking [2]					
No	reference				
Yes	0.81	0.19	<0.001	0.43	1.20
Alcohol consumption [3]					
No	reference				
Yes	1.25	0.28	<0.001	0.71	1.79
Total physical activity (MET-hour/week)	0.01	0.00	<0.001	0.01	0.01

SE: standard error; CI: confidence interval; GDM: Gestational Diabetes Mellitus, classified according to The World Health Organization(World Health Organization 2013); MET: metabolic equivalent task

** Coefficients from fitting stepwise multiple linear regression model*

[1] BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004)

[2]Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.

[3]Alcohol consumption: any consumption of beer or wine

4.4.7. Antenatal EPDS scores and birth outcomes

Table 4.14 presents antenatal EPDS scores by birth outcomes. There were no significant differences in mean EPDS scores between mothers with and without caesarean section, whose baby has low birthweight or not, and whose baby was admitted to neonatal intensive care unit or not. Indeed, the Spearman rho was -0.17 (p=0.45) between EPDS and the continuous birthweight variable. Only a weak negative association was found between EPDS and length of hospital stay, jaundice, and maternal complication. In view of such lack of univariate associations, multiple regression analyses were not performed for these birth outcomes in relation to antenatal depression.

Table 4. 14. Antenatal EPDS scores by birth outcomes

Variable		n	Mean	SD	Median	IQR	Min	Max	p*
Caesarean section									
	No	1178	5.27	4.34	4	6	0	27	0.14
	Yes	728	5.03	4.37	4	7	0	22	
NICU admission									
	No	1851	5.18	4.36	4	7	0	27	0.91
	Yes	55	5.02	4.13	4	7	0	14	
Low birthweight									
	No	1828	5.11	4.37	4	7	0	26	0.61
	Yes (<2500g)	78	5.53	4.98	4	8	0	27	
Maternal complications [1]									
	No	1866	4.20	3.95	4	7	0	26	0.02

Variable		n	Mean	SD	Median	IQR	Min	Max	p*
	Yes	40	2.7	4.21	1	4	0	19	
Jaundice [2]									
	No	1724	4.27	3.97	4	7	0	26	0.01
	Yes	182	3.21	3.77	2	5	0	19	

SD: standard deviation; IQR: interquartile range; NICU: Neonatal intensive care unit

**p value based on rank sum test*

[1] Complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain

[2] Jaundice: According to medical record

Table 4.15 shows relations of one-month postpartum EPDS and APGAR scores, birthweight and length of hospital stay. However, there were no statistically significant relations between one-month postpartum EPDS score and these factors.

Table 4. 15. One-month postpartum EPDS scores and APGAR scores, birthweight and length of hospital stay

Variable	n	Spearman rho	p*
APGAR score 1 minute	1857	-0.038	>0.05
APGAR score 5 minutes	1857	-0.055	>0.05
Birthweight	1857	-0.047	>0.05
Length of hospital stay	1857	-0.013	>0.05

** p value based on Spearman test*

4.5. Depressive symptoms at one month postpartum

This section examines depression at one month postpartum and its association with maternal demographic, clinical and lifestyle factors, as well as birth outcomes. Again, the Edinburgh Postnatal Depression Scale-Vietnamese version (EPDS-V) questionnaire was used to assess the depressive symptoms at one month postpartum; see Section 3.6 for details on the instrument.

4.5.1. Distribution of EPDS scores at one month postpartum

Figure 4. 3 describes the distribution of EPDS scores of the cohort at one month after delivery. Similar to the antenatal EPDS distribution, EPDS scores at one month postpartum were skewed to the right with the mean (3.5) greater than the median (2.0), while the great majority of participants (93.4%) having a score below 10. Overall, the EPDS scores ranged from 0 to 24. Like antenatal EPDS, if a cutoff of 13 for postnatal depression (Murray, Dunne et al. 2015) were adopted, the observed prevalence of postnatal depression would be very low at 2.8% (n=52). Therefore, the EPDS at one month postpartum will be presented and analyzed as a continuous score rather than being classified as a binary variable (depressed versus not depressed) in subsequent sections, unlike some studies in the literature.

4.5.2. One-month postpartum EPDS scores by participant characteristics

Table 4.16 reports EPDS scores of the cohort at one month postpartum in relation to demographic and lifestyle factors. Younger mothers had a significantly higher postnatal mean EPDS score at one month after delivery. Mothers under 25 years old reported approximately 5.5% and 30% significantly higher mean EPDS scores, when compared to those aged 25-35 and over 35 years old, respectively. Similarly, the mean

EPDS scores at one month postpartum were significantly different between occupational groups, with the highest mean score observed for housewives or those unemployed and the lowest mean score for general workers. In addition, pregnant women exposed to passive smoking reported a significantly greater mean EPDS score at one month postpartum than those without such exposure. There were no significant differences in mean EPDS scores with respect to marital status, educational level, body mass index, parity and alcohol drinking during pregnancy. These univariate results will be taken into consideration when assessing factors affecting postnatal depression in Section 4.5.7.

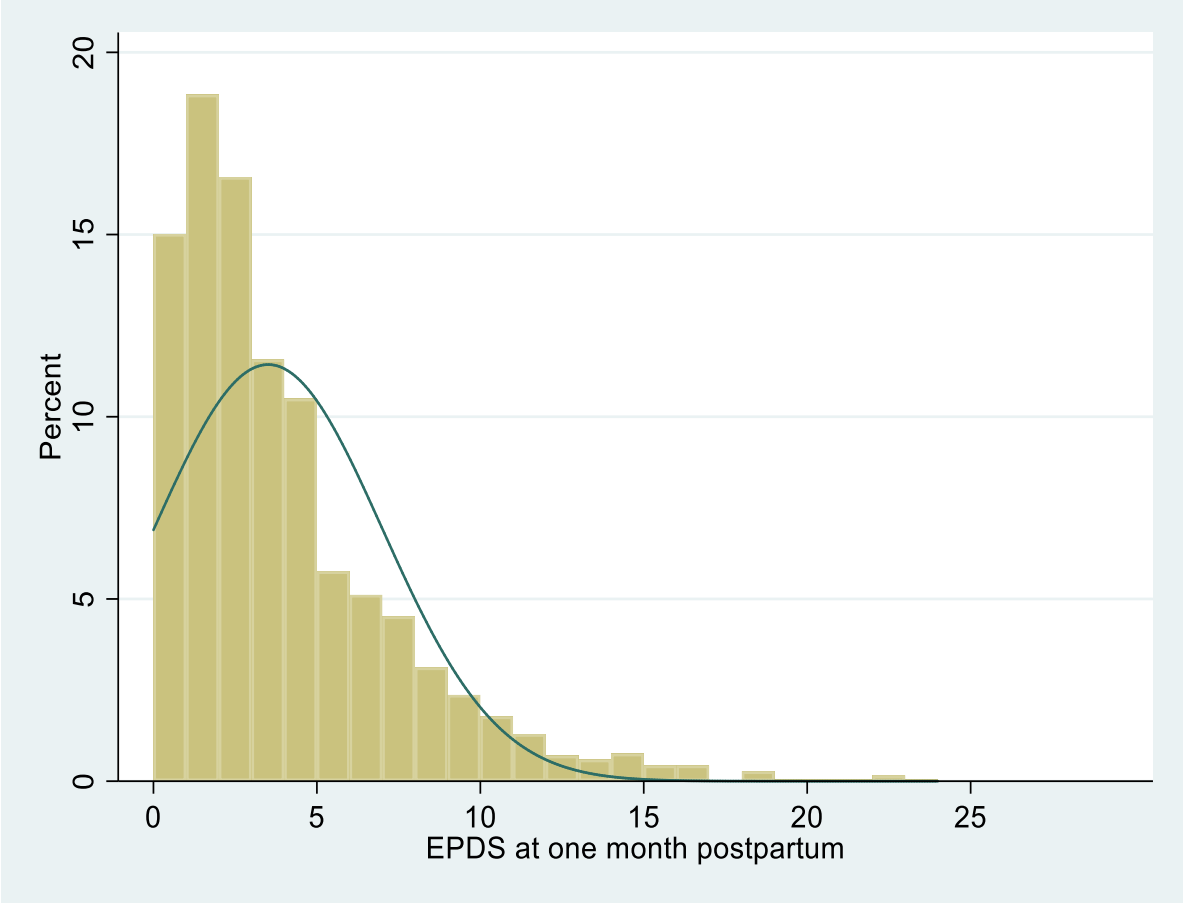

Figure 4. 3. Distribution of EPDS scores at one month postpartum

Table 4. 16. One-month postpartum EPDS scores by demographic and lifestyle characteristics

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Age (years)								
< 25	586	3.69	3.47	3	4	0	22	0.04
25-35	1125	3.50	3.58	2	4	0	24	
> 35	147	2.85	2.72	2	3	0	13	
Marital status								
Single/divorced/ separated/widowed	1846	3.50	3.49	2	4	0	24	0.20
Married	12	4.33	3.08	3.5	5	0	10	
Occupation								
Farmer	283	3.61	3.31	3	4	0	18	0.02
Worker	741	3.28	3.19	2	4	0	22	
Office/technical staff	426	3.35	3.61	2	3	0	24	
Housewife/unemployed	305	4.06	4.06	3	5	0	22	
Sales	103	3.96	3.53	3	5	0	16	
Educational level								
Less than secondary school	146	3.91	3.50	3	4	0	18	0.16
Secondary school	485	3.51	3.35	3	4	0	18	
High school graduate	486	3.38	3.23	2	4	0	19	
College/university	741	3.52	3.74	2	4	0	24	
Parity								
0	715	3.64	3.53	3	4	0	24	0.10
1	689	3.57	3.62	2	4	0	22	
≥ 2	454	3.21	3.20	2	4	0	18	
Pre-pregnancy BMI (kg/m^2) [1]								
Underweight (<18.5)	472	3.80	3.79	3	5	0	24	0.30
Normal (18.5 to <23.0)	1160	3.43	3.39	2	4	0	22	
Overweight/obese (≥23.0)	226	3.32	3.33	3	3	0	19	
Passive smoking [2]								
No	735	3.16	3.23	2	3	0	24	0.001

Variable		n	Mean	SD	Median	IQR	Min	Max	p*
	Yes	1123	3.74	3.63	3	4	0	22	
Alcohol consumption [3]									
	No	1604	3.51	3.47	2	4	0	22	0.67
	Yes	254	3.51	3.64	3	4	0	24	

SD: standard deviation; IQR: interquartile range

**p values based on rank sum tests for binary variables or Kruskal Wallis tests for categorical variables with three levels*

[1] BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004)

[2]Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.

[3]Alcohol consumption: any consumption of beer or wine

4.5.3. One-month postpartum EPDS scores by physical activity during pregnancy

Table 4.17 presents EPDS scores at one month postpartum stratified by physical activity levels during pregnancy. EPDS scores were not significantly different between women meeting and not meeting the recommended level of physical activity, and across tertiles of total physical activity. As demonstrated in Table 4.18, except for occupational physical activity that showed a weak negative association with the EPDS scores, other physical activity domains and physical activity intensities did not appear to be associated with the EPDS scores one month after giving birth. Therefore, physical activity during pregnancy posed little influence on postnatal depression at one month.

Table 4. 17. One-month postpartum EPDS scores by physical activity level

Physical activity	n	Mean	SD	Median	IQR	Min	Max	p*
Meeting physical activity guidelines [1]								
No	1472	3.53	3.56	2	4	0	22	0.68
Yes	386	3.43	3.23	3	4	0	24	
Total level (MET-hour/week)								
1st tertile (8.4 to <94.3)	601	3.63	3.57	3	4	0	22	0.42
2nd tertile (94.3 to <144.2)	623	3.48	3.42	2	4	0	22	
3rd tertile (144.2 to 362.8)	634	3.43	3.48	2	4	0	24	

SD: standard deviation; IQR: interquartile range; MET: metabolic equivalent task

**p values based on rank sum test or Kruskal Wallis test*

[1] >7.5 MET-hour/week in sports/exercise activities of moderate-intensity (American College of Obstetricians and Gynecologists 2015)

Table 4. 18. One-month postpartum EPDS scores and physical activity domain and intensity

Physical activity	n	Spearman rho	p*
Total level (MET-hour/week)	1858	-0.02	0.21
Domain			
Household/care giving	1858	-0.01	0.75
Occupation	1858	-0.05	0.04
Sport/leisure activity	1858	-0.17	0.38
Travel	1858	0.01	0.96
Intensity			
Sedentary	1858	0.01	0.64
Light	1858	-0.01	0.59
Moderate	1858	-0.38	0.13
Vigorous	1858	0.03	0.13

MET: metabolic equivalent task

**p values based on Spearman test*

4.5.4. One-month postpartum EPDS scores and gestational diabetes mellitus

Table 4.19 compares postnatal EPDS scores at one month between mothers with and without GDM. The mean EPDS scores were not significantly different between women with and without GDM. The EPDS scores in the former group ranged between zero and 24, and the latter group from zero to 22. There were also no apparent association between EPDS scores and the continuous glucose levels; the Spearman rho being -0.01, 0.04 and 0.02 ($p > 0.05$) for fasting, 1-h and 2-h, respectively.

Table 4. 19. One-month postpartum EPDS by gestational diabetes mellitus

GDM	n	Mean	SD	Median	IQR	Min	Max	p*
No	1467	3.54	3.53	2	4	0	24	0.77
Yes	385	3.40	3.34	2	4	0	22	

SD: standard deviation; IQR: interquartile range; GDM: Gestational Diabetes Mellitus, classified according to The World Health Organization(World Health Organization 2013)

**p value based on rank sum test*

4.5.5. One-month postpartum EPDS scores and birth outcomes

Table 4.20 displays EPDS scores at one month after delivery by birth outcomes. Mothers experiencing caesarean section reported a significantly higher mean EPDS score than those with virginal delivery ($p = 0.01$). Similarly, mothers with complications had a significantly higher mean EPDS score than others without any complication. Mothers whose infants admitted to neonatal intensive care unit were more likely to incur depressive symptoms when compared to those without such admission. In addition, mothers who delivered babies with low birthweight or jaundice reported higher mean EPDS than those without such conditions. Table 4.21 shows that the continuous APGAR scores at one minute and five minutes, together with

birthweight, were weakly and negatively associated with the EPDS scores, besides a weak negative association being observed for the mother's length of hospital stay.

Table 4. 20. One-month postpartum EPDS score by birth outcomes

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Caesarean section								
No	1147	3.30	3.34	2	3	0	22	0.01
Yes	710	3.85	3.70	3	5	0	24	
NICU admission								
No	1802	3.44	3.42	2	4	0	24	0.001
Yes	55	5.80	4.69	5	6	0	19	
Low birthweight								
No	1784	3.45	3.44	2	4	0	24	0.001
Yes (<2500g)	74	4.96	4.35	3.5	5	0	19	
Maternal complications [1]								
No	1817	3.48	3.48	2	4	0	24	0.001
Yes	40	4.90	3.77	4	5.5	0	14	
Jaundice [2]								
No	1677	3.39	3.45	2	4	0	24	<0.001
Yes	180	4.64	3.65	4	5	0	15	

SD: standard deviation; NICU: Neonatal intensive care unit

**p value based on rank sum test*

[1] *Complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain*

[2] *Jaundice: According to medical record*

Table 4. 21. One-month postpartum EPDS scores and APGAR scores, birthweight and length of hospital stay.

Variable	n	Spearman rho	p*
APGAR score 1 minute	1858	-0.05	0.02
APGAR score 5 minutes	1858	-0.05	0.02
Birthweight	1858	-0.05	0.03
Length of hospital stay	1858	-0.04	0.06

**p value based on Spearman test*

4.5.6. One-month postpartum and antenatal EPDS scores

Table 4.22 shows a significant association between antenatal and postnatal EPDS scores; however, the rho value was quite small (0.12). It means that only small change of one-month postpartum EPDS was contributed by antenatal EPDS.

Table 4. 22. One-month EPDS score and antenatal EPDS score

Variable	n	Spearman rho	p*
Antenatal EPDS score	1858	0.12	<0.001

EPDS: Edinburgh postnatal depression scale

**p value based on Spearman test*

4.5.7. Factors affecting postnatal depression at one month postpartum

Multiple linear regression analysis was undertaken to ascertain demographic, lifestyle and other risk factors associated with postnatal depressive symptoms, using the one-month postpartum EPDS as the main outcome. Variables were initially chosen based on the above univariate analyses and plausible risk factors from the literature (Boyce 2003, Mohamad Yusuff, Tang et al. 2015, Murray, Dunne et al. 2015) as described in Chapter 2. The full model initially comprised of 15 predictors, but due to lack of association, the following variables were subsequently dropped from the full model:

GDM, APGAR score 1 and 5 minutes, and length of hospital stay. As a result, ten risk factors remained in the final model. As shown in Table 4.23, antenatal EPDS, passive smoking, caesarean section, maternal complications, jaundice, birthweight, NICU admission and total physical activity level were significantly and positively associated with EPDS scores at one month postpartum, which elevated the risk for postnatal depression. However, both older mothers and more educated women appeared to be less susceptible to postnatal depressive symptoms, as reflected by their negative regression coefficients. Overall, the ten influencing factors explained about 70% of the variance in postnatal EPDS scores.

Table 4. 23. Factors associated with one-month postpartum EPDS scores

Variable	Coefficient	SE	p	95% CI	
				Lower	Upper
Intercept	5.83	0.86	<0.001	4.146	7.518
Antenatal EPDS	0.13	0.02	<0.001	0.092	0.166
Age (years)	-0.05	0.02	0.001	-0.081	-0.020
Birthweight (g)	0.01	0.00	0.031	-0.001	0.000
Total physical activity (MET-hour/week)	0.01	0.00	0.042	-0.006	0.000
Education level					
Less than Secondary school	reference				
Secondary school	-0.44	0.32	0.171	-1.070	0.190
High school graduate	-0.76	0.33	0.02	-1.409	-0.119
College/university	-0.64	0.32	0.042	-1.266	-0.022
Passive smoking [1]					
No	reference				
Yes	0.37	0.16	0.022	0.055	0.695
Caesarean section					

Variable		Coefficient	SE	p	95% CI	
					Lower	Upper
	No	reference				
	Yes	0.65	0.17	<0.001	0.330	0.979
Maternal complications [2]						
	No	reference				
	Yes	0.65	0.17	<0.001	0.330	0.979
Jaundice [3]						
	No	reference				
	Yes	1.10	0.27	<0.001	0.580	1.627
NICU admission						
	No	reference				
	Yes	1.87	0.48	<0.001	0.930	2.810

SE: standard error, CI: confidence interval; EPDS: Edinburgh postnatal depression scale; MET: metabolic equivalent task; NICU: Neonatal intensive care unit

[1]Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.

[2]Maternal complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain

[3]Jaundice: according to medical record

4.6. Depressive symptoms at three months postpartum

This section examines the EPDS scores at three months after giving birth and influencing factors including maternal demographic, clinical and lifestyle characteristics, as well as the association between depressive symptoms and birth outcomes and infant health problems.

4.6.1. Distribution of EPDS scores at three months postpartum

Figure 4. 4 shows the distribution of EDPS scores at three months postpartum. Similar to antenatal EPDS scores and those at one month postpartum, the EPDS distribution

at three months was skewed to the right, with the mean (3.50) greater than the median (3.0). Most of the mothers (93%) had a score below 10. Overall, the EPDS scores varied from 0 to 29. Same as EPDS at one month postpartum, if a cutoff of 13 were adopted for postnatal depression (Murray, Dunne et al. 2015), the observed prevalence of postnatal depression would be 3.2% (n=59). Therefore, the EPDS at three months postpartum will be presented and analyzed as a continuous score rather than being classified as a binary variable (depressed versus not depressed) in subsequent sections.

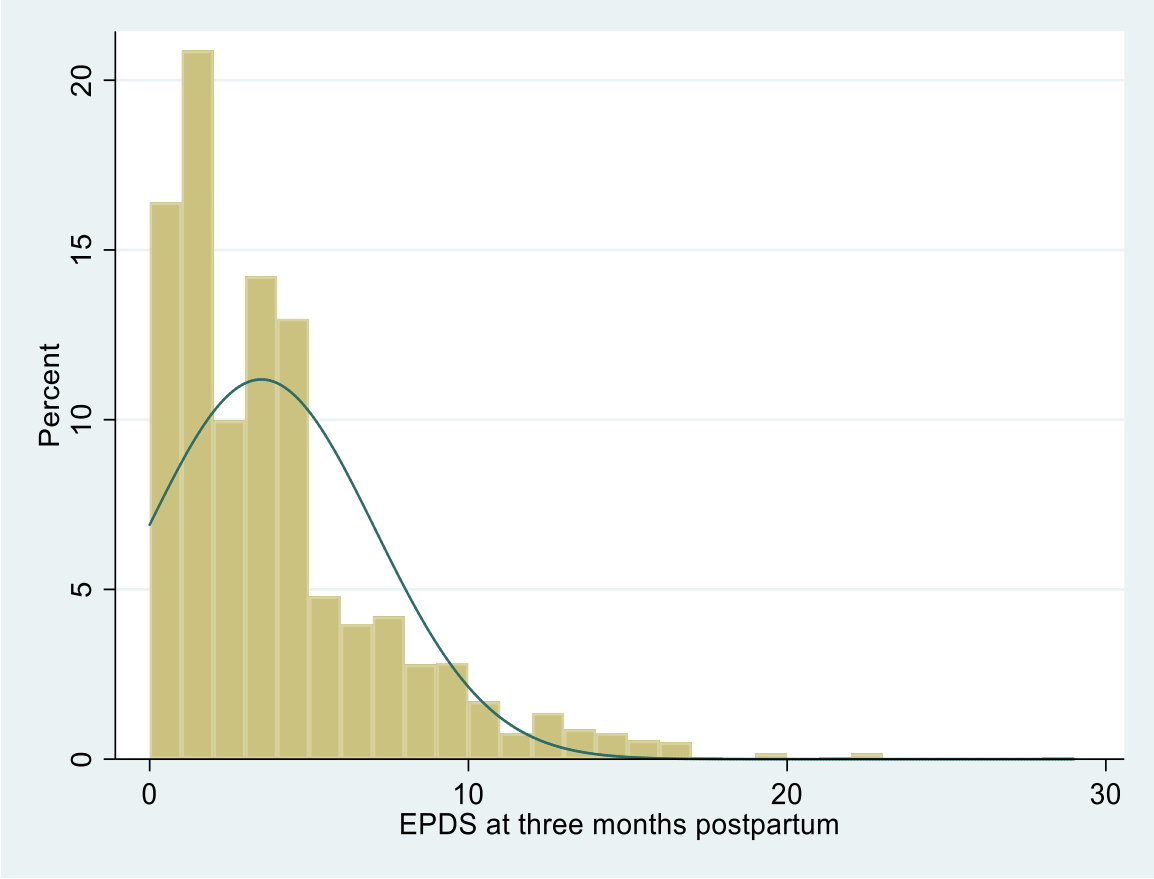

Figure 4. 4. Distribution of EPDS scores at three months postpartum

4.6.2. Three-month postpartum EPDS scores by participant characteristics

Table 4.24 shows the EPDS scores at three months postpartum according to maternal demographic and major lifestyle factors. EPDS scores were seemingly lower for

mothers with older age, higher pre-pregnancy BMI and less children, though the differences were not statistically significant. Mean EPDS scores were not significantly different across levels of other maternal socio-demographic and lifestyle factors ($p>0.05$).

Table 4. 24. Three-month postpartum EPDS scores by demographic and lifestyle characteristics

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Age (years)								
< 25	581	3.61	3.53	3	4	0	19	0.46
25-35	1108	3.48	3.62	3	4	0	29	
> 35	146	3.27	3.30	2	3	0	15	
Marital status								
Married	1823	3.51	3.57	3	4	0	29	0.32
Single/divorced/separated/widowed	12	2.67	3.34	1.5	3.5	0	12	
Occupation								
Farmer	281	3.68	3.56	3	3	0	22	0.37
Worker	725	3.40	3.39	3	4	0	19	
Office/technical staff	422	3.45	3.77	3	4	0	29	
Housewife/Unemployed	304	3.56	3.71	2	4	0	19	
Sales	103	3.79	3.53	3	5	0	19	
Educational level								
Less than secondary school	142	3.49	3.28	3	4	0	14	0.65
Secondary school	478	3.25	3.29	3	3	0	22	
High school graduate	478	3.61	3.55	3	4	0	19	
College/university	737	3.60	3.80	3	4	0	29	
Parity								
0	705	3.39	3.50	3	3	0	21	0.39
1	681	3.54	3.58	3	4	0	29	
≥ 2	449	3.63	3.65	3	4	0	22	
Pre-pregnancy BMI (kg/m^2)[1]								

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Underweight (<18.5)	470	3.74	3.77	3	4	0	22	0.17
Normal (18.5 to <23.0)	1147	3.47	3.47	3	3	0	22	
Overweight/obese (≥23.0)	218	3.19	3.62	2	3	0	29	
Passive smoking [2]								
No	726	3.37	3.39	3	3	0	29	0.5
Yes	1109	3.59	3.67	3	4	0	22	
Alcohol consumption [3]								
No	1583	3.51	3.60	3	4	0	29	0.71
Yes	252	3.47	3.38	3	3	0	21	

SD: standard deviation; IQR: interquartile range

**p values based on rank sum test or Kruskal Wallis test*

[1] *BMI: body mass index, classified for Asian populations according to World Health Organization (WHO Expert Consultation 2004)*

[2]*Passive smoking: inhalation of tobacco smoke or environmental tobacco smoke from partner, household members, colleagues, etc.*

[3]*Alcohol consumption: any consumption of beer or wine*

4.6.3. Three-month postpartum EPDS scores by physical activity during pregnancy

Table 4.25 presents EPDS scores at three months postpartum stratified by physical activity levels during pregnancy. EPDS scores were not significantly different between women meeting and not meeting the recommended level of physical activity, and also across tertiles of total physical activity. As demonstrated in Table 4.26, with the exception of occupational physical activity that showed a weak negative association with the EPDS scores, other physical activity domains and physical activity intensities did not appear to be associated with the EPDS scores at three months. Therefore, physical activity during pregnancy posed little influence on postnatal depression at three months.

Table 4. 25. Three-month postpartum EPDS scores by physical activity level

Physical activity	n	Mean	SD	Median	IQR	Min	Max	p*
Meeting physical activity guidelines								
No	1453	3.48	3.55	3	4	0	29	0.63
Yes [1]	382	3.53	3.65	3	4	0	29	
Total level (MET-hour/week)								
1st tertile (8.4 to <94.3)	592	3.32	3.45	2	3	0	22	
2nd tertile (94.3 to <144.2)	617	3.46	3.47	3	4	0	22	
3rd tertile (144.2 to 362.8)	626	3.72	3.76	3	4	0	29	

SD: standard deviation; IQR: interquartile range; MET: metabolic equivalent task

[1] >7.5 MET-hour/week in sports/exercise activities of moderate-intensity (American College of Obstetricians and Gynecologists 2015)

**p values based on rank sum tests for binary variables or Kruskal Wallis tests for categorical variables with three levels or more*

Table 4. 26. Three-month postpartum EPDS scores and physical activity domain and intensity

Physical activity	n	Spearman rho	p*
Total level (MET-hour/week)	1835	0.049	0.034
Domain			
Household/care giving	1835	0.045	0.053
Occupation	1835	-0.002	0.901
Sport/leisure activity	1835	0.011	0.645
Travel	1835	0.055	0.655
Intensity			
Sedentary	1835	-0.016	0.512
Light	1835	0.017	0.455
Moderate	1835	0.086	0.002
Vigorous	1835	0.041	0.081

MET: metabolic equivalent task

4.6.4. Three-month postpartum EPDS scores and gestational diabetes mellitus

Table 4.27 compares EPDS scores at three months postpartum between mothers with and without GDM. Although the mean EPDS score of gestational diabetic mothers was about 10% lower than their counterparts without GDM, the difference was not statistically significant. The EPDS scores among mothers with GDM ranged between zero and 16, while those among mothers without GDM ranged from zero to 29. There were no apparent associations between EPDS scores and the continuous glucose levels; the Spearman rho being -0.01, -0.03 and -0.02 ($p > 0.05$) for fasting, 1-h and 2-h, respectively.

Table 4. 27. Three-month postpartum EPDS scores by gestational diabetes mellitus

GDM	n	Mean	SD	Median	IQR	Min	Max	p*
No	1453	3.57	3.66	3	4	0	29	0.25
Yes	376	3.20	3.14	3	3	0	16	

SD: standard deviation; IQR: interquartile range; GDM: Gestational Diabetes Mellitus (World Health Organization 2013).

**p value based on rank sum test.*

4.6.4. Three-month postpartum EPDS scores and birth outcomes

Table 4.28 summaries EPDS scores at three months postpartum by birth outcomes. Compared to mothers who had no pregnancy related complications, those experiencing complications such as bleeding and infections reported significantly higher EPDS scores; the difference in mean EPDS being approximately 1.4 ($p = 0.04$). Similarly, mothers who delivered low birthweight babies had a significantly higher mean EPDS score than those giving birth to normal weight babies ($p = 0.01$). However, there were no significant differences in mean EPDS scores with respect to caesarean section, neonatal intensive care admission status or presence of jaundice. According to Table

4.29, APGAR scores at one and five minutes appeared to be weakly but positively associated with EPDS scores, whereas birthweight and length of hospital stay were weakly but negatively associated with the EPDS scores.

Table 4. 28. Three-month postpartum EPDS scores by birth outcomes

Variable		n	Mean	SD	Median	IQR	Min	Max	p*
Caesarean section									
	No	1131	3.50	3.55	3	4	0	29	0.86
	Yes	702	3.52	3.60	3	4	0	22	
NICU admission									
	No	1780	3.49	3.56	3	4	0	29	0.36
	Yes	53	4.02	3.82	3	5	0	15	
Low birthweight									
	No	1762	3.47	3.56	3	4	0	29	0.01
	Yes (<2500g)	73	4.29	3.56	4	5	0	15	
Maternal complications [1]									
	No	1793	3.47	3.54	3	4	0	29	0.04
	Yes	40	4.85	4.61	4	6	0	22	
Jaundice [2]									
	No	1655	3.45	3.47	3	3	0	22	0.19
	Yes	178	4.02	4.35	3	5	0	29	

SD: standard deviation; IQR: interquartile range; NICU: Neonatal intensive care unit

**p values based on rank sum test.*

[1] *Complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain.*

[2] *Jaundice: According to medical record.*

Table 4. 29. Three-month postpartum EPDS scores and APGAR scores, birthweight and length of hospital stay

Variable	n	Spearman rho	p
APGAR score 1 minute	1833	0.06	0.02
APGAR score 5 minutes	1833	0.06	0.01
Birthweight	1833	-0.05	0.04
Length of hospital stay	1833	-0.11	0.001

**p values based on Spearman test.*

4.6.5. Three-month and one-month postpartum EPDS scores

Table 4.30 reveals a significantly positive relationship between the one-month and the three-month EPDS. One-month EPDS contributed about one-third of change of the three-month EPDS value.

Table 4. 30. Three-month EPDS score and one-month EPDS score

Variable	n	Spearman rho	*p
One-month EPDS score	1834	0.363	<0.001

EPDS: Edinburgh postnatal depression scale

**p values based on Spearman test.*

4.6.6. Factors affecting postnatal depression at three months postpartum

Multiple regression analyses were performed to identify risk factors associated with depressive symptoms at three months postpartum. Potential risk factors were initially chosen based on results of univariate analyses undertaken in previous sections with $p<0.2$, together with plausible factors from the literature. A full model began with twelve risk factors including mother's age, education level, EPDS score at one-month postpartum, physical activity during pregnancy, GDM status, jaundice, length of hospital stays, caesarean section, maternal complications, infant birthweight, neonatal intensive care unit admission. Due to lack of association, the following variables were

subsequently dropped from the regression model: age, education level, jaundice and length of hospital stay. The final model comprised of eight factors after the stepwise selection procedure, as shown in Table 4.31. Depressive symptoms scores at one month and physical activity level during pregnancy were significantly and positively associated with the three-month postpartum EPDS, after accounting for the effects of other confounding factors. Mothers who reported a high depressive symptom scores at one month were more susceptible to postnatal depression later at three months postpartum. The seven independent factors together explained about 16% of the variance in the outcome variable.

Table 4. 31. Factors associated with three-month postpartum EPDS score

Variable		Coefficient	SE	p	95% CI	
					Lower	Upper
Intercept		2.91	0.66	<0.001	1.62	4.21
One-month EPDS score		0.41	0.02	<0.001	0.37	0.45
Birthweight (g)		0.01	0.00	0.075	0.01	0.01
Total physical activity (MET-hour/week)		0.01	0.00	0.017	0.01	0.01
GDM						
	No	reference				
	Yes	-0.26	0.19	0.167	-0.64	0.11
Caesarean section						
	No	reference				
	Yes	-0.13	0.16	0.402	-0.45	0.18
Maternal complications [1]						
	No	reference				
	Yes	-0.37	0.33	0.253	-1.01	0.27
NICU admission						
	No	reference				
	Yes	-0.56	0.49	0.252	-1.53	0.40

SE: standard error, CI: confidence interval; GDM: Gestational Diabetes Mellitus (World Health Organization 2013); MET: Metabolic Equivalent Task; NICU: Neonatal intensive care unit

[1] *Complications: any of high fever, increased bleeding, painful or frequent urination, severe pain in abdomen, chest pain*

4.6.7. Three-month postpartum EPDS scores and infant health at six months

Table 4.32 shows EPDS summary statistics at three months postpartum according to infant health conditions within the first six months. Overall, depressive symptom scores at three months postpartum were significantly higher in mothers whose infants experienced health problems at six months postpartum. Specifically, mothers with infants who were admitted to hospital due to illness in the first six months reported a significantly higher EPDS mean score when compared to mothers without any infant hospitalization. Similarly, mothers who had infants with diarrhea or lower respiratory tract infection reported higher EPDS mean score than mothers whose infants incurred no such diseases within the first six months. Therefore, some association was evident between postnatal depressive symptoms and infant health problems.

Table 4. 32. Three-month EPDS scores by infant health at six months postpartum

Variable	n	Mean	SD	Median	IQR	Min	Max	p*
Hospitalization								
No	1468	3.27	3.40	3	3	0	22	<0.001
Yes	241	4.29	3.92	3	4	0	22	
Diarrhea								
No	1453	3.29	3.36	3	3	0	22	0.005
Yes	256	4.16	4.14	3	5	0	22	
Lower respiratory tract infection								
No	1275	3.26	3.34	3	3	0	22	0.007
Yes	434	3.89	3.90	3	4	0	22	

SD: standard deviation; IQR: interquartile range.

**p values based on rank sum test.*

CHAPTER 5: DISCUSSION

This chapter discusses the research findings in relation to the literature and previous reports, together with the strength and limitations of the study.

5.1. Findings in relation to the literature

5.1.1. Antenatal depression

In this large prospective cohort study in Vietnam, the observed antenatal depression prevalence was 7.04% (n=143), based on the EPDS cut-off score of 13. There appears a lack of consistency between our result and findings from previous studies conducted in Vietnam, with a few studies reporting lower while others showing higher prevalence of antenatal depression. For instance, in a prospective cohort study including 1337 women from Dong Anh District conducted during 2014-2015, the prevalence of antenatal depression was estimated at 4.9% using the EPDS cut-off score of 10 (Van Ngo, Gammeltoft et al. 2018). In contrast, antenatal depression prevalence in the present study was much lower than past data reported in Vietnam. A cross-sectional study of 419 pregnant women in a typical Red River delta rural province in the north of Vietnam reported 22.4% of participants experiencing depressive symptoms during early pregnancy (12-20 weeks of gestation), defined using the EPDS cut-off-point of 4 (Fisher, Tran et al. 2013). A similar result was obtained by Hue and colleagues among 1260 pregnancy women who sought antenatal care at four obstetric hospitals from January to September 2019 (Hue, Nguyet Van et al. 2020). They found that pregnant women were at high risk of antennal depression (24.5%). Such discrepancy on antenatal depression prevalence in Vietnam might be due, in part, to the selection

of EPDS cut-off points. Another possibility would be related to the time at which depressive symptoms were assessed, i.e., the first, second or third trimester.

The reported prevalence of antenatal depression above appeared to be lower than the global estimates which varied from 15% to 64% (Dadi, Miller et al. 2020), with a pooled prevalence of approximately 21% from a recent meta-analysis (Yin, Sun et al. 2021). The EPDS was the predominant screening tool for assessing antenatal depression, despite heterogeneity of the cut off scores being used (Levis, Negeri et al. 2020). In South-Asia, the pooled prevalence of antenatal depression was estimated at 24.3%, with a wide range (6.1% to 75.1%), while different screening tools were used for the assessment of antenatal depression (Mahendran, Puthussery et al. 2019). Some East-Asian countries reported a range of 4.8% to 20% (Schatz, Hsiao et al. 2012). Notably, a meta-analysis of 95 primary studies comprising 96,096 women in China showed an overall antenatal depression of 19.7% (Nisar, Yin et al. 2020). The discrepancy in rates might again be attributed to the different EPDS cut-off scores applied for depression ascertainment and study participant characteristics together with cultural factors.

GDM was associated with lower antenatal depressive symptoms scores. Besides GDM diagnosis, the levels of glucose from the oral glucose tolerance tests have strengthened our evidence regarding the apparent association between hyperglycaemia during pregnancy and antenatal depressive symptoms. Our finding concerning Vietnamese women appears to be different from previous studies in other populations. In the literature, it has been argued that the negative effect of GDM on perinatal depression may be due to the stress from GDM and its adverse birth outcomes, or to the biochemical changes as a result of GDM (Talbot and Nouwen 2000). Moreover,

women with GDM are prone to increased inflammation and adipokine concentrations (Fasshauer, Bluher et al. 2014). These conditions are known to be associated with major depression and may possibly related to perinatal depression as well (Osborne and Monk 2013). In view of our finding contrary to the literature, further studies are required to confirm the impact of GDM regarding reducing antenatal depressive symptoms.

Except for recreational physical activity, positive association was evident between physical activity subtypes during pregnancy and antenatal depressive symptoms. This finding was consistent, to some extent, with a recent study of 820 Latina women on domain-specific physical activity (Szegda, Bertone-Johnson et al. 2018). However, a multiethnic cohort study involving 1144 Asian women found a significantly reduce risk of probable antenatal depression for women who undertook sufficient levels of total physical activity (≥600 MET-min/week) (Padmapriya, Bernard et al. 2016). Such discrepancy may be attributed to fundamental differences in characteristics of the populations being examined, as well as other instruments/questionnaires (instead of PPAQ and EPDS) adopted to ascertain physical activity exposure and the antenatal depression outcome. The observed positive correlation between total physical activity level and antenatal depression scores could be influenced by household/care giving – a habitual activity among pregnant women in Asia including Vietnam.

The present study indicated that several socio-demographic factors, including age, occupation, and education, were significantly associated with depressive symptoms scores. Specifically, the mean score of antenatal depression were lower among older mothers and those with occupations requiring light-intensity physical activity (e.g.,

housewife, salesperson) as well as less education individuals. Consistent with this study, a large body of literature has found a significant association between young age and depression during pregnancy. However, several other studies reported a significant positive association between advancing age and antenatal depression scores (Gavin, Melville et al. 2011, Ali, Azam et al. 2012, Fisher, Tran et al. 2013, Raisanen, Lehto et al. 2014). Indeed, no association between age and antenatal depression was apparent according to a systematic review (Biaggi, Conroy et al. 2016). In line with our data, past research have indicated that antenatal depression is more prevalent in women with low educational achievements (Biaggi, Conroy et al. 2016), or inversely associated with literacy (Stewart, Umar et al. 2014). One study in Vietnam found mothers with education level beyond high school had a lower mean EPDS score than others with high school education or below (Hue, Nguyet Van et al. 2020). Less educated women may be unable to access timely and affordable health care during pregnancy including mental health support, and thus are more vulnerable to gestational depression. Similarly, several previous investigations found depressive symptoms to be more common among unemployed women (Dibaba, Fantahun et al. 2013, Lydsdottir, Howard et al. 2014, Rubertsson, Hellstrom et al. 2014) and housewives (Balestrieri, Isola et al. 2012, Yanikkerem, Ay et al. 2013). It is conceivable that women with financial difficulties or feeling bored doing housework may be more susceptible to depressive disorders during pregnancy.

Elevated adiposity is commonly accompanied by increased levels of subclinical inflammatory markers, which has been implicated in the pathogenesis of depression (Belmaker and Agam 2008, Payne and Maguire 2019). Body mass index is an indicator of adiposity, and therefore overweight or obese women are more likely to experience

depressive symptoms during pregnancy. However, we found mothers with a high BMI (≥ 23 kg/m2) before pregnancy had a significantly lower mean EPDS score when compared to underweight mothers.

This result appears to align with a Hispanic cohort of nearly 1000 pregnant women in the USA where the risk of elevated depressive symptoms during pregnancy (EPDS ≥ 13) was about halved in overweight women (BMI 25–<30 kg/m^2) compared with their normal-weight counterparts (BMI 18.5 –<25 kg/m^2) (Ertel, Silveira et al. 2015). In fact, the association between pre-pregnancy or early pregnancy BMI and antenatal depression remains inconsistent. For example, a study of 1621 Australian women reported a significant relationship between pre-pregnancy BMI and antenatal depression (Holton, Fisher et al. 2019), though another study comprising 7824 women (3514 white British and 4310 South Asian) exhibited no such association between early pregnancy BMI and depression (Insan, Slack et al. 2020). Inconsistent findings of maternal pre-pregnancy overweight in association with prenatal depressive symptoms are evidenced in two meta-analyses (Molyneaux, Poston et al. 2014, Dachew, Ayano et al. 2021), with one suggesting a positive association while another one found null association. Moreover, primary studies included in the two meta-analyses above were mainly conducted in Western countries where classification of BMI to define overweight/obesity is not similar to criteria used in the Asian population (WHO Expert Consultation 2004). In view of the lack of sufficient scientific evidence, further research is required to elucidate the relationship between BMI level before pregnancy and depression during pregnancy in lean female populations, including Vietnamese women.

The present study found passive exposure to tobacco smoking during pregnancy was positively associated with antenatal depression scores. Such finding is comparable to a Japanese study of 1183 women whose second-hand smoke exposure incurred a significant 50% odds of developing depressive symptoms during pregnancy (Kawasaki, Miyake et al. 2017). Likewise, an earlier study of 929 minority pregnant women who were non-smokers in Washington, DC, USA, suggested a significant positive association between second-hand smoke exposure and depressive symptoms (Beck Depression Inventory Fast Screen) (Tan, Courtney et al. 2011). In addition, another prospective cohort study of 236 pregnant women in Florida found mean EPDS score was significantly higher amongst passive smoking mothers than their non-smoking counterparts (mean ± SD: 5.3±5.5 versus 4.8±4.8, respectively) (Mbah, Salihu et al. 2013). The biological mechanism linking passive smoking to antenatal depression remains unclear but may partly be a consequence of the adverse effect of nicotine and tobacco particulate matter on the function and expression of the dopamine and norepinephrine transporters (Danielson, Putt et al. 2014). It is posited that depression may be linked to dopaminergic system dysregulation (Papakostas 2006). Another possibility is that passive smoking may increase levels of pro-inflammatory markers (Jefferis, Lowe et al. 2010), which have been implicated in the pathogenesis of depression (Miller, Maletic et al. 2009, Felger and Lotrich 2013, Kim, Na et al. 2016).

Despite a low proportion of mothers with alcoholic beverage consumption, those who drank alcohol was more likely to experience depressive symptoms. We are not aware of any literature investigating the association between alcohol drinking during pregnancy and prenatal depression, and thus it is difficult to make a direct comparison.

Given that depression and perinatal depression share some potential mechanisms (Belmaker and Agam 2008, Hasler 2010, Meltzer-Brody 2011), our result appears to be consistent with previous reports suggesting a J-shaped relationship between alcohol consumption and depression (Manninen, Poikolainen et al. 2006, Graham, Massak et al. 2007, Awaworyi Churchill and Farrell 2017). In any case, the observed inverse correlation between alcohol drinking and prenatal depression scores should be elucidated in other populations.

Prenatal depression is a common depressive disorder that can affect pregnancy outcomes (Dadi, Miller et al. 2020). Nonetheless, we found no significant differences in EPDS mean scores with respect to delivery method, NICU admission and low birthweight (< 2500 g). On the contrary, Ngo and colleagues observed a significantly higher odds of giving birth to low birthweight babies for mothers with antenatal depression (EPDS score ≥ 10), than others experiencing no depressive symptoms during pregnancy (Van Ngo, Gammeltoft et al. 2018). Moreover, depressive symptoms (EPDS score ≥ 3) were found to be significantly associated with low birthweight in another Vietnamese study(Niemi, Falkenberg et al. 2013). Findings from the literature have been generally inconsistent (Grote, Bridge et al. 2010, Grigoriadis, VonderPorten et al. 2013, Accortt, Cheadle et al. 2015). In a meta-analysis of eleven studies evaluating the association between antenatal depression and low birthweight, 6 studies showed no significant association, despite the overall relative risk being 1.18 (95% CI 1.07-1.30) (Grote, Bridge et al. 2010). The lack of association was also reported in another meta-analysis of eleven studies (Grigoriadis, VonderPorten et al. 2013). Additional research is therefore warranted to clarify the

relationship between prenatal depressive symptoms and low birthweight, particularly in lean Asian populations including Vietnamese.

Consistent with our finding, a systematic review and meta-analysis of six studies found no significant association between prenatal depression and NICU admission (Grigoriadis, VonderPorten et al. 2013); the pooled relative risk being 1.43 (95% CI 0.83-2.47). This result is reassuring given that pregnant women commonly experience episodes of depressive symptoms (Dadi, Miller et al. 2020). The null association between prenatal depression and caesarean delivery seems to concur with previous studies that reported mode of delivery was unrelated to antepartum mental health (Wu, Viguera et al. 2002, Coker, Sanderson et al. 2004). However, a Malaysian study of 799 pregnant women suggested an independent association between antenatal depressive symptoms and caesarean section or instrumental deliver (odds ratio 1.55; 95% CI 1.06-2.26) (Nasreen, Pasi et al. 2019). In the present study, caesarean section due to pregnancy complications or maternal preference could not be distinguished, while preference for caesarean section is relatively common in low- and middle-income countries (Mazzoni, Althabe et al. 2011). It may be argued that those mothers wishing to have caesarean section are more prepared for giving birth, and consequently are less likely to be depressed during pregnancy. However, the mean EPDS score among pregnant women with elective caesarean section was significantly higher than their counterparts who underwent normal delivery (Olieman, Siemonsma et al. 2017). Considering the high prevalence of antenatal depression and caesarean section, elucidation of their causal links can contribute to developing appropriate prevention measures.

5.1.2. Postnatal depression

The observed postnatal depression prevalence of 2.8% (n=52) at one month and 3.2% (n=59) at three months postpartum , based on the EPDS cut-off score of 13, was lower than previous reported rates varying from 8.2% to 33% using EPDS cut-off points of 10 and 13 respectively to indicate depression status for Vietnamese mothers (Fisher, Morrow et al. 2004, Murray, Dunne et al. 2015, Van Vo, Hoa et al. 2017, Do, Nguyen et al. 2018, Tho Tran, Nguyen et al. 2018). In the literature, only one study in Vietnam reported a low prevalence of 1.9% based on the EPDS cut-off score of 13 (Wesselhoeft, Madsen et al. 2020). Moreover, our observed rate was much lower than the 16% overall prevalence of postnatal depression among Asian mothers assessed by screening instruments (Shorey, Chee et al. 2018). The discrepancy may be due to differences in living conditions, stability of partnership arrangements, and access to public health services, stressful life events, as well as underlying methodological differences between studies.

Our finding of a positive association between antenatal depression scores and postnatal depression scores is in general agreement with the literature. A meta-analysis of 84 studies published in the 1990s, comprised of eleven studies which addressed the link between history of depression and postnatal depression. The pooled finding suggested a moderate relationship between history of depression and postnatal depression (Beck 2001). More recently, a systematic review of 16 primary studies totalling 35,419 women estimated that about 39% of pregnant women with antennal depressive symptoms also experienced postnatal depression after giving birth (Underwood, Waldie et al. 2016). In the review, most of the included studies (n = 13) used EPDS to assess depressive symptoms. It is noted that the majority of studies reviewed were

conducted in Europe, with one exception from Thailand (Limlomwongse and Liabsuetrakul 2006). The connection between prenatal depression and postnatal depression has been consolidated by an updated umbrella review (Zhao and Zhang 2020). Because postnatal depression can adversely affect the mother and infant's physical and mental health together with their interactions (e.g., bonding, breastfeeding, and the maternal role) (Slomian, Honvo et al. 2019), it is important to prevent and manage depression during pregnancy.

Consistent with antenatal depression, the apparent positive association between total physical activity level and postnatal depression can be attributed to the stress and pressure from household work for Vietnamese women during pregnancy and after giving birth. Similar to our result, a prospective cohort study of 550 mothers in North Carolina, USA, reported moderate to vigorous physical activity was positively associated with EPDS-defined postnatal depression (Demissie, Siega-Riz et al. 2011). In addition, the general population whose work stress may lead to higher risk of depressive symptoms (McKercher, Schmidt et al. 2009). It should be noted that our participants spent their highest energy expenditure on household chores and/or care giving activities (59.3 MET-hour/week), whereas the corresponding values for occupational and travel activities were 31.4 and 11.5 MET-hour/week, respectively. On average, only 6.1 MET-hour/week spent were devoted to sport or leisure activities. It appears that physical activity can play a role in perinatal depression among Vietnamese women. Nevertheless, more research is needed to confirm our finding and to understand the underlying biological mechanism.

As with antenatal depressive symptoms, we observed that higher postnatal EPDS score was significantly associated with younger age and higher maternal education level. The inverse association between maternal age and depression scores after childbirth is in accordance with previous investigations that showed the risk of postpartum depression was higher among young mothers (<24 years) (Viguera, Tondo et al. 2011, Pooler, Perry et al. 2013, Sidebottom, Hellerstedt et al. 2014, Lara, Navarrete et al. 2015), as well as data indicating the correlation between young age and antenatal depression (Biaggi, Conroy et al. 2016), a predictor of postnatal depression (Underwood, Waldie et al. 2016). Young mothers generally have less experience in parenthood, and thus they may be more mentally vulnerable than their older counterparts.

In general, low socioeconomic status is associated with adverse health outcomes, including depression. However, the present study suggested a positive association between maternal education level, the most frequently used indicator of socioeconomic status (Lorant, Deliege et al. 2003), and postnatal depression scores. Compared to less educated mothers, those with higher level of education may experience greater pressure in life and career together with family issues, in light of the rapid economic transition in Vietnam (Nguyen and Trevisan 2020). Prior studies in Vietnam revealed that higher education was associated with lower prevalence of postnatal depression (Do, Nguyen et al. 2018, Tho Tran, Nguyen et al. 2018). Although age and maternal education are non-modifiable factors, they may be used to develop prediction models for postnatal depression in Vietnam (Zhang, Wang et al. 2021).

Our finding of a positive association between passive smoking during pregnancy and EPDS scores at one month postpartum is supported by past research (Khan, Arif et al. 2015, Song, Li et al. 2019). In a large population-based cohort study conducted in China (n = 8,842), women exposed to passive smoking during pregnancy had higher odds of postnatal depression when compared with those not exposed (OR 1.43, 95% CI: 1.16–1.77) (Song, Li et al. 2019). Similarly, a larger-scale study undertaken in Korea (n = 34,693) among women aged over 18 years observed a significant association between passive smoking exposure and depressive symptoms in a dose-response manner (Jung, Shin et al. 2015). Similar finding was also confirmed in European women (Raisanen, Lehto et al. 2014, Vivilaki, Diamanti et al. 2016). The potential mechanism remains unclear, though there are some plausible explanations. Nicotine is one of the major biochemicals in the tobacco smoke, and chronic exposure to this substance can desensitize nicotinic acetylcholine receptors (Bockman, Zeng et al. 2018), consequently affecting. the activities of the neuroendocrine system and functions of the hypothalamic-pituitary-adrenal axis, which is involved in depression (Belmaker and Agam 2008). Another possibility is the direct impact of nicotine on oestrogen and their interactive effect, which had been reported to be associated with depression (Ghaedrahmati, Kazemi et al. 2017, Payne and Maguire 2019).

Delivery by caesarean section is common in high and low- and middle-income countries, and its effect on postpartum depression has been extensively documented (Carter, Frampton et al. 2006, Xu, Ding et al. 2017, Moameri, Ostadghaderi et al. 2019, Sun, Wang et al. 2020). We found 38.2% of mothers had caesarean section and this delivery mode was positively and significantly associated with the EPDS scores. The first meta-analysis including 24 studies, of which five exhibited a significant inverse

association, 15 showed no significant association, and four found mixed results between caesarean section and postnatal depression (Carter, Frampton et al. 2006). A decade later, another meta-analysis of 28 studies comprising 532,630 mothers found those with caesarean section had a significant 26% higher likelihood of developing postnatal depression versus mothers with normal delivery; the association being more pronounced for emergency caesarean section (Xu, Ding et al. 2017). Such apparent relationship has also been confirmed in two updated systematic review and meta-analyses, in which the pooled odds ratio varied between 1.15 and 1.33 (Moameri, Ostadghaderi et al. 2019, Sun, Wang et al. 2020). A possible explanation is the impact of caesarean section on pro-inflammatory markers including interleukin 6 (Hebisch, Neumaier-Wagner et al. 2004), which has been suggested to increase the risk of depression (Khandaker, Pearson et al. 2014). Another reason is the stress as a result of surgery, since surgical stress can make susceptible subjects prone to depression (Dinan 1994, Edwards, Porter et al. 1994). Moreover, pain associated with caesarean section may increase the mother's susceptibility to depression (Goesling, Clauw et al. 2013, Han and Pae 2015).

Besides caesarean section, we noticed a positive association between maternal complications (e.g., any of high fever, increased bleeding, pre-eclampsia, painful or frequent urination, severe pain in abdomen, chest pain) and postpartum depressive symptoms scores. Similarly, a population-based cohort study involving nearly 5000 mothers showed that several complications during pregnancy (such as pre-eclampsia, induced hypertension, and hospitalisation) are significant predictors of depressive symptoms at two months postpartum. (Blom, Jansen et al. 2010). Likewise, a small study in Argentina found complications during pregnancy and birth were significantly

associated with postpartum depressive symptoms (Mathisen, Glavin et al. 2013). The observed association may be explained by physical morbidity as a result of maternal complication(s), while poor health is a well-known stressor because of pain, tiredness and limitations. Another possibility is the reduction of serotonin in the brain due to pre-eclampsia, thereby leading to depressive symptoms (Bloch, Schmidt et al. 2000). An alternative explanation is that elevated inflammation levels related to maternal complications during pregnancy (e.g., hypertension, infection) are posited to augment the risk of postpartum depression (Payne and Maguire 2019).

Mother–infant bonding is the emotional relationship established between a mother and her new-born, so that factors influencing the child can impact on maternal postpartum depressive disorders. The present study suggested that low birthweight and NICU admission were independently associated with the EPDS scores at one month postpartum. The findings are compatible with previous studies which suggested that mothers who gave birth to very low birthweight infants (<1500 g) or babies requiring NICU admission were more likely to experience depressive symptoms in the early postpartum period (Blom, Jansen et al. 2010, Helle, Barkmann et al. 2015). In a sample of 403 parents (230 mothers and 173 fathers), very low birthweight was found to be the most powerful predictor of postpartum depressive symptoms assessed using the EPDS (Helle, Barkmann et al. 2015). Similarly, infant hospitalisation (within the first week after delivery) was 1.45 times more likely among mothers who subsequently developed depressive symptoms at two months postpartum (Blom, Jansen et al. 2010). Conceivably, most mothers expect to have a healthy pregnancy, safe delivery and normal postpartum period. Unexpected or sudden life events such as preterm birth, low birthweight neonates or hospital admission of the new-born can cause worries and

feelings of disappointment and failure (Robertson, Grace et al. 2004, Beck 2006, Hopkins and Campbell 2008). In addition, parents with low birthweight infants often worry about their infant's health, development and future, which in turn might trigger depressive symptoms. Mothers with infants admitted to NICU generally express distress and concern that their parental role are affected (Affleck, Tennen et al. 1991, Miles, Funk et al. 1992, Ionio, Colombo et al. 2016). As a result, women may find it difficult to adapt in the postpartum period, and thus likely to incur depressive symptoms.

Postnatal depression is a serious mental health problem that have negative consequences for both infants and mothers. The present study showed that the mean EPDS score at three months postpartum was higher for mothers whose infants were hospitalised, had diarrhea or contracted lower respiratory tract infection, than mothers giving birth to infants without the aforementioned problems within 6 months postpartum (Goodman 2019, Slomian, Honvo et al. 2019). These results are in accordance with accumulating evidence from other countries, suggesting that infants of mothers with postnatal depression tend to have elevated risks of common health problems (Waqas, Elhady et al. 2018, Jacques, de Mola et al. 2019, Slomian, Honvo et al. 2019, Dadi, Miller et al. 2020). In a systematic review and meta-analysis of 6 studies (one in Taiwan, one in China, two in the USA, one in the UK and one in Ghana), three reports investigated the association between prenatal/postnatal depressive symptoms or depression and infant hospitalisation up to one year (Jacques, de Mola et al. 2019). The pooled relative risk estimate of hospitalisation was 1.44 (95% CI 1.10–1.89) times greater in children whose mothers were prenatally and postnatally depressed. In another pooled analysis of eight studies on postnatal depression (as part

of a meta-analysis including 10 studies), infants born to mothers with postnatal depression sustained nearly two-fold increase in risk of diarrhea (odds ratio 1.90; 95% CI 1.39–2.61) (Waqas, Elhady et al. 2018). The overall risk of diarrheal illness also appeared to be higher among mothers with prenatal depression (odds ratio 2.70, 95% CI: 0.92–7.94), a predictor of postnatal depression.

An updated systematic review and meta-analysis comprising 75 studies, with 17 on postnatal depression, reported the risk of infant health problems was 31% significantly higher among mothers with postnatal depression than others without the condition (Dadi, Miller et al. 2020). Common infant health illnesses included acute respiratory infections (e.g., pneumonia, fever, and cough), malaria, measles, and diarrhea. The observed risk was consistent across all forms of measuring instruments and clinically diagnosed depression, in both hospital-based and population-based studies, and in both high- and low-income countries, irrespective of the underlying population characteristics. Potential mechanisms underlying the positive associations found between 3-month postnatal EPDS scores and the infant's hospitalisation, diarrhoea and lower respiratory tract infection remain to be elucidated. It is plausible that child health depends on parental care and support, especially from the mother. Postpartum depression can negatively impact on the maternal attitude towards the infant, leading to impaired mother-child bonding, poor caregiving, and lack of safety practices (Nakano, Upadhyaya et al. 2019). A depressed mother may have low self-efficacy, which can have repercussions on exclusive breastfeeding abandonment and malnutrition (Surkan, Kawachi et al. 2008, Surkan, Kennedy et al. 2011, Machado, Assis et al. 2014, Tuominen, Junttila et al. 2016, Slomian, Honvo et al. 2019). These will weaken the infant immune system to protect against infections such as diarrhoea

(Dennis and McQueen 2009). Another possibility is the potential impact of the dysregulated hypothalamic pituitary adrenal axis in depressed mothers on the infant's immune and neuroendocrine development (Groer and Morgan 2007). Infants with such impaired immune system will have increased susceptibility to infection. The apparent association between postnatal depression scores and adverse infant outcomes has provided evidence for developing effective measures to prevent the onset and subsequent consequences of postnatal depression.

5.2. Measuring instruments

The EPDS was originally developed as an instrument for screening and not for the actual clinical diagnosis of depression (Cox et al, 1987). Therefore, adopting a specific cut-off point to classify individuals as "depressed" or "non-depressed" states can potentially result in misclassification. There is still no consensus on the optimal ("best") cut-off-point in the literature, with EPDS cut-off scores from 9 to 13 being frequently used, so that comparisons of results become difficult between studies. Even if the same cut-off point is adopted across studies, sensitivity and specificity will vary considerably (from 34% to 100% and 44% to 100%, respectively) because of the intrinsic disparities in methodology, language/dialect, and characteristics such as socio-economic status and cultural attitudes in feeling and expressing distress (Gibson et al, 2009). In the present study, a tentative cut-off-point of 13 was used to estimate the prevalence of antenatal and postnatal "depression". However, important information may be lost by dichotomising of the EPDS, since women who are not clinically depressed may span over a continuum from euphoria to misery (Green, 1998). Therefore, the linear regression analyses using the continuous EPDS scores as the outcome variable has the benefit of face validity to reflect depressive symptoms

instead of making a subjective decision on a particular cut-off point for determining depression.

The repeated measurements on the depressive symptoms also provided valuable evidence on the longitudinal changes in the EPDS scores over the entire study period throughout pregnancy and postpartum. Specifically, the mean EPDS decreased from 5.1 during pregnancy to 3.5 at one month and three months after hospital discharge. However, an inherent limitation is the non-diagnostic aspect of EPDS for assessing perinatal depression. Information was also missing on history of major depression before pregnancy, which can by a risk factor for perinatal depression (Castro e Couto et al., 2016), resulting in inaccurate estimation of the depression prevalence. Moreover, analogous to other observational studies, residual confounding could not be avoided even though plausible confounding factors have been controlled in the regression models with EPDS as the continuous outcome variable.

Similar to depressive symptoms, physical activity was assessed using a self-reported questionnaire, PPAQ, which might result in non-differential misclassification of both the exposure variable (physical activity) and outcome (EPDS). In the future, studies should consider adopting objective measurements of physical activity to complement the PPAQ, such as pedometer or accelerometer.

5.3. Strengths and limitations of the study

5.3.1 Strengths

A major strength of the study was its multi-centre prospective cohort design with a relatively large sample size of 2030 participants from six hospitals in Northern and Southern Vietnam. The long follow-up period from 24-28 weeks of pregnancy to six months postpartum with five face-to-face interviews was another strength of the study. Previously, few prospective cohort studies had been conducted in Vietnam, either with smaller sample size, shorter following up duration, or the sample was collected only in one region of Vietnam. Another strength of this study was that it assessed various modifiable maternal risk factors for adverse pregnancy outcomes. Particularly, physical activity was not only quantified by its total magnitude, but also examined in terms of intensity and domain using an appropriate instrument. In addition, this study had higher response (90%) and retention rates (85%) than previous studies.

Our study represented the first multiple-centre cohort study in Vietnam investigating the associations between perinatal depression and birth outcomes; and risk factors of perinatal depressive symptoms such as GDM and physical activity. The participants were also assessed for a variety of characteristics including social demographic factors, pregnancy outcomes and postpartum maternal and child health, in order to adjust for plausible confounding variables. Importantly, this study used the Edinburgh Postnatal Depression scale (EPDS), which is the most common instrument to identify the presence and magnitude of perinatal depressive symptoms, despite its shortcomings as alluded in previous sections.

5.3.2 Limitations

Although the study has several strengths, there are several weaknesses, which need to be considered when interpreting the results. Firstly, participants were mainly recruited from urban and suburban areas in three big cities, who might not represent rural women in Vietnam, and thus could introduce some degree of selection bias. There are other mountainous or remote areas in Vietnam with different backgrounds and cultural characteristics. Therefore, caution should be taken before generalizing our findings to the entire population, due to variations in GDM prevalence, levels of physical activity during pregnancy, rates of hospitalisation and infant diseases. However, for the study objectives focusing on the associations between maternal risk factors and perinatal depression, such selection bias should be deemed negligible. As mentioned in Section 5.2, the non-diagnostic assessment of perinatal depression was an inherent limitation, while information was lacking on the history of major depression before pregnancy, so that residual confounding could not be ruled out.

Second, the study did not include pregnant women in private health facilities and general practitioners. Compared to those giving birth at public facilities, more women stay at least three days at private facilities after delivery (75% private versus 70.4% public) (General Statistics Office and UNICEF 2015). Caesarean deliveries are more prevalent at private hospitals (45%) than public hospitals (32.6%) (General Statistics Office and UNICEF 2015). These data suggest potentially the presence of different maternal characteristics between public and private facilities in Vietnam. However, information on the provision of reproductive health services in the private sector, including the characteristics of Vietnamese women using such services, is not available, probably owing to the low proportion of women giving birth at private health

facilities (3.9%) when compared to public health facilities (89.7%) (General Statistics Office and UNICEF 2015).

Thirdly, data on maternal lifestyle were obtained from self-report of participants which might introduce recall bias. We have minimised this type of error by using validated questionnaires for the Vietnamese population and conducting direct interviews by experienced interviewers with supportive materials. The use of self-reported pre-pregnancy weight might also lead to inaccuracy. However, a high level of concordance between measured weight and self-reported pre-pregnancy weight has been demonstrated, particularly in examining their associations with several pregnancy outcomes (Han, Abrams et al. 2016, Bannon, Waring et al. 2017). The questionnaires were also administered by trained data enumerators to reduce potential estimation errors.

Family or social support is one of the most significant risk factors of perinatal depression. Although this variable was not included in our regression analysis, such information should be incorporated and considered when modelling the depression scores in future studies

Finally, data collections were conducted five times at 24-28 weeks of gestation, before hospital discharge, and at one, three and six months postpartum by several interviewers, so that interviewer bias was plausible. To minimise this bias, all interviewers employed were health workers and well-trained for the study. In addition, during data collection they were supervised by the candidate and other experienced

researchers. The study might lack sufficient statistical power to ascertain the association between maternal factors, perinatal depression and birth outcomes. However, within the scope of the doctoral study, a longer timeframe of follow up in conjunction with a large sample survey was not feasible.

CHAPTER 6: CONCLUSION

This chapter summarises the main findings from the study and gives conclusion, and provides recommendations and implications for maternal health practice and directions for future research.

6.1. Main findings

The aim of the study was to investigate antenatal and postnatal depression and associated risk factors among Vietnamese women. This prospective cohort study enrolled 2030 pregnant women during the baseline survey from six hospitals located in three large cities in Vietnam. Mothers were followed up at hospital discharge (n = 1906), at one month (n = 1858), at three months (n = 1835), and at six months postpartum (n = 1807). Antenatal and postnatal depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS) in an interviewer-administered format. In the baseline survey, maternal characteristics and lifestyle factors were also ascertained with face-to-face interviews using validated data instruments. Gestational diabetes status was determined via fasting glucose and/or glucose tolerance tests. In addition, medical records were retrieved with respect to pregnancy and infant health outcomes.

All six objectives of this study have been successfully addressed. In relation to objective 1, our review of the literature on the epidemiology of perinatal depression in Asia suggested that its prevalence was higher than the rates reported in Western countries; the overall pooled prevalence for antenatal and postnatal depression was approximately 30% and 16%, respectively. An array of risk factors has been identified,

which can be classified as socio-demographic and cultural factors, lifestyle/biological factors, psychological factors and obstetric/paediatric parameters.

In relation to objective 2, the antenatal depressive symptoms scores followed a right skewed distribution (mean 5.1, median 4.0, range 0-27). The observed prevalence of antenatal depression was 7.04% (n=143) if adopting a cut-off score of 13 for EPDS. According to linear regression analysis, age was weakly and negatively associated with antenatal EPDS, whereas a positive association was found for total physical activity level. Women with GDM appeared to experience significantly less depressive symptoms during pregnancy when compared to their non-GDM counterparts. More educated women reported significantly higher EPDS scores. Body mass index was significantly and inversely associated with EPDS, while passive smoking and alcohol drinking during pregnancy showed significant positive associations with EPDS. In relation to objective 3, there was no association between antenatal EPDS and birth outcomes such as caesarean section, low birthweight and admission to NICU.

To address objective 4, data from the one-month postpartum interviews were utilised. The corresponding EPDS scores were skewed to the right (mean 3.5, median 2.0, range 0-24). The prevalence of postnatal depression at one month was low at 2.8% (n=52) based on the cut-off score of 13 for EPDS. Mothers with adverse birth outcomes (caesarean section, maternal complications, low birthweight, NICU admission or jaundice) reported significantly higher mean EPDS scores than those without such experience. After adjusting for antenatal EPDS, linear regression analysis showed that passive smoking, caesarean section, maternal complications, jaundice, birthweight, NICU admission and total physical activity level were significantly and positively associated with EPDS at one month postpartum, which elevated the risk for postnatal

depression. However, both older mothers and more educated women appeared to be less susceptible to postnatal depressive symptoms at one month.

To address objective 5, data from the three-month postpartum interviews were utilised. The EPDS distribution was again right skewed (mean 3.50, median 3.0, range 0-29). The observed prevalence of postnatal depression at three-month would be 3.2% (n=59) using a cut-off score of 13. In terms of risk factors, linear regression analysis found that EPDS at one month and physical activity level during pregnancy were significantly and positively associated with the three months postpartum EPDS. Mothers who reported a high depressive symptom score at one month were more susceptible to postnatal depression later at three months.

Finally, in relation to objective 6, some positive association was evident between the three-month postpartum EPDS and infant health problems (hospitalisation, diarrhoea and lower respiratory tract infection) within the first six months.

6.2. Conclusion

This thesis reported findings from the first multi-center prospective cohort study of perinatal depression in Vietnam. More than 2000 pregnant women were recruited at 24-28 weeks gestational and followed up until six months postpartum. Together with the literature review (Chapter 2), the study has provided updated knowledge about perinatal depression in Vietnam and helped to understand risk and protective factors associated with antenatal depression and postnatal depression. The results confirmed that the prevalence of perinatal depression remained low in Vietnam. However, the results indicated that younger women and those experiencing adverse birth outcomes were more susceptible to depressive symptoms. Meanwhile, education and physical

activity during pregnancy also played important roles influencing the mental condition of the mothers.

The findings could contribute to the effective identification of those women at inflated risk of developing depressive symptoms during pregnancy and after childbirth. Because of this research, evidence-based recommendations can be made for formulating health promotion strategies and intervention programs to deal with perinatal depression, in order to improve the health status of Vietnamese mothers and their offspring. Therefore, the study has important implications on maternal and child health policies, particularly in terms of appropriate education, screening, and early detection to prevent the onset of perinatal depression for Vietnamese women.

6.3. Recommendations

6.3.1. Implications for maternal health practice

Based on the findings of our study, some recommendations are suggested to improve maternal and child health outcomes in Vietnam, which are summarised as follows. All pregnant women are encouraged to attend antenatal classes which should include information on dietary intake and physical activity during pregnancy, in order to meet standard requirements for both energy intake and appropriate energy expenditure during pregnancy. Depression education programs should be conducted at regular intervals throughout pregnancy to control perinatal depression. All pregnant women are encouraged to undertake an EPDS screening test during pregnancy to detect the presence of depressive symptoms early, and to seek appropriate treatments, if necessary, to prevent adverse health outcomes for both mothers and their offspring. National guidelines on diagnosis, treatment, and management of maternal depression

should be disseminated to all hospitals and clinics in both public and private sectors for universal implementation. Appropriate educational programmes targeting pregnant women and women of reproductive age should be performed nationwide. Moreover, moderate-intensive activity, household/caregiving activity, and various types of physical activity should be highlighted to meet the guidelines for pregnancy and women during the postpartum period.

Maternal mental health care services have been scarce in Vietnam; therefore, training about depression and mental health should be emphasized to the midwives and nurses, who have strong connection with pregnant women. Specialized services and centres should be established to help screening, treating and control mental health issues at communal health centres, which operate national health programs at ward/commune level.

Pregnant women should be informed about depression prevention services during the periconceptional period. Such early information may help women who exhibit depressive symptoms during and after the pregnancy. In addition, it is necessary to refer these at-risk women to community health care workers for further recommendations or guidelines regarding better management and control of their condition. These referrals for health services will require effectiveness assessments as this process will necessitate strong collaboration and supports from government and other stakeholders.

It has been revealed by the thesis that physical activity subtypes can contribute to the occurrence of antenatal and postnatal depressive symptoms. Healthcare providers

should advise the impacts of physical activity during pregnancy in relation to controlling perinatal depression, maintaining a healthy lifestyle postpartum, and aiming to improve women's awareness of maternal depression.

The screening for perinatal depressive symptoms is not mandatory yet in Vietnam while the prevalence of perinatal depression is still relatively high compared to other countries in the region. Therefore, applying an appropriate tool to screening for perinatal depression among pregnant women is needed to early identify and diagnose perinatal depression. This would be an extremely useful tool in a resource-limited setting like Vietnam.

6.3.2. Directions for future research

Since Vietnam has 54 ethnic groups with more than 90 different dialects, depression problems might differ from one place to another. To determine the relationship between perinatal depression and maternal factors such as GDM, physical activity, and weight gain during pregnancy at the population level, future studies should be conducted in different parts of Vietnam. Comparisons between rural and urban areas should also be made to clarify the role of maternal factors on perinatal depression among different ethnic groups. A longer follow up period (beyond six months postpartum) and more frequent interviews are required to accurately measure the prevalence and trajectory of depression over time. Furthermore, to ensure sufficient statistical power for analysing depression data, similar prospective cohort studies with a larger sample size are recommended. Interventions on mothers who have high EPDS scores during pregnancy should be considered in future research. Finally, more research on GDM and physical activity during pregnancy and their effects on maternal

depression are recommended, due to limited information available from Vietnam and other developing countries.

The present thesis only assessed maternal participation in physical activity during pregnancy. Future studies are recommended to repeatedly measure maternal participation in physical activity at different time points after giving birth (e.g., when returning to work) in conjunction with postnatal depression. In addition, future studies should differentiate the role of physical activities for relaxation (sport/ leisure) and work. Due to the repeated measurements on maternal depression, repeated measures regression analysis is recommended in future investigations to examine the trajectory of change of depression scores over time and in relation to the risk factors, from antenatal to the postnatal period.

Perinatal depression is known to inflict long-term adverse effects on maternal and child health. However, no study has examined such impact in Vietnam. Since little is known about women and health workers' knowledge and practice on perinatal depression, future studies evaluating these aspects will assist the development of appropriate intervention programmes.

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APPENDIX A: ETHIC APPROVAL 1

MEMORANDUM

Curtin University

To:	Prof Andy H Lee Public Health
CC:	
From	Professor Peter O'Leary, Chair HREC
Subject	Ethics approval Approval number: HR32/2015
Date	16-Feb-15

Office of Research and Development
Human Research Ethics Office

TELEPHONE 9266 2784
FACSIMILE 9266 3793
EMAIL hrec@curtin.edu.au

Thank you for your application submitted to the Human Research Ethics Office for the project: 4873

Maternal lifestyle and nutritional status in relation to pregnancy and child health outcomes: A multi-centre prospective cohort study in Vietnam.

Your application was reviewed by Human Research Ethics Committee at Curtin University at their meeting on the 9/12/2014

Thankyou for providing the additional information requested by the Human Research Ethics Committee. The information you provided was satisfactory and your proposal is now approved.

Please note the following conditions of approval:

1. Approval is granted for a period of four years from **17-Feb-15** to **17-Feb-19**
2. Research must be conducted as stated in the approved protocol.
3. Any amendments to the approved protocol must be approved by the Ethics Office.
4. An annual progress report must be submitted to the Ethics Office annually, on the anniversary of approval.
5. All adverse events must be reported to the Ethics Office.
6. A completion report must be submitted to the Ethics Office on completion of the project.
7. Data must be stored in accordance with WAUSDA and Curtin University policy.
8. The Ethics Office may conduct a randomly identified audit of a proportion of research projects approved by the HREC.

Should you have any queries about the consideration of your project please contact the Ethics Support Officer for your faculty, or the Ethics Office at hrec@curtin.edu.au or on 9266 2784. All human research ethics forms and guidelines are available on the ethics website.

Yours

Professor Peter O'Leary
Chair, Human Research Ethics Committee

APPENDIX B: ETHIC APPROVAL 2

MINISTRY OF HEALTH
HAIPHONG UNIVERSITY OF MEDICINE AND PHARMACY

SOCIALIST REPUBLIC OF VIETNAM
Independence-Freedom-Happiness

No: 05 /HPUMPRB
Issue: Approval of HPUMPRB

CERTIFICATE OF APPROVAL

Basing on the Decision No. 580A/QD-YHP on June 22nd 2012 by The Rector of Haiphong Medical University on the foundation of the HPMU Review Board and secretariat for reviewing the ethical issues in Bio-medical researches;

Basing on the Decision No. 2153/2013/QĐ-TTg on November 11th 2013 by Prime Minister on rename of Haiphong Medical University to Haiphong University of Medicine and Pharmacy.

Basing on the Agreed Minutes (enclosured) of the Haiphong University of Medicine and Pharmacy Review Board (HPUMPRB) and the ratification and assessment committee on August 20th 2015.

HAIPHONG UNIVERSITY OF MEDICINE AND PHARMACY
REVIEW BOARD (HPMURB)
IN BIO-MEDICAL RESEARCH

approves the ethical issues of the following research proposal:

- Research title: ***Maternal lifestyle and nutritional status in relation to pregancy and child health outcomes: A multi-centre prospective cohort study in Viet Nam***
- Principal Investigators: ***Prof. AnDy Lee***
  Chu Khac Tan, MD
  Nguyen Cong Luat, MD
  Nguyen Hoang Phung, MD
  Ha Vo Van Anh, MD
- Research Institution: ***Curtin University, Australiaa***
- Site for research: Vietnam
- Research Period: From August 2015 to December 2017

Date of approval: August 25th, 2015

IRB Chair
Haiphong University of Medicine and Pharmacy

Assoc.Prof. Tran Quang Phuc, M.D, PhD

Rector
Haiphong University of Medicine and Pharmacy

Prof. Pham Van Thuc, M.D, PhD

APPENDIX C: INFORMATION LETTER

School of Public Health

GPO Box U 1987

Perth, WA 6845, Australia

Project title:

Antenatal and postnatal depression in Vietnam: A Prospective Cohort Study

A PhD student from the School of Public Health at Curtin University is conducting research into maternal and child health in Vietnam. The purpose of this study is to investigate the prevalence and associated factors of antenatal and postnatal depression among Vietnamese mothers, as well as their consequences.

In this project, we interview pregnant women of last trimester gestation. We are interested to find out your lifestyle such as physical activity during pregnancy and cigarette smoking. We will also ask you several questions regarding your health status and demographic details. The initial interview will take about 30 to 40 minutes to complete. We would like to measure your weight, height to check your health status. We will collect your blood samples to examine your gestational diabetes status. We will also check your medical records to collect additional information about your health during pregnancy and after childbirth.

After your delivery, an assistant researcher will contact you to ask you some further questions about your health and your baby's health. The weight and length of your infant will be measured at discharge from hospital. Similar follow up interviews will be conducted at one month, three months, and six months after delivery.

In all interviews, we will also ask you ten specific questions (Edinburgh postnatal depression scale questionnaire - EPDS) to identify possibly antenatal and postnatal depression symptoms.

Your participation in this research is voluntary. You can refuse any specific question that you are uncertain or find it difficult to answer. During the initial or follow up interviews, if you decide to withdraw from the study, please feel free to do so because there will be no negative consequences.

After you have signed the enclosed consent form, we will assume that you have agreed to participate, and you allow us to use your data in this research project. The information you provided are confidential, and your identity will remain anonymous. Only aggregated and de-identified data from all participants will be analysed and reported.

Please be assured that only the information you provided will only be accessed by the chief investigators of this project, and not anyone else. In particular, it will not be released to the medical staff and authority of the maternity hospital. Your completed questionnaire and other documents will be kept in a locked cabinet at Curtin University for seven years before being destroyed.

This study has been approved by the Curtin University Human Research Ethics Committee (Approval Number HR32/2015). The Committee is comprised of members of the public, academics, lawyers, doctors and pastoral carers. If needed, verification of approval can be obtained either by writing to the Curtin University Human Research Ethics Committee, c/- Office of Research and Development, Curtin University, GPO Box U1987, Perth, 6845 or by telephoning +61-8-9266 9223 or by emailing hrec@curtin.edu.au

If you have any concern or questions about this study, please contact the following project staff:

- Chu Khac Tan, Project officer and PhD student, on +849002086658 or chukhac.tan@postgrad.curtin.edu.au
- Dr. Ngoc Minh Pham, Main supervisor, on +61 423 934 328 or minh.n.pham@curtin.edu.au
- Professor Andy Lee, Co-supervisor, on +61 8 92664180 or andy.lee@curtin.edu.au
- Professor Colin Binns, Associate supervisor, on +61 8 92662952 or c.binns@curtin.edu.au

Thank you very much for your cooperation.

APPENDIX D: CONSENT FORM

Project title:

Antenatal and postnatal depression in Vietnam: A Prospective Cohort Study

You have been invited to participate in this study because you are a pregnant woman in the last trimester of gestation and aged ≥ 18 years. Please read the information document carefully and ask any questions you wish. Do not sign this informed consent form unless you fully understand the nature of the study and the commitment you may need to make over the next two years.

I, ..., agree to participate in the above study. I have read and understood the Information Letter given to me. I understand the requirements for participation in this study. I have been given the opportunity to ask questions about the study. I fully understand that my participation is voluntary. I may withdraw from the study at any time without any negative consequences.

Signed ..... Date .....

Name of witness

……

Signature of witness ..... Date .....

Address and contact numbers (home phone/mobile)	Address: No.: ……..… Street/Hamlet: …… Commune/Ward: …….…..……..… Phone: You …..... Your husband ……..... Your mother ……..….... Your mother-in-law ...……...……

APPENDIX E: BASELINE QUESTIONNAIRE

Interview Date: _____/_____/_____(DD/MM/YYYY) Interviewe☐☐
Hospital code: ☐ Mother identification number: ☐☐☐☐
Mother's name:☐ _____

A. DEMOGRAPHIC INFORMATION

A1.	Address	
	Number: ; Street: commune:	
	District: ; Province:	
A2.	Contact numbers (home phone/mobile)	You …../..... Your husband ……..... Your mother ……... You mother-in-law …….
A3.	Date of Birth	_____/_____/ _____ (dd/mm/yyyy) …….....years
A4.	Marital status	0 [ ] Never married 1 [ ] Married/de facto 2 [ ] Widowers/divorced/separated
A5.	Parity	_____
A6.	Occupation (before pregnancy)	0 [ ] Farmer 1 [ ] Labour/Manual worker 2 [ ] Office clerk 3 [ ] Teacher 4 [ ] Housewife 5 [ ] Other:……..
A7.	What is the highest level of education you have completed?	0 [ ] No formal education 1 [ ] Primary school 2 [ ] Secondary school 3 [ ] High school 4 [ ] College/vocational school/University

B. ANTHROPOMETRIC MEASUREMENTS

D1.	Height	___ ___ ___.___	cm
D2.	Weight at first antenatal visit (_____ weeks gestation) [Check medical record]	___ ___ ___ . ___	kg

C. EDINGBURH POSTNATAL DEPRESSION SCALE QUESIONNAIRE

B1. **I have been able to laugh and see the funny side of things**

As much as I always could 0
No quite so much now 1
Definitely not so much 2
Not at all 3

B2. **I have looked forward with enjoyment to things**

As much as I ever did 0
A little less than I used to 1
Definitely less than I used to 2
Hardly at all 3

B3. **I have blamed myself unnecessarily when things went wrong**

No, never 0
Not very often 1
Yes, some of the time 2
Yes, most of the time 3

B4. **I have been anxious or worried for no good reason**

No, not at all 0
Hardly ever 1
Yes, sometimes 2
Yes, very often 3

B5. **I have felt scared or panicky for no very good reason**

No, not at all 0
Hardly ever 1
Yes, sometimes 2
Yes, very often 3

B6. **Do you feel that you have too many tasks to manage?**

No, I have been coping as well as ever 0
No, most of the time I have coped quite well 1
Yes, sometimes I haven't coped as well as usual 2
Yes, most of the time I haven't been able to cope at all 3

B7. **I have been so unhappy that I have had trouble sleeping**

No, not at all 0
Not very often 1
Yes, sometimes 2
Yes, most of the time 3

B8. **I have felt sad or miserable**

No, not at all 0
Not very often 1
Yes, quite often 2
Yes, most of the time 3

B9. **I have been so unhappy that I have been crying**

No, never.....0
Only once in a while.....1
Yes, quite often.....2
Yes, most of the time.....3

B10. **The thought of harming myself has occurred to me**

Never.....0
Hardly ever.....1
Sometimes.....2
Yes, quite often.....3

D. PHYSICAL ACTIVITY

It is very important you tell us about yourself honestly. There are no right or wrong answers. We just want to know about the things you are doing during last month.

During last month, when you are NOT at work, how much time do you usually spend :

A1. Preparing meals (cook, set table, wash dishes)

None.....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day..4
2 to almost 3 hours per day..5
3 or more hours per day 6

A2. Dressing, bathing, feeding children while you are <u>sitting</u>

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day.....6

A3. Dressing, bathing, feeding children while you are <u>standing</u>

None....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day.....6

A4. Playing with children while you are <u>sitting or standing</u>

None.....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day..4
2 to almost 3 hours per day..5
3 or more hours per day 6

A5. Playing with children while you are <u>walking or running</u>

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A6. Carrying children

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A7. Taking care of an old adult

None.....1
Less than 1/2 hour per day..2

A8. Sitting and using a computer or writing, while <u>not</u> at work

None.....1
Less than 1/2 hour per day.....2

A9. Watching TV or a video

None....1
Less than 1/2 hour per day.....2

1/2 to almost 1 hour per day..3
1 to almost 2 hours per day..4
2 to almost 3 hours per day..5
3 or more hours per day 6

1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

1/2 to almost 2 hour per day.....3
2 to almost 4 hours per day.....4
4 to almost 6 hours per day.....5
6 or more hours per day..6

A10. Sitting and reading, talking, or on the phone, while <u>not</u> at work

None.....1
Less than 1/2 hour per day..2
1/2 to almost 2 hours per day..3
2 to almost 4 hours per day..4
4 to almost 6 hours per day..5
6 or more hours per day 6

A11. Playing with pets

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A12. Light cleaning (make beds, laundry, iron, put things away)

None....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A13. Shopping (for food, clothes, or other items)

None.....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day..4
2 to almost 3 hours per day..5
3 or more hours per day 6

A14. Heavier cleaning (vacuum, mop, sweep, wash windows)

None.....1
Less than 1/2 hour per week.....2
1/2 to almost 1 hour per week.....3
1 to almost 2 hours per week.....4
2 to almost 3 hours per week.....5
3 or more hours per week.....6

Going Places…

During last month, how much time do you usually spend :

A15. Walking <u>slowly</u> to go to places (such as to the bus, work, visiting) <u>Not</u> for fun or exercise

None....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day 4
2 to almost 3 hours per day 5

A16. Walking <u>quickly</u> to go to places (such as to the bus, work, visiting) <u>Not</u> for fun or exercise

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A17. Riding a bicycle to go places (such as the bus, work, or school) <u>Not</u> for fun or exercise

None....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day 4
2 to almost 3 hours per day 5

3 or more hours per day.....6

3 or more hours per day.....6

A18. Driving or riding in a motorbike or bus

None....1
Less than 1/2 hour per day..2
1/2 to almost 1 hour per day..3
1 to almost 2 hours per day 4
2 to almost 3 hours per day 5
3 or more hours per day.....6

For Fun or Exercise…

During last month, how much time do you usually spend :

A19. Walking <u>slowly</u> for fun or exercise

None.....1
Less than 1/2 hour per week.....2
1/2 to almost 1 hour per week.....3
1 to almost 2 hours per week.....4
2 to almost 3 hours per week.....5
3 or more hours per week.....6

A20. Walking more <u>quickly</u> for fun or exercise

None.....1
Less than 1/2 hour per week.....2
1/2 to almost 1 hour per week.....3
1 to almost 2 hours per week.....4
2 to almost 3 hours per week.....5
3 or more hours per day..6

A21. Walking <u>quickly up hills</u> for fun or exercise

None....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A22. Jogging

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A23. Prenatal exercise class

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

A24. Swimming

None....1
Less than 1/2 hour per day.....2
1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

Doing other things for fun or exercise? Please tell us what they are.

A25. Dancing

None.....1
Less than 1/2 hour per day.....2

A26. _____
Name of Activity
None.....1
Less than 1/2 hour per day.....2

A27. _____
Name of Activity
None....1
Less than 1/2 hour per day.....2

1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

1/2 to almost 1 hour per day.....3
1 to almost 2 hours per day.....4
2 to almost 3 hours per day.....5
3 or more hours per day..6

Please fill out the next section if you work for wages, as a volunteer, or if you are a student. If you are a homemaker, out of work, or unable to work, you do not need to complete this last section.

At work……

During last months, how much time do you usually spend:

A28. Sitting at working or in class

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 2 hours per day.....3
2 to almost 4 hours per day.....4
4 to almost 6 hours per day.....5
6 or more hours per day..6

A29. Standing or slowly walking at work while carrying things (heavier than a 1 gallon milk jug)

None.....1
Less than 1/2 hour per day..2
1/2 to almost 2 hours per day.....3
2 to almost 4 hours per day..4
4 to almost 6 hours per day..5
6 or more hours per day 6

A30. Standing or <u>slowly</u> walking at work <u>not</u> carrying anything

None....1
Less than 1/2 hour per day..2
1/2 to almost 2 hours per day 3
2 to almost 4 hours per day 4
4 to almost 6 hours per day 5
6 or more hours per day.....6

A31. Walking <u>quickly</u> at work while <u>carrying</u> things (heavier than a 1 gallon milk jug)

None.....1
Less than 1/2 hour per day.....2
1/2 to almost 2 hours per day.....3
2 to almost 4 hours per day.....4
4 to almost 6 hours per day.....5
6 or more hours per day..6

A32. Walking <u>quickly</u> at work <u>not</u> carrying anything

None.....1
Less than 1/2 hour per day..2
1/2 to almost 2 hours per day.....3
2 to almost 4 hours per day..4
4 to almost 6 hours per day..5
6 or more hours per day 6

E. EXPOSURE TO CIGARETTE SMOKING AND ALCOHOL CONSUMPTION

B1.	**Before** you became pregnant, did you smoke?	0 [ ] No *GO TO C3* 1 [ ] Yes

B2.	On average, how many of the following tobacco products did you smoke per day **before pregnancy**?	Manufactured cigarettes? Hand-roll cigarettes? Pipes full of tobacco? Cigars, cheroots or cigarillos? Number of water pipe sections? Any others? Specify…… ……	……..... per day ……..... per day ……..... per day ……..... per day ……. per day ……..... per day
B3.	**While** you are pregnant, do you smoke?	0 [ ] No *GO TO C5* 1 [ ] Yes	
B4.	On average, how many of the following tobacco products do you smoke per day **during pregnancy**?	Manufactured cigarettes? Hand-roll cigarettes? Pipes full of tobacco? Cigars, cheroots or cigarillos? Number of water pipe sections? Any others? Specify…… ……	……. per day …….. . per day ……..... per day ……..... per day ……..... per day ……..... per day
B5.	Did your relatives/people living with you smoke at home **before** you were pregnant?	0 [ ] No 1 [ ] Yes	
B6.	Are your relatives/people living with you smoking at home **while** you are pregnant?	0 [ ] No 1 [ ] Yes	
B7.	While you are pregnant, do you drink alcohol (beer, wine)	0 [ ] No 1 [ ] Yes	

Type	**frequency (month/week/day)**	**Unit**	**Units/time**	**Duration**
Beer	___time / [ ]**month** [ ]week [ ]**day**	*cup 300ml*		
Wine	___time / [ ]**month** [ ]week [ ]**day**	*cup 30ml*		

THANK YOU VERY MUCH FOR YOUR PARTICIPATION!

APPENDIX F: DISCHARGE QUESTIONNAIRE

Interview Date: _____/_____/_____(DD/MM/YYYY) Interviewer Code: ☐☐

Hospital code: ☐ Mother identification number: ☐☐☐☐

Mother's name: _____

Please inspect the medical record for information in this section

Baby's Date of Birth: _____/_____/_____(DD/MM/YYYY)

Baby's gender: Male.....1 Female.....2 ☐

Baby's birthweight: ___ ___ ___ ___ gram

Gestation: _____weeks _____days

Weight at last examination (delivery day): ___ ___ ___. ___ kilogram

Delivery method: Vaginal delivery without forceps or suction.....1 ☐

Vaginal delivery with forceps or suction.....2

Caesarean section.....3

Did the baby stay at intensive care unit?

No.....0

Yes.....1 (_____days)

Did the baby have any health problems while at hospital? ☐

No.....0

Yes.....1 (Health problems:_____ _____)

Did the mother have any health problems during this pregnancy? ☐

No.....0

Yes.....1

(Complications: _____)

Did the mother have any complications during delivery?

No.....0

Yes.....1

(Complications: _____)

APPENDIX G: FOLLOWING-UP

QUESTIONNAIRE

Interview Date: _____/_____/_____(DD/MM/YYYY) Interviewer Code:

Health institution code: ☐ Mother identification number: ☐☐☐☐

Mother's name: _____ Baby's Date of Birth: _____/

_____/_____

A. HEALTH OF INFANT

C1. Has your baby experienced any hospital admission since I spoke to you last time?
No 0
Yes .....1 ☐

C2. Has your baby experienced any health problem since I spoke to you last time, what is/are the health problem(s)?

	NO…0	YES…1	
1. Lower respiratory tract infection			☐
2. Diarrhoea			☐
3. Other infant health problems			☐

Lower respiratory tract infection: *at least one specific lower respiratory tract sign (fast or difficulty breathing, chest wall indrawing) and/or abnormal auscultatory findings (crackles/crepitations or bronchial breath sounds)*
Diarrhoea: *the passage of three or more loose or liquid stools per day, or more frequently than is normal for the individual*

C3. Did you take your baby to see any health professionals regarding this problem?
No GO TO QC7.....0
Yes.....1 ☐

C4. If YES, who did you take your baby to?

	NO…0	YES…1
1. General practitioner in community health centre		
2. Doctor in hospital		
3. Private practitioner		
4. Other (Please specify)		

C5. Total number of visits to health professionals since last interview?
_____Times

C6. Total days of hospitalisation since last interview? _____
___Times

C7. How do you feel about your baby's weight change since last interview?

Satisfied/pleased 1

A little concerned ..... 2 ☐

Very concerned 3

Don't know 4

B. EDINGBURH POSTNATAL DEPRESSION SCALE QUESIONNAIRE

B1. **I have been able to laugh and see the funny side of things**

As much as I always could 0
No quite so much now ..... 1 ☐
Definitely not so much 2
Not at all 3

B2. **I have looked forward with enjoyment to things**

As much as I ever did 0
A little less than I used to ..... 1 ☐
Definitely less than I used to 2
Hardly at all 3

B3. **I have blamed myself unnecessarily when things went wrong**

No, never 0
Not very often ..... 1 ☐
Yes, some of the time 2
Yes, most of the time 3

B4. **I have been anxious or worried for no good reason**

No, not at all ..... 0 ☐
Hardly ever 1
Yes, sometimes 2
Yes, very often 3

B5. **I have felt scared or panicky for no very good reason**

No, not at all ..... 0 ☐
Hardly ever 1
Yes, sometimes 2
Yes, very often 3

B6. **Do you feel that you have too many tasks to manage?**

No, I have been coping as well as ever ..... 0 ☐
No, most of the time I have coped quite well 1
Yes, sometimes I haven't coped as well as usual 2

Yes, most of the time I haven't been able to cope at all 3

B7. **I have been so unhappy that I have had trouble sleeping**

No, not at all 0
Not very often 1
Yes, sometimes 2
Yes, most of the time 3

B8. **I have felt sad or miserable**

No, not at all 0
Not very often 1
Yes, quite often 2
Yes, most of the time 3

B9. **I have been so unhappy that I have been crying**

No, never 0
Only once in a while 1
Yes, quite often 2
Yes, most of the time 3

B10. **The thought of harming myself has occurred to me**

Never 0
Hardly ever 1
Sometimes 2
Yes, quite often 3

THANK YOU VERY MUCH FOR YOUR PARTICIPATION!

Contact numbers (Home phone/mobile)	You …...../..... Your husband ……..... Your mother ……... Your mother-in-law...…….

APPENDIX H: COHORT PROFILE PAPER

Open Access Cohort profile

BMJ Open

Cohort profile: maternal lifestyle and diet in relation to pregnancy, postpartum and infant health outcomes in Vietnam: A multicentre prospective cohort study

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ABSTRACT

Purpose To determine modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam.

Participants This prospective cohort study included pregnant women seeking prenatal care at six hospitals in three large cities in Vietnam. After enrolment, eligible participants who gave their consent to participate in the study were interviewed at 24–28 weeks' gestation. Glucose testing was conducted and blood pressure was measured during this period. Each participant will be assessed prospectively during their postnatal visits at delivery, 1, 3, 6, 12, 18 and 24 months, and will be followed up for 5 years.

Findings to date Of 2248 eligible pregnant women, 2030 were recruited (participation rate 90.3%) between August 2015 and July 2016. All participants completed the baseline assessment. Their mean (SD) age was 27.6 (5.3) years. The mean pre-pregnancy body mass index (BMI) was 20.2 (SD 2.6) kg/m^2, with nearly two-thirds of participants having a normal pre-pregnancy BMI (18.5 to <23.0 kg/m^2) and one-quarter being underweight (pre-pregnancy BMI <18.5 kg/m^2). Overweight or obese mothers (pre-pregnancy BMI ≥23.0 kg/m^2) accounted for 12.8%. No pregnant women reported smoking during their pregnancy while 13.4% of them had continued drinking. 22.8% of participants had hyperglycaemia. Their mean systolic blood pressure was 105.6 (SD 8.2) mm Hg, and diastolic blood pressure was 67.4 (SD 7.5) mm Hg.

Future plans The relationships of maternal lifestyle and nutritional status with the health outcomes of pregnancy, postpartum maternity and infants will be analysed. Meanwhile, participants will be closely tracked to minimise loss to follow-up.

Strengths and limitations of this study

- This is the first multicentre, prospective cohort study of maternal and child health in Vietnam, with a large sample size over a relatively long period of follow-up.
- The study investigates multiple modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam.
- All questionnaires used for data collection have been validated for Vietnamese people.
- Potentially high rates of loss to follow-up in more affluent settings.
- Lack of participants from rural and remote areas.

INTRODUCTION

Pregnancy and the first 2 years after giving birth are critical periods for mother and child health. Maternal lifestyle and dietary intake are known to be associated with metabolic disorders, such as gestational diabetes mellitus (GDM). These conditions increase the risk of adverse pregnancy and infant health outcomes.[1 2] In particular, overeating or sedentary behaviour during pregnancy has been positively associated with a risk of GDM.[3–6] Development of maternal GDM increases the risk of adverse health in mothers (gestational hypertension and pre-eclampsia, subsequent type 2 diabetes),[2] in infants (stillbirth, macrosomia, neonatal hypoglycaemia)[7] and in children (obesity, diabetes, hypertension and cardiovascular diseases).[8]

Vietnam is a middle-income country in Southeast Asia with a population of over 90 million.[9] It is undergoing epidemiological transition. A high burden of infectious diseases remains and the prevalence of chronic non-communicable diseases is increasing. The prevalence of overweight and obesity (BMI ≥23.0 kg/m^2) among Vietnamese adults has risen from 11.7% to 16.3% between 2000 and 2005.[10] The prevalence of GDM is reported to range from 6.1% to 20.3%, and women with GDM tend to deliver

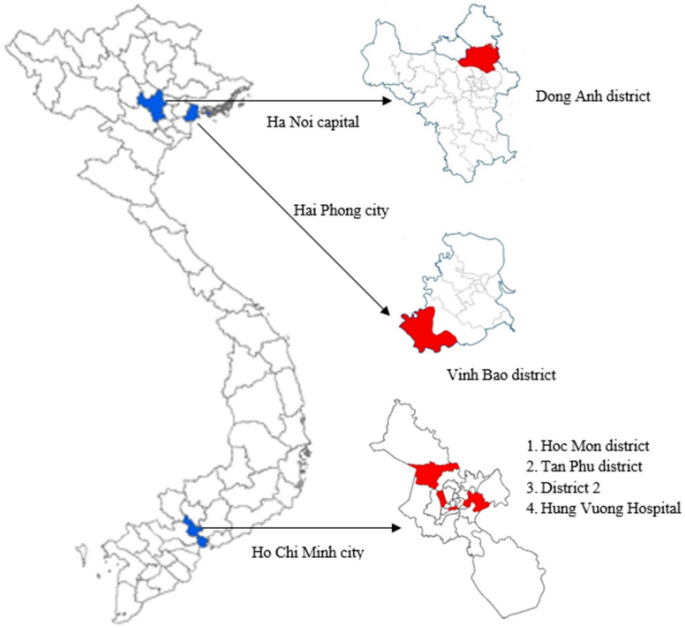

Figure 1 The location of study centres.

Recruitment

Recruitment began in August 2015 and ended in July 2016. During that period, all pregnant women from the participating hospitals were consecutively approached and invited to participate in the study if they met the eligible criteria. According to the Vietnam 2014 Multiple Indicator Cluster Survey, nearly 94% of the pregnant women delivered in hospitals.[24] Gestational age was determined using ultrasound during the first trimester and was available from medical records. A total of 2248 pregnant women who met the inclusion criteria were invited, 218 (9.7%) refused participation, and 2030 (90.3%) consented to take part in the study. No significant difference in mean age was found between participants and non-participants (p=0.991).

Baseline interview at 24–28 gestation weeks

After enrolment, pregnant women were interviewed face to face by trained personnel to obtain detailed information on demographic and personal characteristics, dietary intakes, lifestyle habits including physical activity, cigarette smoking and alcohol drinking, antenatal depressive symptoms and attitudes to breastfeeding. Standard or validated questionnaires for Vietnamese adults were used to collect information.

Dietary assessment

The Food Frequency Questionnaire for Vietnamese adults was applied to investigate habitual diet.[25] It consists of various food and beverage items grouped into categories, with frequencies and quantities consumed recorded in detail. The frequency recorded is either per day, per week, per month or never, with a standard portion or utensil defined for each food/beverage item listed.

Physical activity assessment

The Pregnancy Physical Activity Questionnaire (PPAQ) was used to examine physical activity.[26] The PPAQ measures the duration, frequency and intensity of physical activity during pregnancy. It is a semiquantitative questionnaire that asks about the time spent participating in 32 activities, including household/caregiving (13 activities), occupational (five activities), sports/exercise (eight activities), transportation (three activities) and inactivity (three sedentary activities). For each activity, respondents are asked to select a category with the closest amount of time spent per day or per week. The possible duration ranged from 0 to 6 or more hours a day. An open-ended section is appended to allow listing of additional activities not covered.

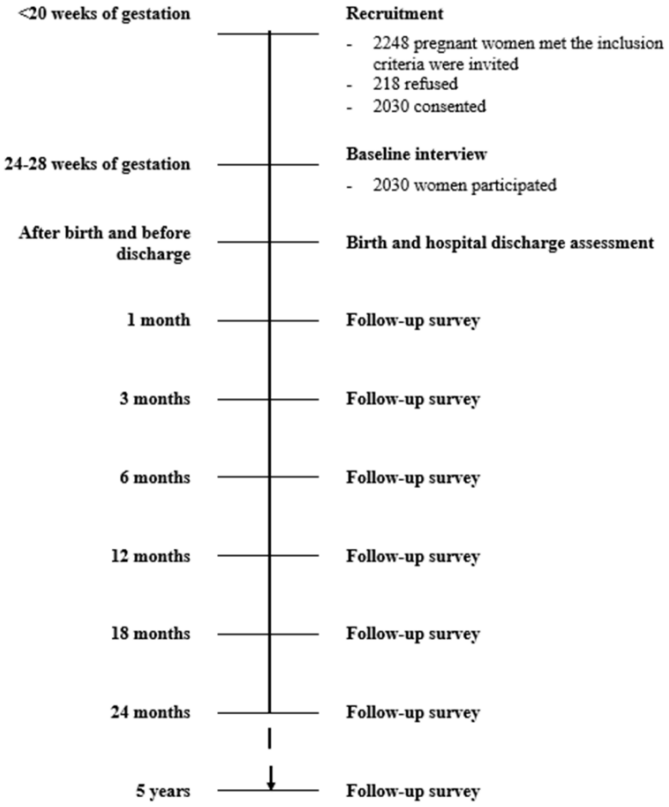

Figure 2 Recruitment and interview schedule planned.

Maternal depressive symptoms assessment

The Edinburgh Postnatal Depression Scale (EPDS) was used.[27] EPDS is a self-administered questionnaire widely used for research into antenatal and postnatal depressive symptoms to explore a woman's feelings within the past 7 days during the antenatal or postnatal period. It comprises 10 items rated on a four-point scale (from 0 to 3), reflecting the degree of agreement, with the total score ranging from 0 to 30.

Assessment of attitude to infant feeding

The Iowa Infant Feeding Attitude Scale was applied to study the breastfeeding attitudes of pregnant women.[28–30] It contains 17 items with a five-point Likert scale, ranging from 1 (strongly disagree) to 5 (strongly agree). Approximately half the items are worded favourably towards breastfeeding and the remaining items favour formula feeding. Items favouring formula feeding are reverse-scored and a total score is computed by summing all items. Total attitude scores range from 17 to 85, with higher scores reflecting attitudes more positive towards breastfeeding. Total scores are grouped into three categories: positive towards breastfeeding (70–85), neutral (49–69) and positive towards formula feeding (17–48).

Assessment of smoking and alcohol drinking

Information on cigarette smoking and consumption of alcohol was acquired using WHO STEPS questions.[31]

Anthropometric assessment

Anthropometric measurements were made during the baseline interview. A digital scale was used to record weight to the nearest 100 g. Height was measured using a stadiometer to the nearest 1 mm. Data on pre-pregnancy weight, retrieved from medical records, were likely to be self-reported. Total gestational weight gain was estimated by subtracting the early first trimester weight from the last measured weight before delivery. Maternal BMI was

calculated using weight and height recorded at baseline (kg/m^2).

Clinical assessment

To determine maternal glucose-metabolic status, all pregnant women were required by the participating hospitals to undergo a 75 g oral glucose tolerance test between 24 and 28 weeks of gestation; three blood samples were collected at fasting, 60 and 120 min. Confirmation of gestational diabetes mellitus was based on the 2013 diagnostic criteria of the World Health Ogarnization.[32] To determine gestational hypertension, blood pressure was measured at the same time as the glucose tolerance test by qualified nurses or physicians using an Omron M5-1 electronic sphygmomanometer according to the WHO procedure. Participants were required to take a short rest (15 min), sitting, feet supported on a flat surface and arm supported at heart level. Two consecutive measurements were taken 3 min apart and a mean value was obtained. WHO diagnostic criteria for gestational hypertension were used.[1] Information on pre-eclampsia was obtained from medical records. Details of obstetric complications during pregnancy were extracted from medical records.

Birth and hospital discharge assessment

At the time of delivery, details including obstetric and neonatal outcomes (eg, type of delivery, Apgar scores, problems/complications, intensive care treatment and length of hospital stay) will be recorded. Infants will be weighed to the nearest 10 g on an electronic scale immediately after birth. Length at birth will be measured on an infantometre. Other physical characteristics, such as head, abdominal and mid upper-arm circumference, will be measured within 72 hours after birth to the nearest 0.1 cm using a standardised measuring tape.

Mothers will be asked about breastfeeding initiation, prelacteal feeds (if any) and breastfeeding self-efficacy at this time using a standardised breastfeeding questionnaire[15 33] and the Breastfeeding Self-Efficacy Scale (BSES).[30] The BSES is a 33-item, self-report instrument developed to measure breastfeeding confidence. The items are preceded by the phrase 'I can always' and anchored with a five-point Likert scale, where 1=not at all confident and 5=always confident. All items are presented positively, and scores are summed to produce a range from 33 to 165. A higher score indicates a stronger confidence in breastfeeding. They will be also interviewed about depressive symptoms using the EPDS.

Follow-up surveys

All mothers will be assessed during their postnatal visits at delivery, 1, 3, 6, 12, 18 and 24 months post partum. Detailed information on infant feeding practices, infant illnesses, anthropometrics, maternal depressive symptoms, maternal diet and physical activity, and other health problems of both mothers and infants will be sought at subsequent follow-ups of the cohort. The follow-up interviews will be conducted at community health centres or at the mother's home. A 48-hour food diary will be used to record the consumption of breast milk, formula, foods and beverages by the infants at 1, 3, and 6 months of age. Symptoms of illness of the child such as fever, infection and diarrhoea, and length of hospitalisation will also be documented in detail based on both self-report and/or medical records.

A follow-up study on these children up to 5 years of age is planned and subject to funding availability.

Statistical analysis

Data will be pooled and combined across study sites. After data screening and cleaning, descriptive statistics will be used to characterise study participants. Group comparisons will be undertaken using X^2 tests for categorical variables, and either t tests/analysis of variance or Mann-Whitney U tests for continuous variables. Independent variables include demographic factors, medical history and maternal lifestyle such as dietary intake, physical activity, smoking and alcohol drinking. The main dependent variables of interest are gestational diabetes status, pregnancy outcomes (eg, stillbirth, pre-eclampsia), delivery outcomes (eg, low birth weight, macrosomia, preterm birth, caesarean section), breastfeeding duration, depressive symptom scores, gestational weight gain and postpartum weight retention, infant growth and child health conditions.

Logistic or Poisson regression models will be fitted to investigate the relationships between selected exposures and binary or discrete outcomes measured at a single point in time. Mixed regression analyses with random effects will be undertaken to assess the association between plausible risk factors and the longitudinal outcomes, such as depressive symptom scores and infant weight, while accounting for the repeated measures and clustering of subjects within study sites (hospitals). Kaplan-Meier test and Cox regression will be performed to determine the effects of influencing factors on the breastfeeding duration. Crude and adjusted coefficients or OR estimates and associated 95% confidence intervals will be reported for regression analyses, and adjusted hazard ratios for survival random-effects models.

Potential confounding variables will be selected with reference to the literature and modelling strategies.[34 35] For instance, to assess the association between gestational diabetes and rates of exclusive breastfeeding, possible confounders might be parity, delivery type, birth weight,[14] in addition to demographic factors, energy intake, energy expenditure and other covariates. Effect modification will also be taken into account in the statistical modelling. All statistical analyses will be performed using the SPSS package version 22 (IBM, Armonk, New York, USA).

Ethics and dissemination

The project has been approved by the Curtin University human research ethics committee (HR32/2015) and the Hai Phong University of Medicine and Pharmacy human research ethics committee (No 05/HPUMPRB/2015).

All participants have been provided with verbal and written information on the study describing its purpose and their requirements. Each participant has a unique ID number with basic information, including name, address, and phone numbers of themselves and partners so that they can be followed up later. Participants could withdraw from the study at any time without prejudice. All identifiable information of participants has been coded and securely stored. Study results will be published in academic journals.

FINDINGS TO DATE

Baseline characteristics of participants are summarised in table 1.

The 2030 pregnant women had a mean age of 27.6 (SD 5.3) years (range 18–48 years). The majority (60.6%) of women were in the age group 25–35 years in all locations. Almost all of the subjects were married (99.3%). Manual work and farming were the main occupations (54.9%) of the participants, followed by office and technical staff (22.5%). More than 60% of the mothers had completed high school and over one-third of them had a degree from college or university. Women in Ha Noi had the highest level of advanced educational level (50.9%) while Ho Chi Minh City had the highest rate of low educational level (18.5%). A majority (61.8%) of the participants had a normal pre-pregnancy BMI (18.5 to <23 kg/m^2) and mean BMI was 20.2 kg/m^2 (SD 2.6). The prevalence of normal BMI was similar among the three centres. However, Ho Chi Minh City had a substantially higher rate of overweight and obesity (20.8%) while Hai Phong city had a higher rate of underweight (31.7%). About one-quarter of the pregnant women were underweight. This rate was similar to a study in Ha Nam (26%)[36] and in Nha Trang (26.1%).[16] No pregnant women smoked during pregnancy but more than one-half were exposed to passive smoking at home. The overall prevalence of alcohol consumption during pregnancy was 13.4% and the highest proportion of women consuming alcohol was found in Ha Noi with 18.0%.

Very few participants had a history of hypertension or pre-eclampsia in each site. During their last pregnancy, the rate of GDM was 1.4%, birth defects (1.8%), macrosomia (3.6%) or preterm delivery (6.3%). The reported rates of stillbirth, abortion and caesarean section were 10.4%, 17.9%, and 21.5%, respectively.

Analysis of the blood test of 2023 participants (excluding seven patients with diabetes before pregnancy) showed that the prevalence of hyperglycaemia was 22.8%, slightly lower than found in a previous cohort study in southern Vietnam.[21] The hyperglycaemia rate was highest in Ho Chi Minh City (31.0%), followed by Hai Phong (19.9%) and Ha Noi (16.4%). The mean systolic blood pressure in all centres was 105.6 (SD 8.2) mm Hg, and the mean diastolic blood pressure was 67.4 (SD 7.5) mm Hg.

Data on physical activity, dietary pattern, breastfeeding and antenatal depressive symptoms are currently being analysed and results will be presented in subsequent articles.

STRENGTHS AND LIMITATIONS

One major strength of this multicentre, prospective cohort study in Vietnam is its large number of patients, followed up over a relatively long period; it is conducted in two principal regions of Vietnam, thus representing the urban Vietnam population. The few previous prospective cohort studies undertaken in Vietnam were either conducted in a single province,[11 15–17 37] or their sample sizes were small[15 17] or their follow-up times were short.[11 17]

Another strength is that it investigates a variety of modifiable maternal risk factors for adverse pregnancy, postpartum maternal and child health outcomes in Vietnam. Unlike previous prospective studies in Vietnam,[11 17 37] this project examines lifestyle, nutritional and metabolic status of pregnant women, including physical activity, smoking, alcohol drinking, dietary intake, pre-pregnancy BMI, gestational weight gain, antenatal and postnatal depressive symptoms and breastfeeding. It will also ascertain the impact of maternal factors (eg, pre-pregnancy BMI, dietary intake, physical activity, gestational weight gain) on obstetric complications (eg, gestational diabetes mellitus, pre-eclampsia, pregnancy-induced hypertension), pregnancy outcomes (eg, preterm delivery, caesarean section, low birth weight, macrosomia and postpartum haemorrhage), postpartum health status (eg, postnatal depressive symptoms, morbidity) and child health and growth for at least 2 years.

The results of our study will provide new evidence on the impact of diet and physical activity on delivery and postpartum health outcomes in Vietnamese women, which can be compared with findings from other developing and developed countries. The research findings will provide significant information for the development of guidelines, policy planning and advocacy, and can be used to formulate appropriate intervention programmes to improve maternal and child health in Vietnam. In addition, all questionnaires used for data collection have been validated for the Vietnamese people, thereby increasing the accuracy of the information.

This study has several weaknesses. First, pregnant women were recruited from hospitals, which may present some selection bias. However, the participation rate was high (90.3%) and thus selection bias should be negligible. Second, recall errors and bias in the assessments of physical activity and dietary intake cannot be ruled out. Nevertheless, we minimise these impacts by using validated questionnaires and experienced interviewers. Third, although contact information of participants and their partners, such as addresses and mobile phone numbers have been recorded, a high rate of attrition in an industrialised city like Ho Chi Minh City is expected. This limitation is reduced by maintaining a regular good relationship with participants during the follow-up. Finally, although farming respondents are recruited from

Table 1 Baseline characteristics of participants

Variables	Ha Noi (n_1=905) n (%)	Hai Phong (n_2=298) n (%)	Ho Chi Minh (n_3=827) n (%)	Total (n=2030) n (%)
Age (years)				
<25, (n (%)	346 (38.2)	97 (32.6)	194 (23.5)	637 (31.4)
25–35, n (%)	499 (55.1)	178 (59.7)	553 (66.9)	1230 (60.6)
>35, n (%)	60 (6.6)	23 (7.7)	80 (9.7)	163 (8.0)
Mean (SD)	26.6 (5.0)	27.4 (5.4)	28.6 (5.3)	27.6 (5.3)
Marital status (married)	902 (99.7)	294 (98.7)	819 (99.0)	2015 (99.3)
Occupation				
Famers	194 (21.4)	44 (14.8)	58 (7.0)	296 (14.6)
Workers	303 (33.5)	139 (46.6)	376 (45.5)	818 (40.3)
Office and technical staff	226 (25.0)	44 (14.8)	186 (22.5)	456 (22.5)
Sales worker	35 (3.9)	10 (3.4)	74 (8.9)	119 (5.9)
Housewife/unemployed	147 (16.2)	61 (20.5)	133 (16.1)	341 (16.8)
Educational level				
Under secondary	15 (1.7)	3 (1.0)	153 (18.5)	171 (8.4)
Secondary	164 (18.1)	98 (32.9)	289 (34.9)	551 (27.1)
High school	265 (29.3)	88 (29.5)	172 (20.8)	525 (25.9)
College/university	461 (50.9)	109 (36.6)	213 (25.8)	783 (38.6)
Parity				
0	361 (39.9)	105 (35.2)	323 (39.1)	789 (38.9)
1	306 (33.8)	110 (36.9)	340 (41.1)	756 (37.2)
≥2	238 (26.3)	83 (27.9)	164 (19.8)	485 (23.9)
Body mass index (BMI) before pregnancy (kg/m^2)* (n=2010)				
Low (<18.5)	244 (27.0)	88 (31.7)	177 (21.4)	509 (25.3)
Normal (18.5 -<23.0)	587 (64.9)	178 (64.0)	478 (57.8)	1243 (61.8)
High (≥23.0)	74 (8.2)	12 (4.3)	172 (20.8)	258 (12.8)
Mean (SD)	19.8 (2.3)	19.5 (2.2)	20.8 (2.8)	20.2 (2.6)
History of previous pregnancy (n=1241)				
GDM	1 (0.2)	1 (0.5)	15 (3.0)	17 (1.4)
Hypertension	0 (0.0)	0 (0.0)	4 (0.8)	4 (0.3)
Pre-eclampsia	4 (0.7)	0 (0.0)	3 (0.6)	7 (0.6)
Preterm birth	43 (7.9)	8 (4.1)	27 (5.4)	78 (6.3)
Macrosomia	29 (5.3)	4 (2.1)	12 (2.4)	45 (3.6)
Birth defects	13 (2.4)	3 (1.6)	6 (1.2)	22 (1.8)
Caesarean section	135 (24.8)	18 (9.3)	114 (22.6)	267 (21.5)
Stillbirth	100 (11.1)	37 (12.4)	75 (9.1)	212 (10.4)
Abortion	207 (22.9)	46 (15.4)	110 (13.3)	363 (17.9)
History of participant's family				
Diabetes	38 (4.2)	6 (2.0)	84 (10.2)	128 (6.3)
Hypertension	74 (8.2)	36 (12.1)	197 (23.8)	307 (15.1)
Smoking and drinking during pregnancy				
Active smoking	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Passive smoking	481 (53.1)	150 (50.3)	439 (53.1)	1070 (52.7)
Drinking	163 (18.0)	29 (9.7)	80 (9.7)	272 (13.4)

Continued

Table 1 Continued

Variables	Ha Noi (n_1=905) n (%)	Hai Phong (n_2=298) n (%)	Ho Chi Minh (n_3=827) n (%)	Total (n=2030) n (%)
Blood glucose test (n=2023)				
Fasting (mean, SD)	4.4 (0.5)	4.4 (0.7)	4.5 (0.4)	4.5 (0.5)
1-Hour 75g OGTT (mean, SD)	7.2 (1.8)	6.9 (1.6)	8.4 (1.8)	7.6 (1.9)
2-Hour 75 OGTT (mean, SD)	6.4 (1.5)	6.1 (1.3)	7.3 (1.5)	6.7 (1.6)
Hyperglycaemia†	148 (16.4)	59 (19.9)	255 (31.0)	462 (22.8)
Blood pressure				
Systolic, mm Hg (mean, SD)	105.0 (7.3)	107.0 (8.3)	105.8 (9.0)	105.6 (8.2)
Diastolic, mm Hg (mean, SD)	64.9 (6.4)	64.3 (6.1)	71.3 (7.3)	67.4 (7.5)
Pulse, bpm (mean, SD)	84.3 (9.3)	79.3 (6.0)	97.0 (9.9)	88.7 (11.5)

Results are shown as number (%) unless stated otherwise.
*BMI cut-off for Asian population was used.[38]
†Hyperglycaemia was classified by WHO 2013.[32]
GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

suburban districts, they may not represent rural women in the country.

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Collaborators There is room for future joint studies. This study will follow-up mothers and their babies until 2 years post partum. This duration can be extended to investigate the effects of maternal factors on the health problems of mothers and their children later in life. In addition, the study is currently performing in two regions (Red River Delta and Southeast), while Vietnam has six socioecological regions. It can be expanded into other regions to increase the sample size and representation. Therefore, the study welcomes all researchers who have the same objectives together with available funding. Study proposals must be submitted to the study research team for review and approval.

Contributors CLN, PTHN, TKC, and AWH participated in the study design and data collection. CLN wrote the draft and edited the manuscript. TKC performed the baseline analysis. NMP provided expert advice on the draft of the manuscript. DVDu, DVDo, HKT, AHL, and CWB were the study supervisors and involved in all aspects of the study. All the authors revised the article and approved the final version to be published.

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Competing interests None declared.

Patient consent Obtained.

Ethics approval The study was approved by the Curtin University human research ethics committee (approval number: HR32/2015) and the Hai Phong University of Medicine and Pharmacy human research ethics committee (approval number: 05/HPUMPRB/2015).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Researchers can access to the cohort data by sending us an applicationvia email () for discussion andapproval at the research team meeting.

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APPENDIX I: ORAL AND POSTER PRESENTATIONS FROM PHD PROJECT

Poster Presentation certificate: The Mark Liveris Health Sciences Research Student Seminar, Faculty of Health Sciences, Curtin University, Sep 28, 2017

Curtin University

Faculty of Health Sciences

CERTIFICATE OF PARTICIPATION

Presented to

Tan Khac Chu

School of Public Health

For presenting a poster at the

THE MARK LIVERIS RESEARCH STUDENT SEMINAR

28 September 2017

Professor Michael Berndt
Pro Vice-Chancellor
Faculty of Health Sciences

Poster: Presented in the Mark Liveris Health Sciences Research Student Seminar, Faculty of Health Sciences, Curtin University, Sep 2017