Perinatal Depression: Epidemiology and Associated Adverse Birth and Infant Health Outcomes in Ethiopia: A Mixed Method study

By

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Thesis

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Abbreviations

ACOG	American College of Obstetrics and Gynaecology
AIC	Akaike Information Criteria
AMSTAR	Assessment of Multiple Systematic Reviews
ANC	Antenatal care
AND	Antenatal Depression
APA	American Psychiatry Association
ARI	Acute respiratory infection
ATE	Average treatment effect
BDI	Beck Depression Inventory
BIC	Bayesian Information Criterion
CED-S	Centre for Epidemiological Depression Scale
CFI	Comparative Fit Index
CMD	Common Mental Disorder
DM	Diabetic Mellitus
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders
Emerald	Emerging mental health system in low-and middle-income countries
EPDS	Edinburgh Postnatal Depression Scale
FMOH	Ethiopian Federal Ministry of Health
FMOH	Federal Ministry of Health
GEE	Generalised estimating equation
GLM	Generalised Linear Model
GSEM	Generalised Structural Equation Modelling
HEP	Health Extension Program
HEWs	Health Extension Workers
HIV	Human Immune Deficiency
IMNCI	Integrated Management of Newborn and Childhood Illnesses
IPV	Intimate Partner Violence

LBW	Low birth weight
LMICS	Low- and Middle-Income Countries
LNMP	Last normal menstrual period
MCH	Maternal and child health
mhGAP	mental health Gap Action Program
MUAC	Middle-Upper Arm Circumference
NOS	Newcastle–Ottawa Scale
ODK	Open Data collection Kit
OR	Odds Ratio
OSSS	Oslo Social Support Scale
PCI	Perinatal Coping Inventory
PDQ	Pitt Depression Questionnaire
PHQ-9	Patient Health Questinaire-9
PNC	Postnatal care
PND	Postnatal Depression
POR	Pooled Odds Ratio
PRIME	A Program for Improving Mental Health care
PRISMA	Preferred Reporting Items for Systematic Review and Meta-analysis
RMSEA	Root Mean Square Error of Approximation
RR	Relative Risk
SBRC	Social and Behavioural Research Ethics Committee
SD	Standard deviation
SDG	Sustainable Development Goals
SEM	Structural Equation Modelling
SRQ-20	Self-Reporting Questionnaire
TLI	Tucker Lewis Index
TMLE	Targeted maximum likelihood estimation
UK	United Kingdom

US	United States
VIF	Variance Inflation Factor
WHO	World Health Organization

Glossary

Terms	Definitions
Health centre	According to the Ethiopian health system it is a health facility at the primary care level that provides preventive and curative services by health officers, nurses, and laboratory and pharmacy professionals.
Urban Health Extension Program	A specially designed community health program to reach every urban household with primary health care services.
Health extension workers	Clinical nurses trained in urban health extension programs for at least three months and deployed in urban kebeles to provide primary health care at household levels.
Antenatal depression	Depression occurring during pregnancy
Postnatal depression	Depression occurring during the postnatal period (measured from two weeks to 12 weeks after birth).
Perinatal depression	Depression occurring during the perinatal period (from pregnancy to the postnatal period).
Adverse birth outcomes	Birth outcomes where infants were preterm, low weight, or stillborn.
Adverse infant health outcomes	Diarrhea, acute respiratory infection, and malnutrition occurring in infants aged to six months.
Kebele	The lowest administrative unit in Ethiopian administrative system.

Executive summary

Introduction: Depression occurring during the perinatal period (from pregnancy through the postnatal period to 12 months postpartum is one of the most common complications of the perinatal period in high- and low-income countries. Perinatal depression has been reported to affect pregnancy, maternal, newborn and child health outcomes. Although several studies have been conducted on perinatal depression in Ethiopia, the mechanisms underlying the relationship between this disorder and risk factors, and the links between the condition and adverse birth and infant health outcomes remain unexplored. Furthermore, there have been no studies conducted to explore how the healthcare system addresses perinatal depression issues in Ethiopia. This PhD thesis has investigated the burden and potential causal mechanisms of perinatal depression and its association with the risk of adverse birth and infant health outcomes in Gondar town, Ethiopia. Health system related barriers and enablers of accessing perinatal depression services in Ethiopia were also explored.

Methods: A mixed-methods study was employed to address research questions as follows: (i) to understand what previous studies had found and to assess any gaps in literature, systematic reviews and primary observational studies published between 2007 and 2018 were systematically searched from relevant databases. The quality of the systematic reviews and primary studies were appraised using the Assessment of Multiple Systematic Reviews (AMSTAR) checklist and the Newcastle–Ottawa scale, respectively. (ii) To assess the epidemiology of perinatal depression (using Edinburgh Postnatal Depression Scale (EPDS)), risk factors and effects of perinatal depression on birth and infant health outcomes, a prospective cohort study was conducted. In total, 916 pregnant women were interviewed from six randomly selected urban districts in Gondar town between June 2018 and March 2019. Face-to-face questionnaires were administered using the online Open Data collection Kit (ODK). Enrolled women were followed from pregnancy to up to six months after birth. Using Stata (release 12) software, a mixed effect linear regression and Structural Equation Modelling (SEM) were used to explore antenatal and postnatal depression risk factors and their potential causal mechanisms. Modified Poisson regression and Generalized SEM were used to estimate the risk of adverse birth outcomes and

potential mechanisms. Targeted Maximum Likelihood Estimation (TMLE) was applied to investigate the causal association between perinatal depression and the risk of adverse infant health outcomes. (iii)To explore barriers to and facilitators of access to services that address perinatal depression, a qualitative study was conducted with 13 health service administrators from different levels of the Ethiopian health system. A thematic content analysis was conducted to analyse the qualitative data aided by NVivo 12 software.

Results: The systematic review findings highlighted the following: (i) The global prevalence of antenatal depression (AND) ranged from 7% to 65% and was highest in low-income countries. (ii) Globally, the risk of LBW and preterm birth was 1.49 (95%CI: 1.32, 1.68) and 1.40 (95%CI: 1.16, 1.69) times higher in women with AND relative to those with no depression. (iii) Nearly one in three pregnant women in low-income and one in five in middle-income countries had depression symptoms. (iv) The risk of low birth weight (LBW) and preterm birth was found to be 1.66 (95%CI: 1.06, 2.61) and 2.41 (95%CI: 1.47, 3.56) times higher in women with AND in low- and middle-income countries (LMICs) relative to those with no depression. (iii) One in four postnatal women in low-income and one in five in middle-income countries had depression symptoms. (iv) The risk of malnutrition (RR=1.39; 95%CI: 1.21, 1.61), non-exclusive breastfeeding (RR=1.55; 95%CI: 1.39, 1.74), and common infant illnesses (RR=2.55; 95%CI: 1.41, 4.61) were found to be high in the infants of postnatally depressed women. (v) Perinatal women with depression were more likely to experience abuse or violence, poor social and/or partner support, a history of common mental disorders (CMDs), economic difficulties, and poor obstetric history relative to those without depression. The review found that there was a lack of information on the potential causal links of antenatal and postnatal depression and their effects on birth and infant health outcomes in Ethiopia.

Findings from the preliminary analysis of cohort study indicated that the prevalence of AND was 6.9% (95%CI: 5.3, 8.7). Unplanned pregnancy (standardised β=0.15), having a history of CMDs (standardised β=0.18), fear of giving birth (standardised β=0.29), and adequate food access for the last three months (standardised β=–0.11) were correlated with depression score. Social support (β=–0.21), marital agreement (β=–0.28), and partner support (β=–0.18) appeared to

partially mediate the link between the identified stressors and the risk of AND. Findings from the cohort study (sample 916) showed that the cumulative incidence of stillbirth, LBW, and preterm birth was 1.90% (95%CI: 1.11, 3.02), 5.25% (95%CI: 3.88, 6.92), and 16.42% (95%CI: 14.05, 19.01), respectively. Depression had no direct effect on birth outcomes but indirectly affected preterm birth via partner support. Partner support moderated the association between AND, preterm birth, and LBW. The risk of stillbirth was 3.22 (95%CI: 1.04, 9.98) times higher in women with AND, and 73% (RR: 0.27; 95%CI: 0.07, 0.99) lower in women with higher coping abilities, but this association was attenuated in path analysis.

The analysis of the cohort study (sample 895) indicated the prevalence and incidence proportion of postnatal depression (PND) to be 9.27% (95%: 7.45, 11.36) and 7.77% (95%CI: 6.04, 9.79), respectively. More than two percent of the women showed depression symptoms both in pregnancy and the postnatal period. Postnatal depression was associated with limited postnatal care services (IRR=1.8; 95%CI: 1.0, 3.2), and was predicted by AND (IRR=1.6; 95%CI: 1.4, 1.7) and CMDs before pregnancy (IRR=2.4; 95%CI: 1.4, 4.3). Antenatal depression (standardised total effect=0.36) and history of CMDs before pregnancy (standardised total effect=0.11) had both a direct and an indirect positive effect on PND scores. Low birth weight (standardised β=0.32) and self-reported labour complications (standardised β=0.09) had only direct effects on PND scores. The cumulative incidence of diarrhea, acute respiratory infection (ARI) and malnutrition during the 6-month follow-up (sample 878) was 17.0% (95%CI: 14.5, 19.6), 21.6% (95%CI: 18.89, 24.49), and 14.4% (95%CI: 12.2, 16.9), respectively. Antenatal depression was not causally associated with the risk of ARI (RD=–1.3%; 95%CI: –21.0, 18.5), diarrhea (RD=0.8%; 95%CI: –9.2, 10.9), or malnutrition (RD=–7.3%; 95%CI: –22.0, 21.8). Similarly, there was no evidence of causal association between PND and the risk of diarrhea (RD=–2.4%; 95%CI: –9.6, 4.9), ARI (RD=–3.2%; 95%CI: –12.4, 5.9), or malnutrition (RD=0.9%; 95%CI: –7.6, 9.5).

The qualitative inquiry identified the following barriers to the delivery of perinatal mental health services: (i) low awareness of perinatal depression among health administrators and community members, and (ii) the absence of policies and/or programs that addressed perinatal depression in Ethiopia. However, the introduction of the new mental health gap action program (MhGap),

the simplicity of available screening programs and health worker motivation were identified as potential opportunities that could be used to address perinatal depression by the health system in Ethiopia.

Discussion: The cohort study findings estimated a lower prevalence of antenatal and postnatal depression estimates than those found in systematic reviews. Higher incidence of adverse birth and infant health outcomes were observed in the current study than in previously conducted studies in Ethiopia. Partner support during pregnancy mediated the link between depression, LBW and preterm births. A strong association was found between depression during pregnancy and stillbirth. History of CMDs before pregnancy, AND, LBW, and self-reported labour complications were found to increase the risk of PND. There was no evidence of direct associations between perinatal depression and the risk of adverse infant health outcomes.

Conclusion and implications: The thesis findings inform the need to develop national mental health policies, guidelines and strategies that incorporate perinatal depression in Ethiopia. Health providers' training and reorientation of mental health service towards a holistic approach that engages the community, especially pregnant women, is crucial for enhancing the mental health and wellbeing of pregnant women and their newborn babies. The thesis findings also provide comprehensive evidence that can be used to inform policies and practices that can address issues of perinatal depression in Ethiopia and in similar settings.

Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief, it does not contain any material previously published or written by another person except where due reference is made in the text.

Abel Fekadu Dadi Date

23/09/2020

Dedication

I dedicate this work to my grandmother, Temegnu Lemma Desta, for her personal sacrifices to raise me, unconditional love and for her every day and night prayers.

Articles published, submitted or presented during the candidature

This thesis informed the following published and under review articles. I confirm that I have made a significant contribution from the inception of idea, designing the study, data collection, analysis, interpretation, and publication of the findings as a first and corresponding author. Additionally, I have also published more than 20 articles during my candidature as an extra activity.

Published articles

1. **Dadi AF**, Miller ER, Woodman RJ, Azale T, Mwanri L. Effect of antenatal depression on adverse birth outcomes in Gondar town, Ethiopia: A community-based cohort study. PLoS One. 2020 Jun 17;15(6).
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Under review article

1. **Dadi AF**, Miller ER, Woodman RJ, Azale T, Mwanri L. Estimating effect of perinatal depression on risk of adverse infant health outcomes in mother–infant dyads in Gondar town using the Targeted Maximum Likelihood Estimation Model; BMC Paediatrics

Manuscripts under review for submission

1. **Dadi AF**, Miller ER, Bisetegn TA, Mwanri L. *"We do not know how to screen and provide treatment*": A qualitative study of health system response, barriers, and opportunities of perinatal depression care in Ethiopia.
2. **Dadi AF**, Miller ER, Bisetegn TA, Mwanri L. *"I do not have any idea about perinatal depression though I am a non-communicable disease officer*": Health administrators' literacy on perinatal depression in Ethiopia.

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1. **Dadi AF**, Miller ER, Woodman R, Azale T, Mwanri L. A causal mechanism between stressors and mediators of antenatal depression among pregnant mothers in Gondar town: Application of a Stress Process Model framework: AFSAAP Conference 2019; Dunedin November 26–27, New Zealand 2020
2. **Dadi AF**, Miller ER, Woodman R, Azale T, Mwanri L. Effect of minor depression during pregnancy on adverse birth outcomes in Gondar town: Flinders University Emerging Leaders Showcase; 21–22 November 2019: Alere Function Centre, Flinders University, Bedford Park, SA. 2019.
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4. **Dadi AF**, Miller ER, Mwanri L. Prenatal depression and its effect on birth outcomes in low and middle-income countries: a systematic review and meta-analysis: 30th EPHA Annual Conference: February 25–27, 2019, Adama, Ethiopia.

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Media opinion

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2. https://medicalxpress.com/search/?search=Abel+Fekadu+Dadi&s=0

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Chapter One: Introduction

1.1. Introduction

This chapter introduces depression by summarising its epidemiology during pregnancy and after birth, and its association with adverse birth and infant health outcomes. The rationale and original contribution of the thesis, the research aim and objectives are then described. The chapter ends by briefly summarising the thesis structure.

1.2. Statement of the problem

Good mental health is crucial for overcoming stressors, living a productive life, and actively participating in day-to-day activities (1). The World Health Organization (WHO) made mental health a priority agenda in its recent publication, *Mental health and development: Targeting people with mental health conditions as a vulnerable group* (2). Depression is a widespread mental health disorder worldwide (3). It is defined in the *Diagnostic and Statistical Manual of Mental Disorders* 5th edition (DSM–V) (4) and the *International Statistical Clarification of Disease* 11th revision (ICD–11) (5) as symptoms manifested by low mood or loss of interest or pleasure for two weeks. Depression symptoms are often accompanied by lack of concentration, reduced energy, changes in sleeping and eating patterns, feelings of worthlessness, psychomotor impairments or suicidal ideation (6). Previous studies have demonstrated that 40% of the cause of depression is genetic while 60% can be attributed to environmental influences (7, 8).

Depression is a common problem, with an estimated 264 million people affected worldwide which is more common in lower income countries and prevalence has been increasing over the last ten years (9, 10). Depression affects people of every age and sex, however, females and older age groups are more vulnerable (11). Depression is predicted to be the second and third leading cause of disease burden in high- and low-income countries respectively by 2030 (12). Nineteen percent of health-related disabilities are due to depression and related mental health disorders (12). Untreated depression can lead to suicide and it is the reason for 90% of suicidal ideation worldwide (13). Depression can increase the treatment costs of chronic diseases such as diabetes mellitus (DM), hypertension, cancer, and HIV through reducing treatment adherence and impairing immunity (14). In general, untreated depression could directly or indirectly affect the attainment of Sustainable Development Goals (SDG) (2).

Pregnancy and the postnatal period are important times of vulnerability for depression (15, 16). The causes of antenatal (AND) and postnatal depression (PND), collectively named as perinatal depression, are explained by genetic, biological, and social constructs such as distressing relationships, difficulty with pregnancy, and caring for the baby (17). Both antenatal and postnatal depression can be accompanied by signs and symptoms of low mood, tiredness, insomnia, lack of energy, forgetfulness, irritability, and poor physical and cognitive functioning (18). The occurrence of depression during pregnancy follows different patterns (19), such as increasing in the first and final weeks and decreasing in mid-pregnancy (20). The range of possible AND prevalence in developed countries is reported to be 5–30%, and varies with socio-demographic, obstetric, and measurement related factors (21-23). Elsewhere, possible AND prevalence has been reported as ranging from 10.4% to 57% in low-income Asian countries (24-34) and between 22.7% and 38.5% among African countries (35-38). In Ethiopia, possible AND prevalence ranges from 11.8% to 31.1% and varies by setting and time of measurement (39).

Biological studies indicate that women with depression during pregnancy produce high levels of stress hormone (cortisol) that affects foetal development (40) and growth leading to adverse birth outcomes (Low Birth Weight (LBW), preterm and stillbirth) (41, 42). It has also been suggested that high levels of cortisol during pregnancy can result in discontinuation of the proper functioning of the placenta and reduced oxygen supply to the foetus, which may cause foetal death or miscarriage (43). Empirical evidence has also supported a biological link between depression during pregnancy and adverse birth outcomes. For instance, systematic reviews have suggested a significant relationship between depression during pregnancy and the risk of adverse birth outcomes (44-47). Similarly, different reviews from LMICs have indicated that the risk of preterm birth is high in women who had depression, anxiety and stress during pregnancy (21, 48-52). Previously conducted studies in Ethiopia, however, found lack of association between adverse birth outcomes and CMDs (53-55). Antenatal depression is also associated with low maternal healthcare service uptake, increased substance use (43, 56, 57), and children's low stress coping ability in later life (58).

Births before 37 weeks of gestation are considered 'preterm' and worldwide about 15 million births annually are preterm (59). Worldwide, preterm complications cause lifetime disability or death in one million children every year (60). Globally, more than 60% of preterm births

occur in Africa and Asia (59). In Ethiopia, 320,000 babies are born preterm each year and 24,000 children die because of preterm complications (61). A study conducted in Gondar, Ethiopia, reported a preterm prevalence of around 4% (62). Low birth weight (birth weight less than 2500gm) is the main cause of perinatal mortality and morbidity (63). More than 15% of all births are low weight, with high prevalence observed in low-income countries (64). In Ethiopia, hospital-based studies have reported a prevalence ranging from 10% to 17.1% (65-67). Low birth weight increases the risk of non-communicable diseases such as DM and cardiovascular disease in later life (68).

Globally, more than two million stillbirths occurred in 2015 and almost all were from low-and middle-income countries (LMICs), with three-quarters occurring in Sub-Saharan Africa and Asia (69). Stillbirth imposes socio-economic and psychosocial burdens on families, communities and nations (70). Globally, Ethiopia is ranked fifth among the top ten countries with the highest number of stillbirths (97,000) (71).

Postnatal depression (PND) starts to manifest four to six weeks after birth, reaching peak prevalence two to three months after birth, and its symptoms can appear up to 12 months after delivery (18, 72-74). Evidence has shown that about 20% of postnatal women in LMICs have possible PND (75). The pooled prevalence of possible PND in Africa is 18.3% (76) with a lower prevalence in Uganda (7.1%) and the highest in Zimbabwe (33%) (77). In Ethiopia, recent studies have reported a prevalence that ranges from 12.2% to 22.1% in rural areas (78, 79) and 22.4% to 33.2% in urban areas (80-82). Postnatal depression is the second cause of disability after HIV and AIDS (83), and is the most known complication of childbirth (84). It is reported to increase costs to the health care system, impair mothers' quality of life (85), and reduce their work efficiency (86). Postnatally depressed women are at risk of back pain, feelings of self-worthlessness, thoughts of self-harm, and suicidal ideation (87). It is very difficult for depressed women to breastfeed their newborn effectively and efficiently, or make optimal use of available health services (88, 89). Postnatal depression can also affect women's emotional regulation and stress coping ability, children's cognitive development (90), and mother–child interaction during infancy and in later life (91).

Providing adequate care and attachment to a newborn baby requires courage, patience, commitment, and concentration (92). However, this could be difficult for depressed women

where there are associated physical, psychosocial and psychological symptoms that affect their relationship with their newborn baby (93). Studies suggest that women with possible PND have a 30% risk of being unresponsive toward their baby (94, 95). Postnatal depression may result in difficulty in getting adequate sleep, negative maternal parenting behaviour and, in severe cases, infanticide (89). Studies from developing and developed countries have reported a higher risk of infant growth impairment and cognitive development among babies of postnatally depressed women (96-98). Reviews of studies conducted in LMICs have indicated that children of perinatally depressed women tend to be stunted, underweight, wasted, and stop breastfeeding early (75, 99-101). However, evidence is inconclusive, possibly because of limited available studies (96, 97, 101, 102). Common mental disorders other than perinatal depression have been linked to child death and illnesses (103, 104) but not malnutrition, diarrhea, or acute respiratory infections (ARI) (104-106) in Ethiopia.

Previous reviews on perinatal depression and associated effects have consistently mentioned issues with methodological quality (76, 107), inconsistencies with tools used for collecting depression data, and the problem of handling confounders (15, 108-110). Despite the fact that 60% of causal factors for depression can be described as environmental characteristics, previous studies in Ethiopia are limited. More importantly, the potential causal mechanisms for antenatal and postnatal depression that could possibly support intervention modalities have not been previously explored. Moreover, studies published from Ethiopia that investigated the association between perinatal depression and risk of adverse birth and infant health outcomes are very limited. As such, research questions associated with perinatal depression and its adverse outcomes in Ethiopia have not well explored.

1.3. The mental health treatment gap for perinatal women in Ethiopia

Universal health coverage is a key target in SDGs to achieve good health and health quality and equity across the globe (111). Mental health services in LMICs are highly compromised in terms of access and quality, with mental health disorders becoming a major public health problem. For example, depression was one of the top five leading causes of years lived with disability globally (9). In Ethiopia, 10.1% of years lived with disability were reported to be due to depression in the year 2015 (11). Existing sparse evidence has shown that there is a huge gap in access to and quality of mental health services in Ethiopia (79). An estimated 90% of

people with mental disorders never receive care from professionals and fewer than 1% receive ongoing care (112). There is also an enormous gap in the availability of psychiatrists and other mental health professionals, with most professionals located in central cities (113). Although there is a clear absence of research exploring the reasons, lack of government commitment, mental health policy, healthcare system, and resources would be hypothesised factors. As such, effective integration of mental health services into primary healthcare in Ethiopia has also been lagging (114, 115).

In Ethiopia, as elsewhere, biologically, depression is more common in females than males and presentations increase during the perinatal period, as stated above. Despite the high burden of the disorder, there are no screening and treatment services designed for perinatal mothers with signs of depression (1). The treatment gap for PND is close to 95% (57) and it is assumed to be similar for AND. There is a global initiative to reach perinatal women with mental health care through the integration of mental health services with existing maternal health services (116, 117). However, situational analysis in five LMICs including Ethiopia has shown limited evidence on feasible detection and treatment strategies for maternal mental health disorders (118). Ethiopia has developed its first mental health strategy aligned with the WHO Mental Health Gap Action Plan (mhGAP) (119) but mental health needs of perinatal women were poorly addressed in it.

Two programs have been running in Ethiopia to support an increase in mental health services including maternal mental health care. The first is Program for Improving Mental Health care (PRIME), which had the general aim to generate evidence on the implementation and scale-up of mental health service integration in Ethiopia (120). The second is the Emerging Mental Health System in LMICs (Emerald), which had the aim of improving mental health outcomes by generating capacity and evidence (121). The Emerald program had a focus on identifying health system barriers and giving solutions to improve the effective delivery of mental health services. In the Ethiopian health system, policy, programs, guidelines, and implementation plans are developed at the federal level and devolved to regional state health bureaus. The Ethiopian healthcare system operates at multiple levels; however, its governance is centrally directed by health policies of the Federal Ministry of Health (FMOH). While it might be possible for regional governments to exercise some sort of autonomy in the implementation

of health services, it is unlikely these would result in health system structures that respond differently to perinatal depression in Ethiopia.

1.4. Rationale and original contribution of the study

Depression is the most common complication of the perinatal period in both high- (50, 122) and low-income countries (76, 77). Depression affects pregnancy outcomes, newborn and maternal health (122) and, cumulatively, has an impact on the economic and social situation of a country (70). In Ethiopia, from published studies, the prevalence of AND ranges from 11% to 31% (39) while the few published studies on PND report a prevalence ranging from 12.3% to 33.2% (78, 81).

Modelling of the stress process can assist in understanding the various pathways and mechanisms by which depression could occur (123, 124) and it is now considered important to enable interventions (123, 124). Although several antenatal and postnatal depression studies have been conducted in Ethiopia (57, 125-127), none of them examined the potential mechanisms underlying the cause of depression. Although studies conducted in high-income countries have tried to establish the link between perinatal depression and the risk of adverse birth and infant health outcomes, limited and unrelated studies from Ethiopia have reported inconsistent findings, for instance, lack of associations between stillbirth, LBW and maternal CMDs in Ethiopia (54, 55, 128). Furthermore, a study in predominantly rural areas that investigated the link between depression during pregnancy and LBW found a lack of association. However, no studies have investigated the relationship between depression during pregnancy and the risk of preterm and stillbirth. Conflicting conclusions have been drawn about the association between maternal CMDs and the risk of infant illnesses and malnutrition (104-106). No study has investigated the association between antenatal and postnatal depression and risk of infant illnesses and malnutrition. So, in conclusion, the link between perinatal depression and adverse birth and infant health outcomes in Ethiopia has remained unclear.

There are interventions for tackling perinatal depression in high-income countries (129), but the opportunities for such interventions for women in low-income countries are fewer because perinatal depression and its consequences have been poorly understood. As such, the integration of mental health into maternal health services at different levels of the

Ethiopian health system is yet to come to the attention of the government. As a result, it is hypothesised that thousands of perinatal women have been suffering from the disorder, resulting in thousands of LBW, preterm and stillbirths, with many more infants developing malnutrition, illnesses and disabilities (118). In this context, it would be challenging for the country to achieve the SDGs related to maternal and newborn health and other developmental agendas (77, 130).

Hence, the originality of this PhD research project is its contribution to evidence derived from the three main research questions: (i) to explore the potential causal mechanisms of antenatal and postnatal depression using the stress process model developed by Perlin (131); (ii) to investigate the link between antenatal and postnatal depression and the risk of adverse birth and infant health outcomes; and (iii) to explore potential barriers to and enablers of perinatal depression health services. The information generated from this study adds to the body of knowledge and can be used to advocate for the importance of introducing perinatal mental health interventions in Ethiopia. In this thesis, adverse birth outcomes refer to LBW, preterm, and stillbirth while adverse infant health outcomes refer to acute respiratory infection, malnutrition, and diarrhea.

1.5. Study aims and objectives

Study aims

1. To investigate the epidemiology of perinatal depression and its association with the risk of adverse birth and infant health outcomes among perinatal women and infants of age up to six months in Gondar town, Northwest Ethiopia.
2. To explore potential barriers to and enablers of perinatal depression health services in Ethiopia.

Study objectives

1. To systematically review the burden of perinatal depression and its association with the risk of adverse birth and infant health outcomes, globally and in LMICs.
2. To assess the prevalence of antenatal depression and its potential causal mechanisms among pregnant women in their second and third trimesters in Gondar town.

3. To estimate the incidence of adverse birth outcomes and to investigate their association with antenatal depression in Gondar town.
4. To assess the prevalence of postnatal depression and its potential causal mechanisms among postnatal women within two to six weeks after delivery in Gondar town.
5. To estimate the incidence of adverse infant health outcomes and to investigate their association with antenatal and postnatal depression in Gondar town.
6. To explore potential barriers to and enablers of perinatal depression health services in Ethiopia.

1.6. Thesis structure

The thesis is presented in nine chapters. Chapter one introduces the thesis and contains the statement of the problem, significance and original contribution of the study, aims and study objectives. Chapter two presents the review of literature summarised under five main sections: the diagnosis; burden; risk factors of perinatal depression; association of AND with the risk of adverse birth outcomes; and association of perinatal depression with the risk of adverse infant health outcomes. In each section, available studies have been chronologically presented from the global to the local context, and from broader to narrower scope. The gaps in the literature have been identified and summarised at the end of each section. Chapter three presents the methodological approaches employed in the thesis. The first section of the chapter contains a theoretical framework used for conceptualising the thesis, study setting, and methodological philosophy. The method section describes three study designs employed for the development of the thesis including (i) systematic reviews and meta-analyses, (ii) a quantitative (a cohort study), and (iii) a qualitative study.

Chapter four presents the findings from the systematic reviews and meta-analysis conducted to assess the epidemiology of antenatal and postnatal depression and their association with risk of adverse birth and infant health outcomes in three sections. The first section presents the method summary and findings from a scoping review conducted to assess the global epidemiology of antenatal depression and its association with the risk of adverse birth outcomes. The second and third sections describe the method summary and findings of the systematic review and meta-analysis of antenatal and postnatal depression and their associations with the risk of adverse birth and infant health outcomes in LMICs, respectively.

Chapter five summarises methods, results, discussion, and conclusion of a cohort study conducted to investigate antenatal depression and its association with the risk of adverse birth outcomes in two sections. The first section of this chapter addresses the prevalence and potential causal mechanisms of AND. The second section describes the association between antenatal depression and the risk of adverse birth outcomes. Chapter six summarises methods, results, discussion, and conclusions of further analysis of the cohort study, whereby the first section of the chapter presents results for prevalence and incidence of PND and its potential causal mechanisms, and the second section summarises the findings of additional analysis to assess the association between antenatal and postnatal depression and risk of adverse infant health outcomes. Chapter seven presents the findings from a qualitative study that explored barriers to and enablers of perinatal depression health services in Ethiopia.

In chapters eight and nine, there is a general discussion of the synthesised findings, conclusions, and implications of the thesis. Relevant documents such as ethics approval, questionnaires, supplementary materials for systematic reviews, and interview guides are attached as an annexe after the list of references.

Chapter Two: Literature review

2.1. Introduction

This literature review addresses the question of what is already known about the epidemiology and consequences of perinatal depression. The findings are thematically presented from the global to the local context, where the current study has been conducted. This chapter covers five sections. The first section provides background on depression during the perinatal period as well as diagnostic approaches to it. The second and third sections describe the burden and risk factors of antenatal and postnatal depression, respectively. Section four discusses the effects of AND on adverse birth outcomes. The final section summarises evidence about the effects of PND on malnutrition, breastfeeding, and infant illnesses. The contents of this chapter provide a background for chapter four of the thesis, where findings from systematic reviews and meta-analyses of studies are further synthesised and presented.

2.2. Depression and its diagnosis in the perinatal period

The experience of pregnancy and childbirth is conventionally described as a happy and joyful period. However, for many women the perinatal period may be experienced as a struggle because of a range of stressors including the associated extra responsibilities, pre-existing health conditions, and facing the new environment of pregnancy and childbirth. Depression is one of the most common health conditions that may manifest during pregnancy and may also continue through to, or emerge during, the postnatal period (132, 133). Depression levels are reported to double during puberty when estrogen and progesterone production start influencing brain function (134, 135). Epidemiological and clinical evidence suggest that depression following pregnancy and childbirth is identical with affective illnesses that occur at other times (136, 137). Depression during pregnancy and the postnatal period is collectively referred to as 'perinatal' depression (138). Perinatal depression typically differs from the emotional changes that are normally associated with pregnancy and the postnatal period. The timing of onset is an area of controversy; however, AND manifests within the first trimester of pregnancy, and PND manifests from the second week after birth up to 12 months afterwards (139-146).

Antenatal and postnatal depression are both generally diagnosed by using standardised interviews or self-report questionnaires (screening tools) (137). The DSM–V and ICD are the two most-known methods of diagnosing depression in clinical settings (147, 148). However, these instruments are perceived to be time-consuming, expensive and not always feasible for general clinical practice (137). For this reason, self-reported questionnaires were introduced for simple screening and identification of women with depressive symptoms in both the clinical and research arenas. Various self-reported scales are available for screening purposes; however, clinical decisions should only be based on diagnostic methods. The most commonly used screening tools are the Edinburgh Postnatal Depression Scale (EPDS) (149), Beck Depression Inventory (BDI) (150), Centre of Epidemiological Study of Depression (CES–D) (151), Hospital Anxiety and Depression Scale (HADS) (152), and Patient Health Questionnaire (PHQ–9) (153).

The EPDS is by far the most widely used instrument for population-based screening in high- (149, 154), middle- and low-income countries (155, 156). Its validity, exclusion of common somatic symptoms, simplicity of administration, high maternal acceptance, and accessibility in various languages make the EPDS preferred to other tools (157, 158). The ten items in the EPDS are scored on a four-point scale with a total score ranging between zero and 30. The cut-off value used to declare positive symptoms varies based on the socio-cultural context of the area. For example, depression is considered likely with a score of 12.5 or over in Australia (159), 7 or over in Lithuania (160, 161), 11 or over in Denmark (162), and 13 or over in Ethiopia (105, 106, 163, 164). These cut-off values are identified based on country-specific validity testing. Moreover, cut-off values also differ across the postnatal period (156). For example, the validated cut-off value during the postnatal period in urban areas of Ethiopia is reported to be 6 (164), while an unvalidated cut-off value of 12 has also been used (127, 165).

Variations in EPDS cut-off values are mainly due to cultural and socio-economic contexts (156). These differences can, therefore, affect the validity of the tool in certain contexts and can present challenges for comparisons across studies. Despite this, a cut-off value of greater than or equal to nine has been considered the most advantageous threshold to reduce false positive scores (137). The EPDS was used for this PhD study, taking its advantages into consideration, and based on the literature that used EPDS to determine the burden of

antenatal and postnatal depression as discussed in section 2.3. It is hoped that this helps to facilitate comparison of findings between the thesis and previous studies.

2.3. The burden of antenatal and postnatal depression

Globally, several studies have been conducted to determine the prevalence of antenatal and postnatal depression. A scoping review found a global prevalence of AND ranging from 15% to 65% (166). The pooled prevalence of AND was found to be higher in low- and middle-income countries (LMICs) (34%) (166) than in high-income countries (17%) (167). However, estimates vary significantly across countries because of measurement challenges (lack of use of validated tool) and socio-economic and cultural differences. For example, AND prevalence ranging from 13.2% to 21.9% (168-173) has been reported in European countries. The highest and lowest prevalences were reported in Italy (21.9%) (168) and Germany (13.2%) (174). AND prevalences ranging from 10.4% to 57% (24-34) and from 11.9% to 24.3% (175-180) have been reported in low- and high-income Asian countries. In Africa, reported AND prevalences range from 22.7% to 38.5% (35-38, 181), whilst in Ethiopia, reported AND prevalences range from 16.3% to 23.5% (39, 125, 182-186). The study setting is reported to be the main reason for variation in AND prevalence in Ethiopia (39, 125, 182, 183). For instance, community-based studies estimated AND prevalences of 19.9% (187) and 11.8% (165). However, cross-sectional studies from health institutions estimated AND prevalences of 24.9% (127), 21.5% (182), and 25.6% (188), all of which were higher than community-based studies. This probable related to low ANC coverage in health fascilities at the time the studies were conducted and selection bias.

Postnatal depression has been reported to be less frequent than AND. A systematic review found a pooled prevalence of PND to be 19.7% (75). The prevalence of PND has also been found to differ across region, type and time of measurement, study design, and the socio-economic context of a country. For instance, PND prevalences ranging from 7.7% to 31.4% were reported in cross-sectional studies (189-196), and prevalences ranging from 11.1% to 12% were reported in follow-up studies (197-199). Postnatal depression prevalence also varies according to the economic status of regions. For instance, PND prevalences ranging from 4.3% to 39.2% have been reported in Asian countries (200-227) and from 11.1% to 12% in high-income countries (197-199). Postnatal depression prevalences ranging from 9.2% to

50% have been reported in African countries (228-234). In Ethiopia, PND prevalences ranging from 15.6% to 33.8% have been reported (80-82, 235-240).

Most studies of antenatal and postnatal depression in Ethiopia were cross-sectional studies from health institutions. These studies were underpowered, used inconsistent screening tools for determining depression, and were very limited in number. The lack of quality evidence places restrictions on the ability to develop clear policy and implementation guidelines. Therefore, further studies using a validated screening tool with a sufficiently powered sample size in a community setting are required (122).

2.4. Risk factors associated with antenatal and postnatal depression

Biological and genetic studies have shown that causal explanations of mental illnesses are complex (8, 241). While genetic vulnerability or predisposition to depression may be more common in females, environmental factors play an even more important role (8, 242). Socio-demographic factors (such as age, income, maternal educational and occupational status, marital status); psychosocial factors (such as previous history of depression or anxiety, violence, lack of support, history of stressful life events); obstetric and newborn factors (such as parity, unintended pregnancy, comorbidities and complications); and maternal behavioural factors (such as tobacco smoking, drug abuse, and alcohol drinking) have all been reported to be associated with antenatal and postnatal depression.

An inconsistent association has been reported between age and antenatal or postnatal depression. Both younger (38, 81, 82, 98, 243-247) and older ages (57, 248-253) have been associated with a high risk of antenatal and postnatal depression. The risk of depression has been shown to increase in women or households with low incomes or food insufficiency (37, 188, 254-257). Depression prevalence was lower in pregnant women with higher levels of education (38, 193, 254, 258-261) relative to lower levels of education. In contrast, a study in India found educated pregnant women to be more depressed (26) than uneducated pregnant women. Pregnant (26, 57, 173, 255, 261) and postnatal women (191, 243, 262, 263) who were employed or self-employed were less depressed than those who had part-time employment or no employment. Maternal marital status has also been reported to affect the development of depression during the perinatal period. For example, depression prevalence was found to

be higher among pregnant (9, 29, 174, 188, 248, 250, 255) and postnatal women (80, 243, 264-266) who were unpartnered relative to those with partners.

The most frequently reported psychosocial risk factors associated with perinatal depression were a previous history of CMDs and intimate partner violence. For instance, the prevalence of AND (75, 125, 127, 165, 182, 183) and the incidence of PND (82, 218, 220, 225, 267, 268) were found to be higher among women with current or previous personal or family history of CMDs. Furthermore, women with signs of depression during pregnancy and the postnatal period were more likely to report intimate partner violence (IPV) (82, 188, 251, 252, 269-272), childhood physical and sexual abuse (273), and history of harassment (176, 274). Social support has also been strongly associated with the risk of depression during pregnancy and the postnatal period. For example, pregnant women who reported low levels of social support from their family, partners, and significant others were found to be more depressed (39, 125, 127, 182, 183, 188, 256, 274, 275) than those with strong support. Similarly, a high prevalence of PND was observed in women reporting low social (192, 218, 220, 270, 276) or partner support (228-230).

The prevalence of depression was higher among perinatal women who reported low satisfaction with marital and family relationships (33, 78, 80-82, 177, 183, 188, 228, 246, 277). A high prevalence of depression was also identified in perinatal women reporting a history of death or severe relationship problems with family members or relatives (36, 78, 183, 217, 218, 277, 278). Perinatal depression was more likely if there was a history of trauma (279). Postnatal women who were anxious about the delivery were more at risk of developing depression symptoms (248). Depression risk was increased among postnatal women who had a newborn with poor sleep quality (230, 280).

Parity is a commonly reported obstetric factor associated with depression, although the direction of the association has been inconsistent. For example, the odds of depression symptoms were found to be high among perinatal women who had multiple pregnancies or a large family (78, 98, 183, 245, 251, 277). In contrast, other studies documented that perinatal women who had experienced multiple pregnancies, births and children were less likely to have depression (57, 75, 281, 282). Parity was also found to be an effect modifier in the association between a history of premenstrual syndrome and PND (199). Unplanned pregnancy, on the other hand, has been consistently positively associated with perinatal

depression (80-82, 165, 246, 260). Associations have also been frequently reported between obstetric-related comorbidities and complications and AND and PND symptoms. Such symptoms were also more prevalent in pregnant women who reported daily use of medications for comorbidities such as gestational diabetes, anemia, hypertension, HIV, or tuberculosis (26, 38, 165, 188, 274). Antenatal depression has also been found to be associated with a history of cesarean deliveries, previous obstetric complications, miscarriages, and stillbirths (274, 275, 283, 284). Postnatal women with perceived poor health status who felt their conception was forced (e.g due solely to partner wishes), and those who had no or a suboptimal number of ANC visits during pregnancy were reported to be at higher risk of PND (78, 81, 98, 183, 245, 267, 277, 285). In Asia, mothers of female infants who had experienced perceived or actual pressure to give birth to a male child were found to be more likely to develop depression (33, 283, 286).

Breastfeeding status has also been linked to PND. For instance, postnatal women reporting difficulty in breastfeeding were more likely to be depressed (98, 226, 245, 276, 287, 288). Adverse birth and poor infant health outcomes were associated with a risk of PND. For example, postnatal women of infants with LBW, preterm births, and poor behavioural attachment (temperament) to the mother were at higher risk of having PND (192, 222, 245, 288). Further, infants in ill health and history of infant death were associated with higher odds of PND (81, 231, 266).

Lifestyle factors, such as smoking and alcohol consumption, were reported to be associated with antenatal and postnatal depression. Smoking exposure during the perinatal period has been reported to increase the risk of depression (248, 289, 290) and the number of cigarettes smoked per day has been positively correlated with increased depression scores (281, 286). It has also been reported that both primary and secondhand smoking interact with maternal age, increasing the risk of depression in pregnancy (29, 176). Drug or alcohol use has been identified as a risk factor for antenatal and postnatal depression. Antenatal (291) and postnatal women (80, 82) who reported drug use during the perinatal period were found to be at increased risk of depression. Perinatal women with previous experiences of alcohol consumption were found to be more depressed than non-drinkers (38, 281, 292). History of alcohol use was also associated with the risk of PND in Ethiopia (80, 82). Roomruangwong et al. (225) reported that postnatal women who consumed caffeine during pregnancy were at

increased risk of PND. Pregnant women with good nutritional status were less likely to develop depression relative to malnourished women (293). Furthermore, lower levels of depression were found in pregnant women reporting a high intake of yogurt, calcium (180), and vitamin D (294). Associations have been found between physical activity and maternal depression, with low AND prevalence reported in women who had undertaken routine physical activity during pregnancy (9, 32)**.** As a gap in the literature, previous studies did not clarify the potential causal mechanisms of antenatal and postnatal depression, which would be essential for prevention and control.

2.5. Association between AND and risk of adverse birth outcomes

Most published studies investigating the links between AND and adverse birth outcomes have been conducted in middle- and high-income countries. The majority of these studies investigated the association between AND and LBW and preterm birth, whilst few investigated stillbirth. Findings from these few studies suggested that there was no association between depression during pregnancy and stillbirth. For instance, Goedhart and Sion et al. reported a non-significant association between AND and stillbirth (295, 296). In Africa, no studies have been published on the association between AND and stillbirth. However, Hanlon et al. (54) found no association between CMDs, not specifically depression, and the risk of stillbirth.

The evidence for AND's effect on birth weight has been replicated yet opposing findings are also reported. For example, AND increased the risk of LBW in prospective cohort studies conducted in high- and middle-income countries (42, 248, 296-305), while other studies from the same countries using the same approach reported a lack of association (170, 306-310). Yang et al. (311) found that depression comorbid with anxiety was associated with LBW in preterm births but not in full-term births. A study conducted in Ghana and Cote D'Ivoire examined the impact of AND on LBW and did not find an association (312). A study in Ethiopia found that social support fully mediated the link between AND and LBW (55). Smoking during pregnancy, gestational age, pregnancy complications, low income, non-use of ANC services, low social support, low mid-upper arm circumference (MUAC), unwanted pregnancy, the gender of the foetus, and maternal age were all reported to be potential confounders for the association between AND and LBW (55, 248, 307, 312).

The third adverse birth outcome investigated by previous studies was preterm birth. A posetive link between AND and preterm birth has been found in several studies, yet there were also contrasting pieces of evidence. For example, eleven studies found in the US investigated the relationship between AND and preterm birth but reported conflicting findings. A higher number of preterm births was found among antenatally depressed women compared with non-depressed women in seven of the studies (42, 297-299, 313-315) while the other four studies reported no association (295, 306, 316, 317). The relationship between depression during pregnancy and preterm birth was investigated in six studies in Asia, and with one exception (309), AND was associated with preterm birth (296, 301, 310, 318, 319). In the only published African study on this issue, no association was found between antenatal depression and preterm birth (312). To date, there have been no studies that assessed the link between AND and preterm birth in Ethiopia. Elsewhere, maternal age, parity, maternal education, previous preterm delivery, maternal hypertension, alcohol and other drug use, comorbid anxiety, violence during pregnancy and maternal smoking (295, 311, 314, 315, 318, 320) were found to confound the link between AND and preterm birth. Stressful life events were also found to mediate the link between maternal depression and adverse birth outcomes (311, 318, 320).

The studies conducted to date had several limitations that might affect the validity of the findings. For example, many of these studies had the potential for residual confounding or recall bias, and/or had small sample sizes. Further, some were primarily descriptive and/or used unvalidated tools for screening AND. More importantly, no studies assessed the link between depression during pregnancy and adverse birth outcomes in Ethiopia, the need for which formed a main driver for the current study.

2.6. Perinatal depression and its effect on adverse infant health outcomes

Women are the main constituent of an infant's social environment and mediate their experience of the external world. Therefore, it is imperative to examine the effects of perinatal depression on the risk of adverse infant health outcomes. A small number of studies have suggested that perinatal depression has a moderate impact on the risk of adverse infant health outcomes.

Infant malnutrition is one adverse infant health outcome that may be significantly influenced by perinatal depression. The limited evidence available indicates a clear relationship between perinatal depression and the risk of infant malnutrition. For example, depressive symptoms were strongly associated with higher odds of nutrition-related short stature in normal birth weight infants in Brazil (321). Furthermore, according to a secondary data analysis from India, a greater number of infants below optimal size was observed among women who were depressed during the postnatal period (322) than among non-depressed women. Similarly, studies conducted in Nigeria (323) and Zambia (324) reported that infants of depressed women had poorer growth and lower height and weight compared with infants of non-depressed women. Moreover, higher odds for underweight and stunted infants were found in postnatally depressed women in Kenya (92, 325) and Ghana (326). In contrast, CMDs identified in perinatal women were not associated with the risk of infant malnutrition in two Ethiopian studies (104, 105).

Other adverse infant health outcomes reported to have links with perinatal depression are breastfeeding difficulties, diarrhea, and acute respiratory illnesses. A small number of studies found a positive correlation between perinatal depression and risk of these infant illnesses. For example, infants of postnatally depressed women were at higher risk of diarrheal disease in Bangladesh (327) and repeated episodes of diarrhea in Nigeria (323). Two further studies from Ghana and Cote d'Ivoire reported that infants of antenatally or postnatally depressed women were more likely to have febrile illnesses (328, 329).

In Ethiopia, four studies investigated the association between CMDs and the risk of adverse infant health outcomes. A study from the demographic and health surveillance site in Ethiopia reported an increased risk of diarrheal disease among infants of women with persistent CMDs (163). Another study found a significant association between maternal CMDs and childhood illnesses in children aged zero to five years (104). In contrast, a lack of association between CMDs in women and infant nutritional status (105) and common infant illnesses (163) was also reported. However, there have been no Ethiopian studies prospectively investigating the effect of perinatal depression on risk of adverse infant health outcomes. A recent cross-sectional study reported PND as a risk factor for stunting in infants aged from 5 to 10 months (237). Studies conducted elsewhere that linked perinatal depression and adverse infant health outcomes reported the following potential confounders: maternal education,

occupation, income, unwanted pregnancy, information about the benefits of breastfeeding, IPV, partner and social support, LBW, newborn age, and vaccination (102, 322, 324, 330-332).

The majority of studies reviewed above had small sample sizes, which can affect the precision and control of potential confounders (330, 333, 334). Furthermore, previous studies used cross-sectional study designs, which makes it hard to investigate temporality (334) or to draw conclusive evidence. There was also the potential for measurement bias because non-validated instruments were frequently used to screen for depression (287). In acknowledging the above limitations, several studies highlighted the need for robust investigations in large sample sizes and using follow-up studies (92, 323, 324). In Ethiopia, no studies have investigated the link between perinatal depression and risk of adverse infant health outcomes. Importantly, none of the identified Ethiopian studies examined the potential causal mechanisms underlying the relationship between AND and adverse infant health outcomes. For this reason, in this thesis a statistical causal model was applied to examine the association between perinatal depression and risk of adverse infant health outcomes.

Chapter Three: Study methodology

3.1. Introduction

This chapter describes the theoretical framework underpinning the study, the methodological approaches, and methods that were used in systematic reviews, quantitative and qualitative studies. The chapter is presented in seven sections. The first section begins by describing the theoretical frameworks underpinning the quantitative and qualitative studies. Section two presents the study setting and section three presents the methodology and its philosophical foundation. The fourth, fifth and six sections present the methods used for the systematic reviews, quantitative and the qualitative studies, respectively. The method content for the systematic reviews include description of the search strategies, inclusion and exclusion criteria, quality assessment, and method of analysis. The method content for the quantitative and qualitative studies include study design, population, sample size, sampling technique, participant recruitment, study variables, data collection and management. The final section presents the ethical issues associated with the studies and ethical approvals granted.

3.2. Theoretical framework

The use of theories and models is of paramount importance in designing and guiding analyses and interpretation of study findings (335). In this project, the stress process model (131) and the multilevel conceptual model (336) were used as conceptual and theoretical frameworks for the quantitative and the qualitative studies, respectively. The stress process model consists of three conceptual domains: stressors, mediators, and stress outcomes. The source of stress (stressor) domain accounts for acute or chronic life events or strains that can lead to stress outcomes. The mediator domain accounts for any factors that can mediate the link between the stressors and stress outcomes; these could be social support or personal coping levels. The stress outcome accounts for any type of manifestation of the stress, such as various mental disorders, which is depression in the case of this study. The stress process model has been tested for depression in pregnant (337) and postnatal (338) populations in China and demonstrated a good predictive value.

The stress process model has not yet been tested in Ethiopian perinatal populations. The model was selected to guide the analysis and interpretation of the quantitative findings in this thesis because of its high predictive ability in accounting for multiple potential predictors

and mediator variables. The model also helped to establish potential causal mechanisms of antenatal and postnatal depression based on previously developed theoretical models. A theoretical stress process model was developed for antenatal and postnatal depression. With AND as an outcome, stressors considered included sociodemographic characteristics, obstetric factors, psychosocial factors and maternal behaviour. The model also accounted for mediator factors such as social support, partner support, and maternal coping ability. For PND as an outcome, stressors considered included sociodemographic factors, obstetric and psychosocial factors before delivery. The PND model also accounted for mediator factors such as mode of delivery, labour complications, PNC services, birth outcomes, and breastfeeding status.

In this thesis, the model was employed to guide the analysis of the etiology of antenatal and postnatal depression. Additionally, the model was adapted and used to explain the effect of antenatal and postnatal depression on adverse birth and infant health outcomes. (Figure 3.1)

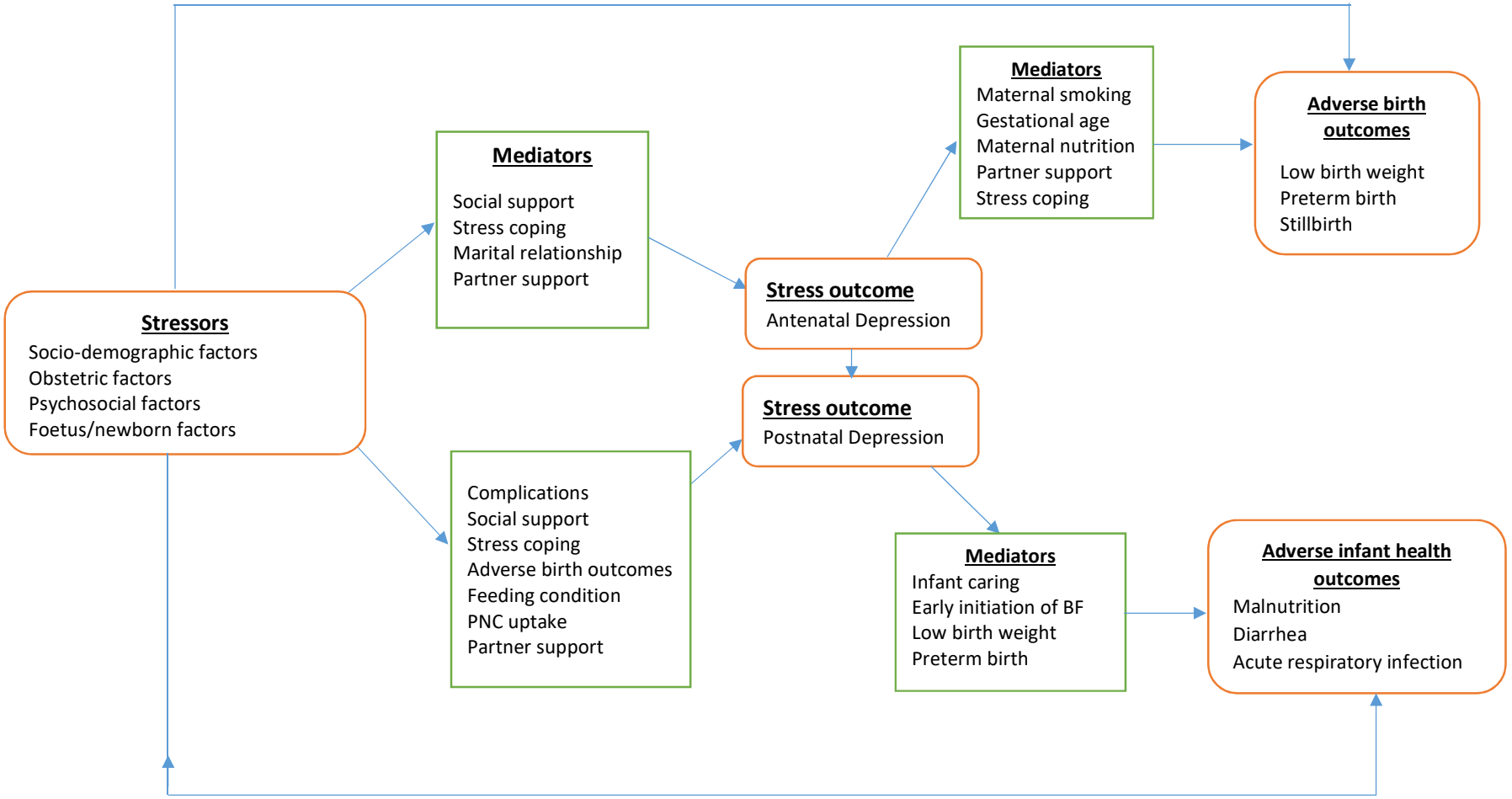


Figure 3.1: Theoretical framework for explaining AND, PND, and adverse birth and infant health outcomes, adapted from stress process model of Pearlin et al (131).

A multilevel conceptual model (MCM) was used to guide the analysis and interpretation of the qualitative study that examined barriers to and enablers for accessing mental health services for perinatal women in Ethiopia (336). The model was selected because of its suitability for exploring the barriers to perinatal depression services in Ethiopia, in preference to other models such as the socio-ecological model (339) or access to health service framework (340). The MCM model was adapted by combining a framework for change by Ferlie et al.(341), health delivery system (342), and a model presented by Smith et al. in a systematic review and meta-analysis of barriers to accessing mental health services for perinatal women (336) in the United Kingdom (UK).

The MCM posits that mental health service delivery and uptake could be affected by individual, organisational, socio-cultural, and structural level barriers. Individual level barriers include women's, health professionals' and administrators' perceptions about perinatal depression, and attitudes and health behaviours of women. Socio-cultural level barriers include language and cultural values of the community. Organisational level barriers include the capacity and readiness of health facilities or organisations to provide maternal mental health services. These include availability of resources (trained workforce, money, time, space), clarity in role and responsibilities, working manuals, screening tools, treatment guidelines, and protocols. Structural level barriers include lack of policies, programs and strategies, clear pathways, systems and structures, and low attention and initiation by the government. Figure 3.2 highlights the multilevel conceptual framework of barriers hindering maternal perinatal mental health services.

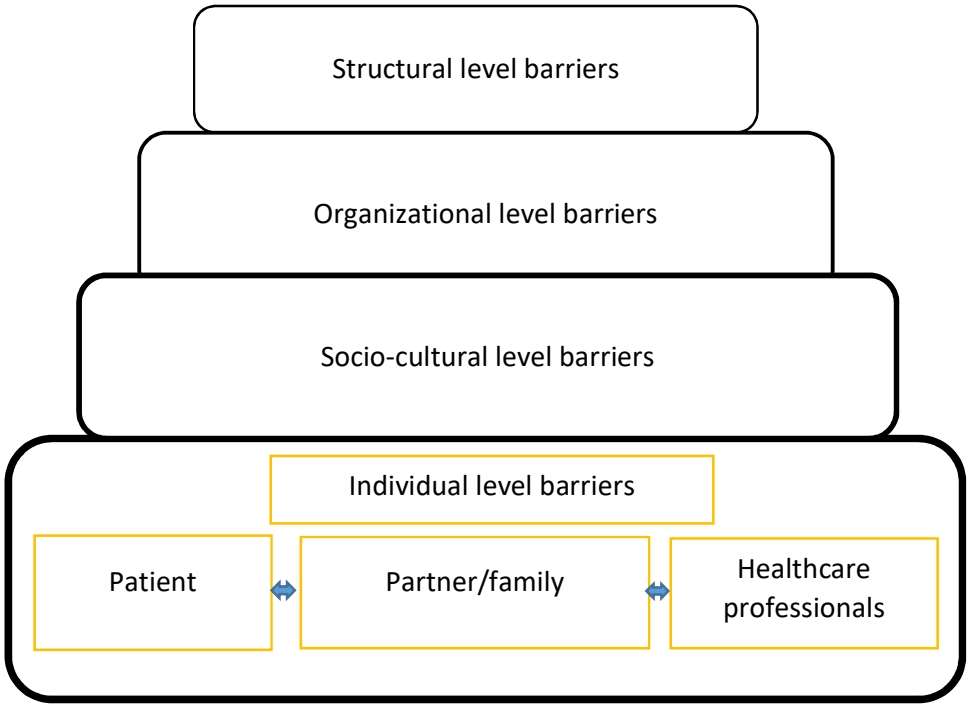


Figure 3.2: Model depicting a multilevel conceptual framework for factors that may hinder services during perinatal period, adapted from MCM (336).

3.3. Study setting

The study was conducted in Gondar town, which is one of the administrative zones of Amhara Regional State, northwest Ethiopia. Ethiopia is the second most populous country in the African continent, with a total population of more than 110,000,000 and a yearly population growth rate of around 2.6% (343). Ethiopia is in the eastern part (Horn) of Africa and is administratively subdivided into ten regional states (kilil) and two administrative cities. Amhara Regional State is the second most populous region located in the northwest part of the country (344). The State is geographically subdivided into 11 administrative zones, one of which is the Gondar Town Administration. Gondar town is in the northern part of Amhara region, being 747 km away from Addis Ababa (Ethiopian capital city) and 170 km from Bahirdar (Amhara region capital city). Gondar town has 12 sub-cities comprised of 12 urban and 10 rural kebeles (the smallest administrative units in the country). At the time data collection commenced, 2017–2018, the town had a total population of 333,103 (343, 345). The expected number of pregnant women in the town was estimated to be 11,225 during the study period, of whom at least 8,913 were living in urban kebeles (Figure 3.3).

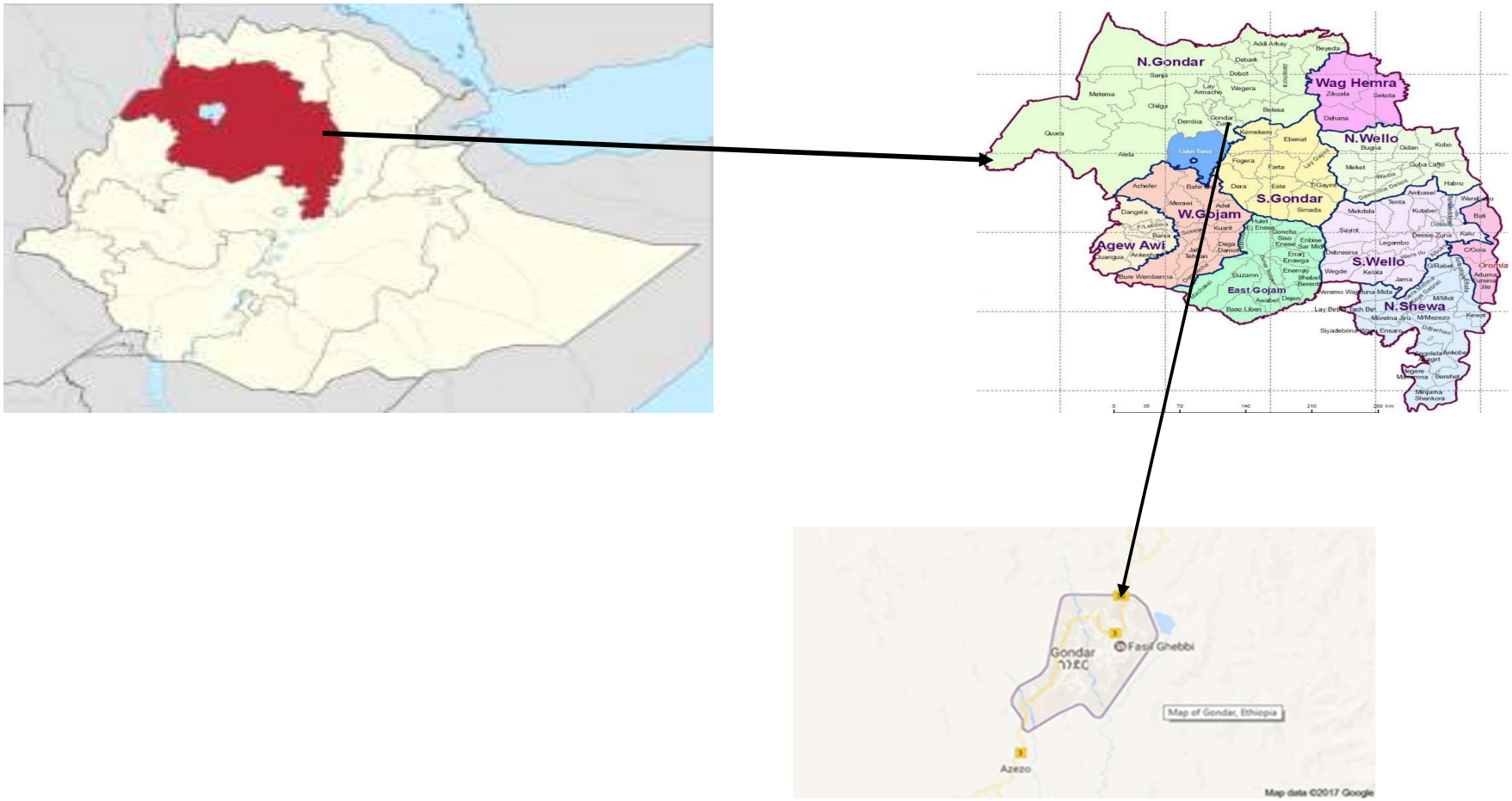


Figure 3.3: Map of Amhara regional state and Gondar town as geographically located in Ethiopia (source, open access (public domain) (344).

3.3.1. The Ethiopian healthcare tier system

Ethiopia is currently facing a challenge from the double burden of communicable and non-communicable diseases (14). To respond to these health challenges, the Ethiopian healthcare delivery system has been structured into three tiers (346). The first tier is the district (woreda) health system that encompasses primary hospitals, health centres and health posts, which form primary health care units that service populations of up to 100,000. The first tier is organised to provide preventive, promotive and essential curative health services. The second and third tiers include general hospitals servicing 1–1.5 million people, and specialised hospitals that service approximately 3.5–5 million people. The second and third tiers of the system are mainly aimed at delivering essential advanced curative health services. Gondar town has one government-operated specialised hospital, more than eight health centres, and 15 private medical clinics (347). However, Gondar University Specialised Hospital is the only facility with a psychiatry clinic that provides mental health services for Gondar town and the catchment area populations. (Figure 3.4)

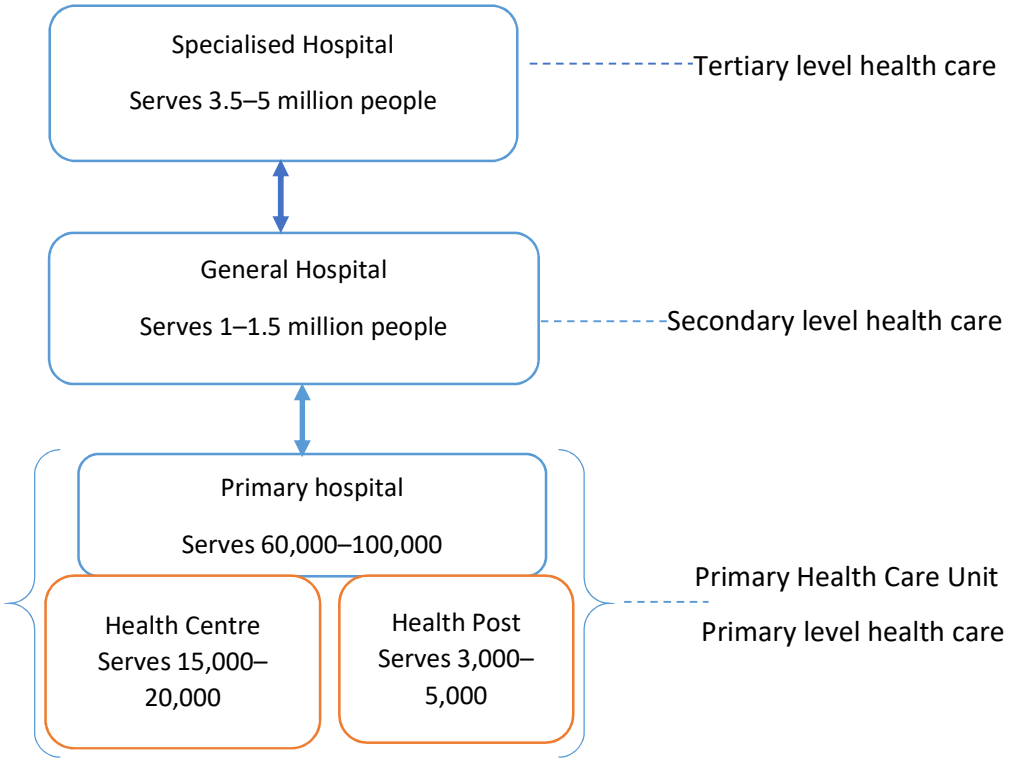


Figure 3.4: Ethiopian healthcare tier system

3.4. Methodological philosophies underpinning the thesis

A methodology is a framework for analysing assumptions (mainly ontological and epistemological), principles, and procedures related to a certain research question (348). The methodology involves two issues, namely the methods (mechanisms or tools applied in answering research questions) and philosophical assumptions (how the research question is conceptualised). Depending on the nature of a research question and its ontological and epistemological perspectives, two research paradigms can be employed, namely quantitative and qualitative (349, 350). Quantitative research draws on the positivist belief that there is only one reality, which can be identified and quantified with an appropriate epistemological approach. Qualitative research is based on constructivist or interpretivist beliefs that there is no single reality; rather the researcher invokes participants' views about reality, believing that environmental and individual differences influence this reality (349, 350).

This PhD study aimed to answer two broad research questions where both qualitative and quantitative research paradigms were used. As such, a mixed methods or pragmatic approach was applied, which helps to fill the gap in methods between the qualitative (interpretive) and quantitative (positivism) paradigms (351). Mixed method designs allow integration of both approaches to answer research questions in a single study (352). In this study, quantitative and qualitative data were collected simultaneously, and information generated from both studies was blended in the interpretation of the findings. The thesis applied the embedded mixed methods approach where qualitative research findings were used to support quantitative findings (352, 353).

3.5. Methods

3.5.1. Methods for the systematic reviews and meta-analysis studies

Three systematic reviews were conducted and published as part of a literature review (discussed in chapter two) to gain a comprehensive understanding of the extent and consequences of perinatal depression and to identify gaps in knowledge. The first systematic review was an umbrella review, aimed at quantifying the global burden and association of AND with adverse birth outcomes by including systematic reviews published in the area. The second and third systematic reviews aimed to quantify the burden and consequences of

antenatal and postnatal depression on adverse birth and infant health outcomes in LMICs, respectively. Detailed methods used in the reviews are presented below.

3.5.1.1. Systematic search strategy

A systematic search of peer-reviewed systematic reviews (for the first review) and primary articles (for the second and third reviews) was conducted in the following seven databases: CINAHL (EBSCO), MEDLINE (via Ovid), PsycINFO, Emcare, PubMed, Psychiatry Online, and Scopus. A range of keywords and database subject headings was used to identify the following key concepts separately and in combination using Boolean and proximity operators and wildcards: (i) depression symptoms during the antenatal period; (ii) AND risk factors; (iii) association of antenatal depression and adverse birth outcomes (mainly LBW, preterm and, stillbirth); (iv) PND symptoms; (v) perinatal depression symptoms; (vi) PND risk factors; (vii) association of PND with adverse infant health outcomes (mainly diarrhea, malnutrition, early cessation of exclusive breastfeeding, malaria, ARI); (viii) association of perinatal depression with adverse infant health outcomes; and (viiii) systematic reviews, observational studies (case-control, cohort, cross-sectional, longitudinal studies). An example of a search strategy for each review is presented as follows:

Below is an example of the full electronic search strategy employed for the umbrella review (systematic review of reviews on antenatal depression and its association with adverse birth outcomes) in PsycINFO via Ovid:

> (((antenatal depression.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]) OR (depression during pregnancy.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]))) AND (((systematic review.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]) OR (meta-analysis.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures] OR (review.mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]))) Sort by: PublicationDate Filters:Publication date from 2007/01/01 to 2017/12/31; Humans; English;MEDLINE; Field: Title/Abstract

Below is an example of the full electronic search strategy for the second review (AND and its association with risk of adverse birth outcomes in LMICs) in the PubMed database.

> Search ((((((Pregnant mothers*) OR (antenatal mothers*) OR (pregnant women*) OR (antenatal period*) OR pregnancy* OR (antepartum women*)) AND ((depression* OR (clinical depression*) OR (depressed

mood*) OR(major depressive disorder*) OR (depressive symptom*) OR (psychological morbidity*) OR (major depression*) OR (unipolar depression*)) AND((exposure* OR (risk factor*) OR correlates* OR (associated factors*) OR predictors*) AND (((cross sectional*) OR (cross sectional*) OR survey* OR(case control*) OR (nested case control*)) Sort by: Publication Date Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; MEDLINE; Field: Title/Abstract

Finally, below is an example of the full electronic search strategy for the third review (PND and its association with adverse infant health outcomes in LMICs) in the MEDLINE database:

(exp POSTPARTUM DEPRESSION/) or (Depress*.tw,id.) AND (postnat* or postnatal wom?n or postpartum wom?n).tw,id.) AND (exp Infant Development/ or exp Morbidity/ or exp Neonatal Development/ or exp Neonatal Disorders/) or ((Common post neonatal illness or neonatal illnes* or malaria or pneumonia or fever or diarrhea or measles).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]) AND ((exp Psychosocial Factors/ or exp Risk Factors/) or (risk*.tw,id.)) AND ((prospective cohort* or retrospective cohort* follow up* or longitudinal* or cross sectional* or case control* or nested-case control).mp.): all Sort by: Publication Date Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female; Field: Title/Abstract

3.5.1.2. Eligibility criteria

For the umbrella review, systematic reviews were included if they: (i) were published as a systematic review/meta-analysis in their title; (ii) stated that antenatal depression and its association with adverse birth outcomes were their primary objective; (iii) systematically searched for primary studies in at least two medical literature databases; (iv) included at least one primary study that aimed to investigate AND and/or its association with birth outcomes; (v) assessed the quality of the included primary studies and considered study quality in the analysis and interpretations; (vi) addressed and reported the methodology, model, publication bias, and heterogeneity issues of any meta-analyses of primary reviews when included; and (vii) were written in English and published between January 1st, 2007 and August 31st, 2018, to have a recent data about the problem.

The second and third reviews included observational studies conducted in LMICs that were written in English and published between January 1st, 2007 and December 31st, 2017. Furthermore, studies were included if they used the following main outcome definitions: (i)

depression during pregnancy and the postnatal period was measured using validated screening or diagnostic tools; (ii) birth weight was measured objectively and LBW was classified as a weight less than 2500grams; (iii) gestational age was measured using Last Menstrual Cycle and/or supported by an ultrasound, and preterm birth was defined as a birth before 37 completed weeks of gestation; (iv) stillbirth was defined as foetal death after 20 completed weeks of gestation and weighing at least 500 grams, or intrauterine death of the foetus prior to the onset of labor, or intrauterine death of the foetus during labor and delivery; (v) malnutrition was measured and reported using standard indices such as wasting, stunting, short stature, or underweight/overweight; (vi) age-related infant feeding practice was reported as exclusive breastfeeding or complementary feeding; and (vii) common infant illnesses such as ARI, malaria, and diarrhea were assessed following the WHO Integrated Management of Newborn and Childhood Illnesses (IMNCI) guideline. Reviews and primary studies conducted in selective populations (obese, overweight, diabetes, mothers with bad obstetric history, unintended pregnancy, primiparous mothers) and articles for which the full text was not available were excluded.

3.5.1.3. Quality assessment of included studies

For the umbrella review, reviews fulfilling the inclusion criteria were assessed for quality using the Assessment of Multiple Systematic Reviews (AMSTAR) (354) checklist scores. AMSTAR contains 11 indicators used to quantify the quality of reviews to be included. Reviews are graded as high quality (score >=8), medium quality (score 4–7), or low quality (score <=3). Risk of bias for the second and third reviews was assessed using the Newcastle–Ottawa Scale (NOS) (355, 356) for observational studies. This includes three categorical criteria with a maximum score of nine points: “selection” with a maximum of four points, “comparability” with a maximum of two points, and “outcome” with a maximum of three points. The quality of each study was rated using the following scoring algorithms: ≥7 points was graded as “good” quality, 2 to 6 points was considered “fair” quality, and ≤ 1 point was considered as “poor” quality. Only studies of good quality (NOS score ≥7 points) were included in these systematic reviews and meta-analyses to generate good quality evidence. Two reviewers independently assessed the quality of each review or primary study, and disagreement between the reviewers was resolved through discussion.

3.5.1.4. Data extraction

A data extraction form was prepared and used in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (357) guideline. The following data were extracted from included studies and summarised in tables: names of authors, year of publication, names of countries in which the study was conducted, country income category using the World bank criteria, study design, sample size, type of screening tool used to identify depression and its cut-off value, and estimates presented (prevalence and odds or risk ratios). The following data were also extracted from included systematic reviews: geographic coverage of the review, databases searched, number of primary studies included, and where meta-analysis had been conducted the pooled number of participants (N), main findings, and AMSTAR score.

3.5.1.5. Risk of bias and adjustment

Cochran Q (I^2), visual inspection of forest plot (358) and Higgins test (359) were used to assess the presence of heterogeneity. DerSimonian and Laird's random-effect model was used to pool odds ratio or relative risk estimates in a subgroup analysis in the presence of heterogeneity (360). Sub-group analyses were used to investigate differences between and within groups in a pooled analysis. Sub-analysis was commonly based on primary study features such as study setting and design, tools used for screening depression, sample size and income of the country. Visual inspection for asymmetry of funnel plots and Egger's regression test were used to check for potential publication bias (361, 362). The L estimator of Duval and Tweedie was used to find and fill missing studies through the procedure called trim-and-fill analysis (363). Meta-analysis was conducted after log-transforming odds ratios and relative risks obtained from the primary studies. Sensitivity analysis was also conducted to test for the presence of outlier estimates.

3.5.1.6. Data analysis and reporting

For the umbrella review, data synthesis was undertaken independently for each outcome of interest. Vote counting and a narrative review were used to summarise and present the global prevalence of antenatal depression and associated factors. Statistical pooling (meta-analysis) was conducted for quantifying the association of AND with LBW and preterm birth. For the

systematic reviews, antenatal and postnatal depression prevalence estimates, odds ratios of associated factors, and relative risks of adverse birth and infant health outcomes were meta-analysed, and their main findings were summarised using tables. For studies that lacked adjusted estimates, crude estimates were extracted. Where primary studies reported estimates for more than one outcome, an independent estimate for each outcome was included in the analysis. The PRISMA (364) statement for reporting systematic reviews and meta-analysis was used to present the study inclusion, exclusion and reasons for exclusion information in a diagram. The STROBE guideline was followed for reporting the findings from the systematic reviews and meta-analyses (357).

3.5.1.7. Protocol registration

All reviews were registered in PROSPERO with protocol numbers CRD42018116267 and CRD42017082624 for the scoping review and systematic reviews, respectively.

3.5.2. Methods for the quantitative study

3.5.2.1. Study design and period

A mother–child closed cohort study was established to register and follow a cohort of pregnant women in selected urban kebeles of Gondar town. Follow-up was conducted from the second or third trimester of pregnancy to six months after delivery. The sample frame included all pregnant women who planned to reside in Gondar town for the study period. Firstly, a community-based cross-sectional study design was employed to determine the prevalence and causal mechanisms of AND (**objective I**). This study further helped to identify pregnant women with symptoms of depression (exposed) and those without symptoms of depression (non-exposed). Secondly, the identified pregnant women with and without AND were prospectively followed until delivery to determine the risk of AND on adverse birth outcomes (LBW, preterm and stillbirth) (**objective II**). Postnatal women were re-screened for PND three to six weeks following delivery to assess the incidence and prevalence of PND and its causal mechanisms (**Objective III**). Finally, mother–infant dyads were followed to six months postpartum to estimate causal associations between antenatal and postnatal depression, and risk of adverse infant health outcomes (malnutrition, diarrhea, and acute respiratory infection) (**Objective IV**). At this phase, the main exposure variables were both antenatal and postnatal depression. (Figure 3.4)

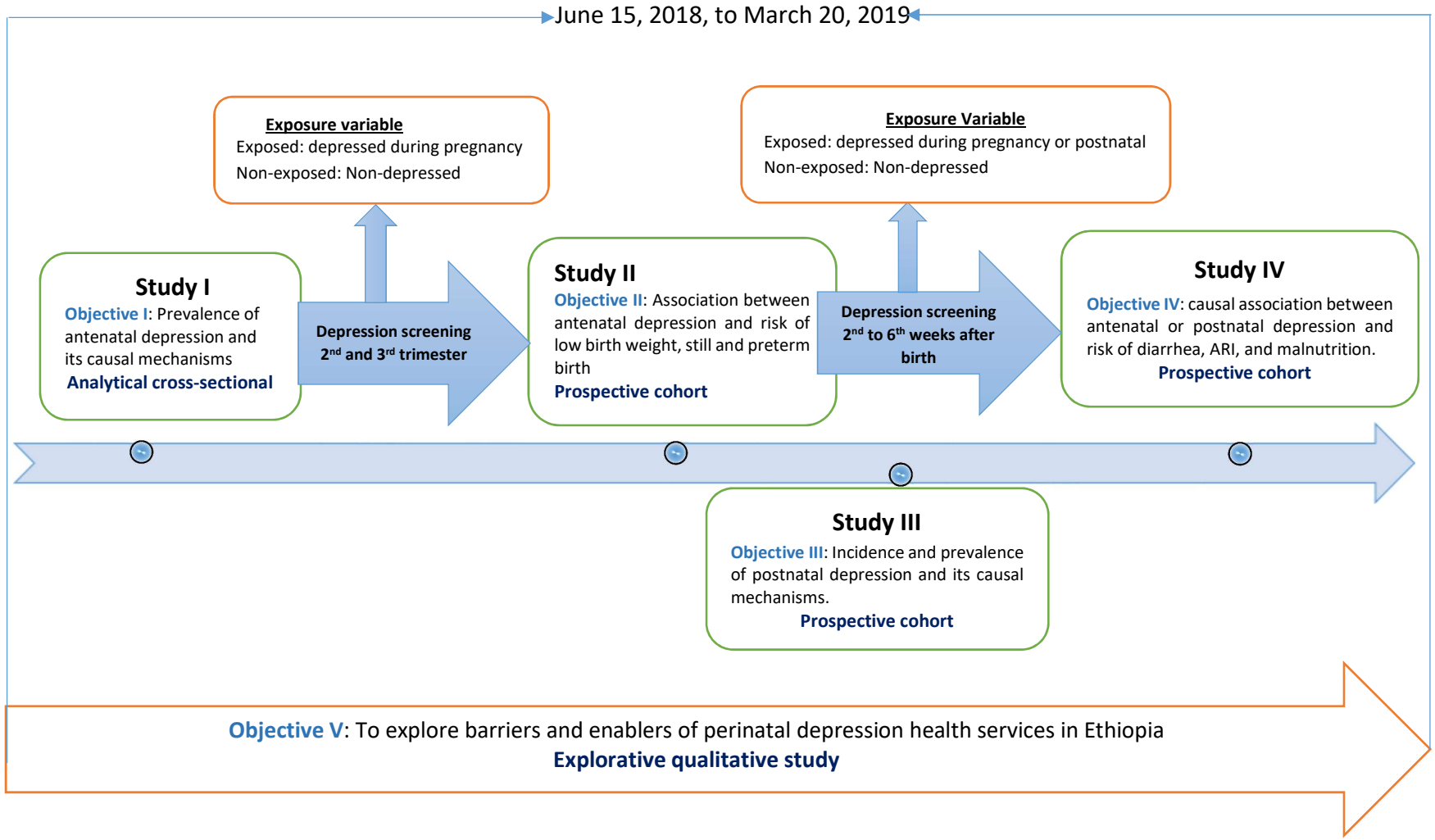


Figure 3.5: Schematic presentation showing the flow of quantitative and qualitative studies in Gondar town, Northwest Ethiopia.

3.5.2.2. Study population, sample size, and recruitment

The study population included all pregnant women aged 18 years and over in their second or third trimester, living in urban kebeles of Gondar town, and who did not intend to leave the town during the follow-up period. Study participants who declined participation in the study or were unable to give consent, those suspected of having severe depression, and thought of suicide were excluded from the study. The sample size required for each objective was determined and the largest of these was considered the final sample size for the thesis. There were four research objectives (described in chapter one). Sample size estimation mostly accounted for the type of research objectives and applied study designs. Epi Info 7 was used to calculate the required sample size (365). Single and double population proportion formulas were used to determine the required sample size for the cross-sectional and cohort studies, respectively. A 90% power and 95% level of confidence were chosen to generate a large sample size and to improve the precision of the study. From the determined sample sizes, the largest was 809. (Table 3.1) After adding a further 20% to account for expected losses to follow up, the final sample size obtained was 970. This sample size was larger than the estimated sample size for the remaining objectives and therefore it was believed that this was adequate to achieve good power and precision. However, because of the cluster sampling, 960 pregnant women were found and included in the cohort. The sample size considered at every stage of the cohort is displayed in figure 3.6.

The process to access and recruit study participants was as follows:

1. A letter of support for the Gondar Town Health Department was obtained from the University of Gondar, Research and Community Service Vice-President's office.
2. A letter of permission from the Gondar Town Health Department was sent to randomly selected kebele administrations.
3. Potential study participants were contacted face-to-face in their homes by data collectors through providing them a letter of introduction (Annex 2.1) and information sheet (Annex 2.2) to request if they were willing to participate in the study.

Table 3.1: Sample size determination methods for each study objective in Gondar town, Northwest Ethiopia, 2018.

Objectives	Confidence level	Power	The ratio of Unexposed: Exposed	% outcome in the unexposed group	RR/OR	Estimated final sample size
Objective I	95%		P=11.8% (165), (1–p)= 88.2%, Z=1.96, d=4%			249.8=250
Objective II	95%	90%	Depressed (1): not depressed (4):	15.8% (prevalence of low birth weight among non-depressed group (55)	1.89	120:479=599
Objective III	To get a sample size that could detect an OR of 2.0 with 90% power using a two-sided 5% test and prevalence of AND (primary exposure variable for PND outcome) of 11.8% (165), a formula was used (366).					354
Objective IV	95%	90%	depressed (1): not depressed (2):	22% (prevalence of underweight among those free from CMDs) (367)	To detect a difference of 1.5	270:539=809

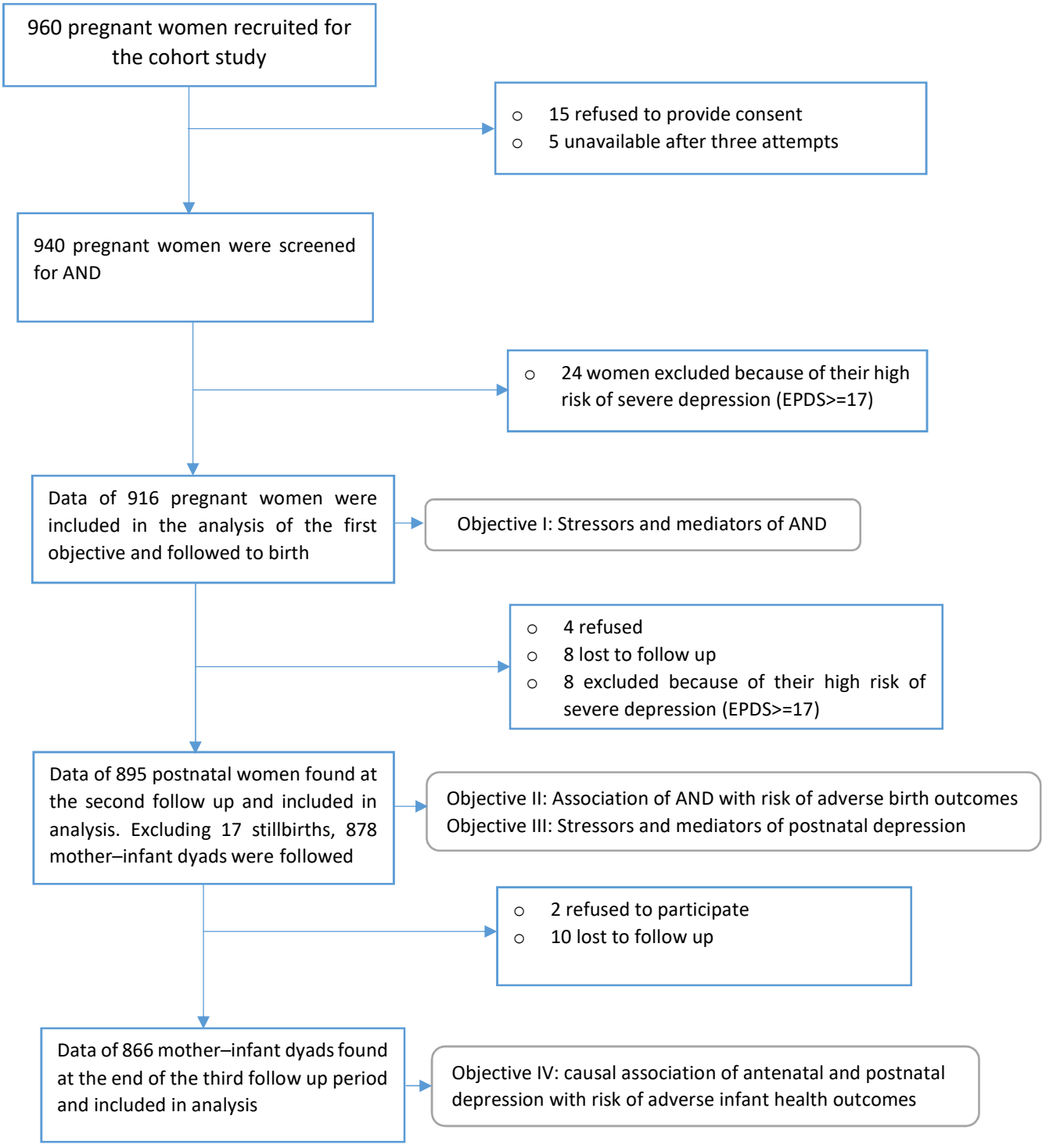


Figure 3.6: Flow chart showing a number of study participants included and excluded at each stage of the cohort in Gondar town, Northwest Ethiopia, 2018.

3.5.2.3. Sampling technique and procedures

Cluster random sampling was used to select the study participants. A cluster of six urban kebeles was randomly selected from twelve using a lottery method, and all pregnant women in their second or third trimester were included in the cohort and contacted through house to house visit. Finally, contact was made with 960 pregnant women who fulfilled the inclusion criteria. Figure 3.7 illustrates the number of study participants found and contacted in each kebele.

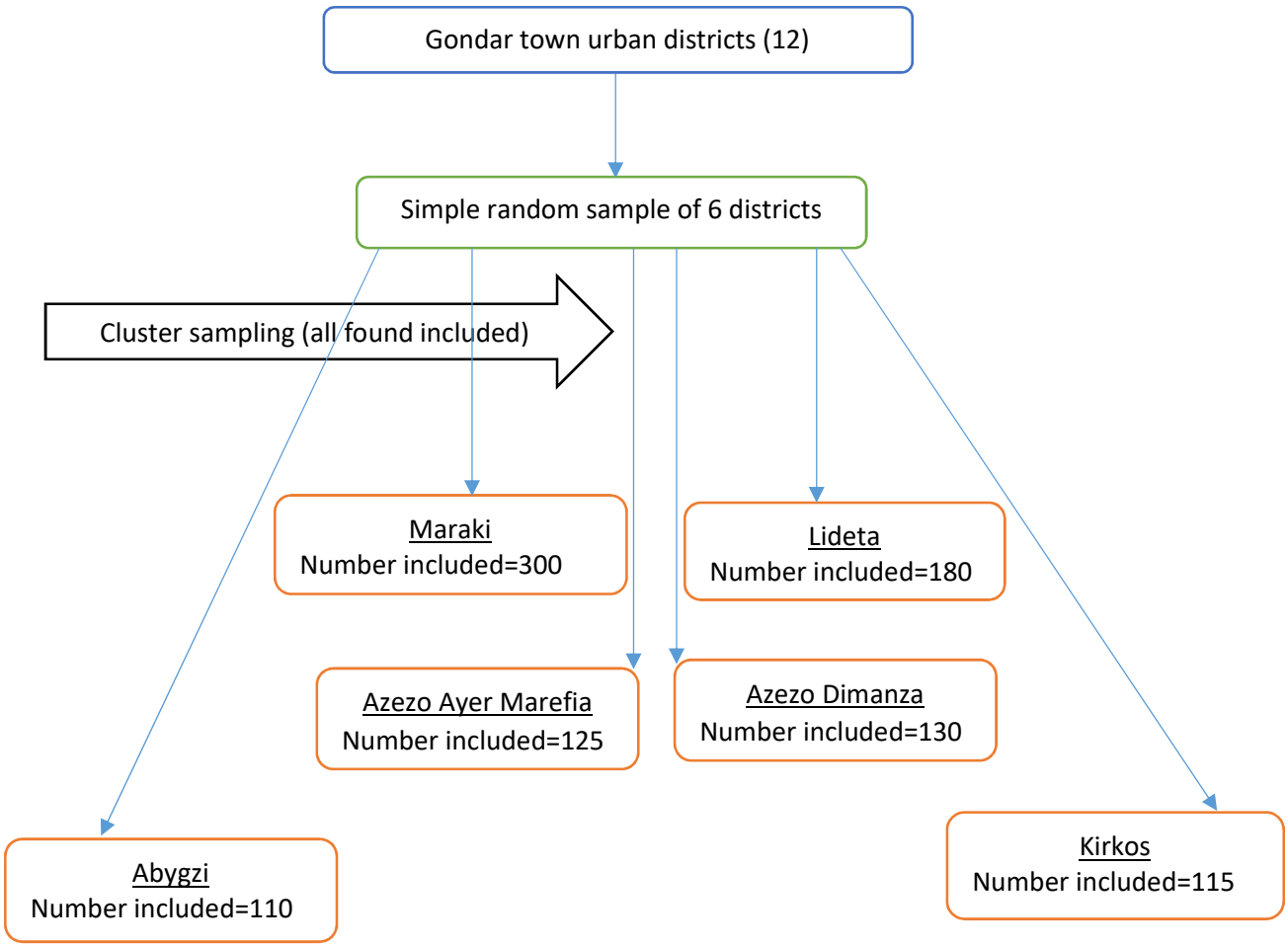


Figure 3.7: Number of study participants included from six randomly selected urban kebeles, Gondar town, Northwest Ethiopia, 2018.

3.5.2.4. Study variables and operational definitions

This thesis addressed four quantitative research objectives. Each objective aimed to measure specific health outcomes and related covariables that were hypothesised to be confounders or mediators. Below, the outcome variables and their hypothesised predictors are presented. (Table 3.2)

Table 3.2: An overview of outcomes and independent variables included in the study of perinatal depression, Gondar town, Northwest Ethiopia, 2018.

Category	**Outcome variables**	
Objective I	Antenatal depression	
Objective II	Stillbirth, LBW, preterm birth	
Objective III	Postnatal depression	
Objective IV	Diarrhea, malnutrition, acute respiratory infection	
Independent (covariate) variables		
Socio-demographic factors	Age of the mother Age of the infant Income of household Religion of the mother	Educational status of the mother Marital status of the mother Occupational status of the mother
Maternal related factors	Parity Type of pregnancy/twin or single/ Pregnancy and birth complications Nutritional status	History of miscarriage History of stillbirth History of infertility
Psychosocial related factors	Fear of giving birth History of CMDs Partner support	Social support Marital relationship Stress coping ability

Women behavioural factors	Tobacco smoking Coffee consumption	Physical activity

Depression: Antenatal and postnatal depression were measured by the EPDS screening tool developed by Cox (149) and revised for use in the Ethiopian context (368). The EPDS is a brief screening tool that contains 10 questions with four Likert scale response options (most of the time, sometimes, not often, never). It is simple and free to use, can be scored by simple addition, and has been validated for measuring postnatal CMDs in urban settings of Ethiopia with a sensitivity and specificity of 84.7% and 77.0%, respectively (164). Globally, the EPDS is the most commonly used depression screening tool in both antenatal (156, 369-372) and postnatal populations (373-375). The tool is intended to measure the experiences of the mother over the previous week. The cut-off value to be used is different for antenatal and postnatal depression but is expected to be higher for pregnancy than the postnatal period (376). A cut-off value of 12/13 has been used for a pregnant population (127, 165), and a cut-off value of 6/7 has been validated for measuring PND (164) in urban settings in Ethiopia.

Adverse birth outcomes: This represented preterm birth, LBW, or stillbirth. The child's gestational age at delivery, birth weight, and birth condition were registered throughout the follow up by participant self-reports confirmed through medical records. LBW was classified as a birth weight of less than 2500grams (377). Preterm birth was considered as a birth occurring before 37 complete weeks of gestation (377). ANC registration was used to get the data of LMP or Ultrasounds for probable time of gestational time. Stillbirth was the death of the foetus after 20 completed weeks of gestation and weighing at least 500grams, or intrauterine death of the foetus before the onset of labour, or intrauterine death of the foetus during labour and delivery (378). The data collectors were nurses and they were able to differentiate between preterm and stillbirth.

Adverse infant health outcomes: This represented ARI, diarrhea, and malnutrition. Malnutrition was assessed using the measurement of Middle-Upper Arm Circumference (MUAC), which is recommended for use when screening for severe acute malnutrition in infants aged under six

months and was defined as a MUAC <110mm (379). Infants were followed for six months after birth for the onset of ARI and diarrhea. Diarrhea was coded as "yes" if the infant moved three or more loose stools in 24 hours (380). ARI positive infants had symptoms of cough/cold accompanied by fever or fast breathing (381). Data collectors were clinical nurses and they used IMNCI guidelines to identify infants with diarrhea and ARI.

Social support: The Oslo Social Support Scale (OSSS-3) (382) was used to assess participants' social support during the perinatal period. Although the tool has not been validated in an Ethiopian context, it has shown good utility in a range of settings including in lower-income countries (53, 165). The OSSS-3 has three items measured with four Likert scales for item one, and five Likert scales for items two and three, summing to 14 points. Social support was categorised as poor if the total score was less than nine and moderate to strong if the score was 9 to 14.

Husband (partner) support: was assessed by a question "My husband helps me a lot" with five response scales, "Always", "Most of the time", "Some of the time", "Rarely", and "Never". Marital agreement was assessed by a question "How often do you discuss and agree with your husband in day to day life?" with a response category, "Most of the time", "Some of the time", "Rarely", and "Never".

Maternal nutritional status: A MUAC tape was used to screen pregnant women for malnutrition, with a cut-off score of 18 to 22 cm as 'underweight' and 22.5 to 31 cm as 'normal' (383).

Physical activity: It is recommended that healthy pregnant women participate in at least two to three hours of moderate intensity physical activity weekly such as brisk walking, dancing, gardening, and usual housework (384). Therefore, the intensity of physical activity was assessed and categorised as "yes" if the participant fulfilled the described criteria and "no" if not.

Tobacco smoking: Exposure to cigarette smoking during pregnancy was assessed by the question, "Have you been smoking since your pregnancy or has there been anybody who smokes near you in your home or your workplace?" with a response category of "yes" or "no" (29).

Coffee drinking: Participants were asked “how often do you drink coffee during pregnancy?” if the answer was “daily” or “sometimes in a week” the mother was labelled as having exposure to coffee.

Maternal stress coping ability: This was assessed by Perinatal Coping Inventory (PCI-4) developed specifically for pregnancy, which has four internally consistent coping subscales (385). Coping styles in this tool include: (i) Preparation for motherhood: “planned how to handle the birth”; (ii) Avoidance: “avoided being with people in general”; (iii) Positive appraisal: “felt that being pregnant has enriched your life; (iv) Prayer: “Prayed that the birth is going well”. Participants were asked to report how often they used the above coping styles, with their responses recorded and categorised in four-item Likert scales; (0) never, (1) rarely, (2) sometimes, and (3) most of the time (386).

3.5.2.5. Data collection tool and methods

Face-to-face interviews were conducted with study participants using a structured and pre-tested electronic-based questionnaire. An Open Data Collection Kit (ODK) application tool was used to collect digital data. The ODK is a suite of open source tools that help to collect, organise, and manage data online (387). The prepared questionnaire was designed on an Excel spreadsheet, converted to XLSForm online, and checked for validity using Enketo. The validated data collection form was downloaded from Enketo and uploaded onto Lenovo 7 tablets, which were then used in the field for data collection. Each trained data collector used a Lenovo 7 tablet to administer the questionnaire to study participants. After completion of each questionnaire, data collectors uploaded data to the Google cloud platform, an online data storage repository designed for this project. This allowed the PhD candidate to download data directly from the Google cloud platform. The electronic-based data collection was helpful to maintain the quality and completeness of the data.

Interviews with each respondent commenced with the data collector’s self-introduction followed by a presentation of the nature and objectives of the study. Data collection occurred at three contact points. In the first contact, AND was assessed during pregnancy (second or third trimester). In the second contact, after birth, the incidence of LBW, preterm and stillbirth were

recorded, and women assessed for postnatal depression. In the third contact, participants were followed to six months post-delivery to identify and record incidence of malnutrition, diarrhea, and ARI. A supervisor working in the Gondar Town Health Office who held a Master's level qualification in public health supervised the data collection process. The supervisor had frequent contact with data collectors to fix issues with the data collection process. The supervisor and the PhD candidate had frequent meetings to fix any issues with the data collection process.

3.5.2.6. Data quality assurance

Instrument development: The questionnaire was developed by the PhD candidate and with supervisors' input, giving due consideration for clarity, logical flow, completeness, and content of the questions, and time needed for the interview (Annex 3.1).

Translation of the questionnaire: The translation of the questionnaire from English to Amharic was accomplished by the PhD candidate and the clarity of the translated questions was reviewed in depth. The re-translation of the Amharic version to English was done by a language expert working in the University of Gondar to ensure the similarity of the Amharic and English versions of the questionnaire. However, the standard translated form of EPDS was used for depression assessment.

Pre-testing of the final questionnaire: A pilot test was conducted with a sample of 50 participants living in kebeles not part of the study sample. After this, the questionnaire was further revised and contents creating apparent ambiguity were clarified.

Data collectors' and supervisor's recruitment and training: The PhD candidate prepared a guide for recruitment and training of data collectors. Based on the recruitment guide, a call for data collectors was announced and screening was undertaken to recruit the best candidates based on agreed criteria. Recruited data collectors fulfilled the following criteria: were clinical nurses who held a Bachelor of Science degree; had previous experience in data collection; were living in Gondar town; were not already engaged in additional duties; were interested in being involved in the research for one year. The resulting nine data collectors and one supervisor were trained by the PhD candidate on the content, interview methods, response recording, and measurement

techniques for two days. Furthermore, data collectors were trained on how to complete the online survey, correct mistakes, and upload the data to the Google cloud platform. The data collectors and supervisor also participated in a practical session about the interview and recording process.

Cut-off value, validity, and internal consistency of the tools: Tools which were previously validated or used in Ethiopian or other African contexts and possessed good internal consistency and reliability were used in the current study. Further, internal consistency, which helps to ensure that tools correctly measured the intended health outcome or related variables, was determined using the Cronbach-α test (388). Lastly, confirmatory factor analysis was performed for testing a fitness of measurement model before fitting the structural models (389)**.**

3.5.2.7. Data analysis

Survey data were downloaded from the Google cloud platform into an Excel spreadsheet, checked for completeness, and imported to Stata version 14 (StataCorp, USA) (390) for further cleaning and analysis. Descriptive statistics such as frequency, mean, median, proportion/percentage, interquartile range, and standard deviation were calculated. Exploratory data analyses were conducted to understand the nature of the data. Chi-squared and t-tests were used to test for crude associations between the covariates and outcomes. Preliminary findings were presented using tables and figures. The mediating and interaction effects of different covariates were investigated. A summary of analysis approaches used for each quantitative objective is presented in the first sections of the result and discussion chapters.

3.5.3. Methods for the qualitative study

3.5.3.1. Study design, sampling, and sample size

A qualitative study allows the exploration of study participants' experiences and perspectives on research questions in a natural setting (350, 391). Health administrators from different levels of the healthcare system were selected and interviewed to explore the barriers to and enablers of perinatal depression health services in Ethiopia. The study was conducted on health administrators to look to barriers and facilitators related to health service provider side. were A

purposive sampling technique was used to recruit study participants with a maximum range of views (349, 392). The aim was to recruit study participants who had been closely involved in the healthcare system to provide better opportunity to potentially explore the barriers to and enablers of perinatal depression health services. Information saturation was used to decide the optimal sample size (350, 392). As such, 13 health administrators from the highest to lower levels of the healthcare system were involved in the study.

3.5.3.2. Recruitment of participants

Figure 3.5 shows the recruitment strategy at each level of the healthcare system. In the Ethiopian healthcare system, in health facilities, a pregnant woman can directly visit the psychiatry clinic for mental health services or maternal health clinics for perinatal services. As such, women with depression symptoms might present at both clinics. Therefore, every health administrator working in the two clinics (maternal and psychiatry) from two referral hospitals was involved. Administratively, the maternal health care team and the mental health care team could be involved in perinatal mental health service delivery. Therefore, health administrators working as mental health and maternal healthcare team leaders at different levels of the Ethiopian healthcare system were involved. The remaining three participants were health professionals leading maternal and child health teams in three health centres.

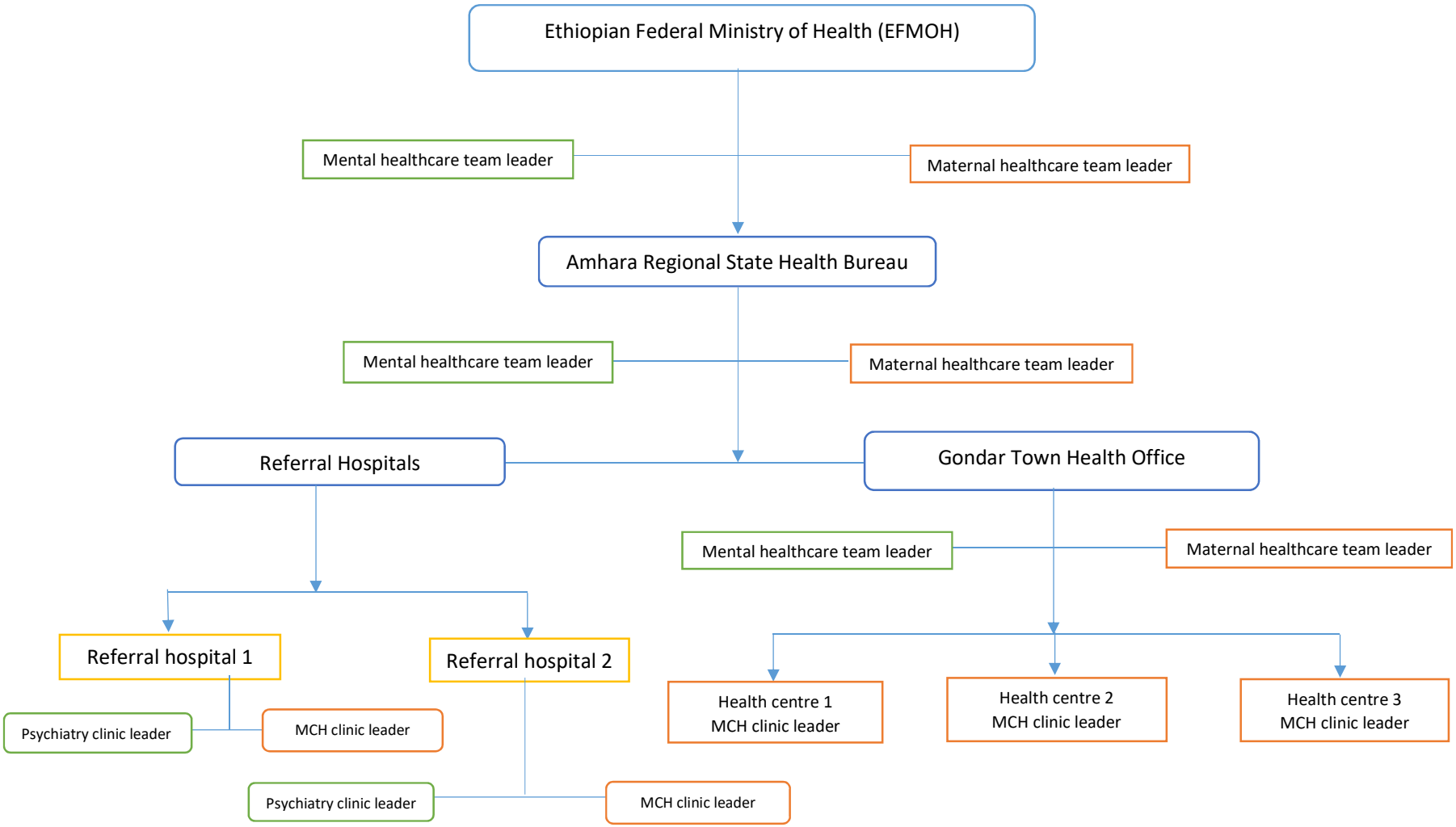


Figure 3.6: Study participants' recruitment procedure for the qualitative study in Ethiopia, 2018.

3.5.3.3. Data collection tool and method

A semi-structured and pretested interview guide was prepared in English and translated to Amharic (local language of the data collection area) and then used to collect the qualitative data. The interview guide was developed to address the main research question. Probes, cues and prompts were used to direct the interviewee into the research topic to get detailed data (393). (Annex 3.2) Face-to-face interviews were conducted by the PhD candidate in participants' private offices (394-396), which were quiet, secure, confidential and deemed comfortable for study participants. Interviews lasted 1between 5 and 35 minutes and were audio-recorded. A summary of essential points was made at the end of each interview to ensure that the responses were correct and thoroughly documented. To provide data triangulation, health policy and mental health strategy documents addressing perinatal mental health service barriers related to the healthcare system were reviewed.

3.5.3.4. Data analysis and presentation

Interviews were audio-recorded and field notes were carefully taken at each interview. Audio-recorded interviews were transcribed verbatim in Amharic and translated back into English. Translated transcripts were imported into NVivo software (397) and analysed using a thematic framework analysis (398) involving the following five steps:

i. **Data familiarisation**: The PhD candidate (PC) familiarised himself with the data by transcribing, repeatedly listening to the audiotapes, and re-reading the transcripts. These helped the understanding of the content of the data and easily identify significant statements, patterns, and initial ideas.
ii. **Coding**: This was achieved through reading the transcripts line by line and then systematically applying a phrase or label (a 'code') to interesting features, patterns, concepts, and ideas in the data. The PC applied open coding, which involved coding of all content or information found in the transcripts that was deemed relevant to fully interpret the data. Different types of coding were applied based on the nature of the response in the transcripts. Attribute coding was used for socio-demographic characteristics of the study participants; emotional coding for hopelessness, pessimism, and denial type of responses; value coding for knowledge and attitude related responses; evaluative coding for judgmental kinds of responses; magnitude

coding for intensive or frequency type of responses, and theming coding for phrases or sentences that gave complete information for the response (394).

iii. **Identifying a thematic framework**: After coding the first two transcripts, discussions were held with supervisors and a draft thematic framework that all supervisors agreed on was developed. Thus, the set of codes and categories (code book) that was applied to other remaining transcripts was identified. Moreover, any subsequent emerging concepts that did not fit the working thematic framework were considered and added to 'other' code created under each category.

iv. **Indexing and charting**: The remaining 10 transcripts were indexed using the defined codes and categories of the identified thematic framework. Indexing in NVivo was completed by dragging and adding concepts and ideas from the transcripts to the related codes and categories created under the working thematic framework. Charting developed a framework matrix that clearly outlined the themes, sub-themes, and descriptions with their respective files and references. Both inductive and deductive approaches were used to account for categories that were known prior and those that were originated from the data (353).

v. **Interpretation**: The themes and sub-themes that emerged, with their clear descriptors, were organised in such a way that they were chronologically linked to provide meaning. Each theme and sub-theme with their central meaning were described and presented, supported by direct quotes from study participants (353, 399-401).

3.5.3.5. Rigour (trustworthiness) of the study

Demonstrating the quality of research process is essential, but the standards used for quantitative and qualitative studies differ (353). The reliability and validity of qualitative research are evaluated by using its credibility, dependability, and confirmability (402). The credibility of this qualitative study was achieved in three ways: (i) building a smooth or trusting relationship between the researcher and the study participants who agreed to participate; (ii) data triangulation using more than one method of data collection, i.e. interviews and the review of health policy and mental health strategy documents; and (iii) selection of participants from different levels of the Ethiopian healthcare system to ensure across-site consistency of the data (394, 396). The dependability of this qualitative study was

attained through documenting, justifying and strictly following the outlined methods in terms of participants recruitment, data collection, analysis, and interpretation of the study findings.

The confirmability of this qualitative study was believed to be realised through: (i) clearly describing the demographic features of study participants; (ii) checking and re-checking the accuracy of information between interview audio, translations and transcripts; (iii) ensuring the accuracy of interview guide translation between English and Amharic (the local language); and (iv) ensuring that the findings represented the data gathered and were not biased by the researcher's personal thoughts, through the inclusion of direct quotations from the study participants. Moreover, the PC is a male professional who was living in the same culture as participants but was not working in the health sector, which also helped to minimise bias in the analysis and interpretation of the data.

3.6. Ethical approval

3.6.1. Ethical issues related to the participants and study design

Research is designed to generate information that contributes to knowledge. However, the knowledge that emerges should be based on individual and collective adherence to core values of objectivity, honesty, openness, fairness, accountability, and stewardship (403). The quantitative study in the project involved perinatal women and their infants of age under six months, to generate information on epidemiology and consequences of perinatal depression. In the research, pregnant women aged 18 years and over were prospectively followed from their second or third trimester of pregnancy through the first six months after delivery. The qualitative research involved interviewing health administrators working at different levels of the Ethiopian healthcare system to explore information on barriers to and enablers of perinatal depression services. The ethical issues in undertaking this research should, therefore, account for the study participants and the nature of the study design.

Concerning study design, the Helsinki declaration applies to all types of research design as stated: "*Medical research involving human subjects includes research on identifiable human material or identifiable data*" (404). The Australian and Ethiopian codes for the responsible conduct of research follow similar ethical principles, as stated in their working guidelines (405, 406). In both countries, a research ethics committee is formed by an accredited body of government and given the responsibility to ensure the ethical and scientific integrity of a

research project to be conducted. A research ethics committee is a group of individuals from different disciplines formally appointed to review, approve, and monitor biomedical and behavioural research involving human participants. The committee is mandated to protect the rights and welfare of study participants as stated in the three basic ethical principles: respect for persons, beneficence, and justice (145).

3.6.1.1. Ethical principles

3.6.1.1.1. Respect for persons

Respect for persons is a fundamental ethical principle that recognises study participants as autonomous, unique, and free individuals. It considers each participant to have the right and capacity to make his or her own decisions to be involved in the research. In terms of study participants, pregnant women and infants are considered individuals with diminished autonomy or vulnerable research subjects. As such, with special emphasis, ethics applications for studies involving this group are required to go through a stringent review process (407), as happened with this study. The vulnerability of perinatal women in this specific study could arise from the naturally stressful condition of pregnancy, women with adverse birth outcomes, and stigma associated with depression in Ethiopian society. Introduction and information sheets were provided for perinatal women a week before the actual consent process (Annex 2.1 & 2.2). It was believed that this gave them adequate time to think, understand, and comprehend critically before making decision to participate in the study. The evidence of external stigma associated with perinatal depression, unlike other severe mental disorders (408), is not documented in Ethiopia. To minimise their internal stigma, recruitment and data collection were conducted in their private homes and they were assured that their screening outcome was confidential.

The other issues that might affect perinatal women's autonomy to give informed consent were the power differences between health care workers and patients, the socio-economic status of participants, and the status of women in Ethiopian society. To resolve the issue of power difference, recruitment and data collection were undertaken by female nurses who were unknown to the participants. The participants were also assured that their participation would not affect their access to clinical services. Furthermore, study participants were

assured about the purpose and benefit of the study for themselves and society. They were also advised that there was no risk associated with the study.

All ethical principles were upheld through following a transparent consent process. As such, potential participants were informed about the purpose, objectives, and their right to participate or not participate in the research activities. The participants were also informed that they had the right to withdraw from the study at any time. The PC made maximum possible efforts in assuring all ethical and scientific standards were upheld. Privacy and confidentiality were maintained during interviews. All data collectors were informed of the need to protect participants' confidentiality. The data collectors assigned a unique non-consecutive code to each participant. Before assigning codes, the PC trained data collectors on the importance and process of assigning unique codes. Only data collectors could link the code to the name of each participant. Participant codes were stored in password-protected computers. The participants were also assured that their information would be treated with the strictest confidence and no identifying information would be published or described in the thesis or other reports or publications.

For the participants in the qualitative interviews, measures were put in place to minimise the potential for perceptions of coercion during the contact and interview process. Firstly, ice-breaker discussion was held to familiarise the study participants by asking their age, occupation, education, and experience. Secondly, the principal investigator informed the participants about the purpose of the study, that it would contribute towards a PhD thesis, and their refusal to participate would not have any effect on their service, work, or personal life. Thirdly, participants were informed that their participation was voluntary, they could withdraw from the interview at any stage, and they had the full right not to answer a question that they were not comfortable with. Fourthly, the participants were informed that they would not receive any direct payment or benefit as a result of their involvement. Participants were asked to read and indicate their understanding of the information sheet before signing the consent form (Annex 2.5 &2.6). They were also asked to raise any issue that was not clear for discussion. Finally, written consent was obtained from participants in both qualitative and quantitative arms of the study (Annex 2.4 & 2.7).

3.6.1.1.2. Beneficence

Beneficence is the act of doing good for participants, and avoiding harm is the minimum standard of this principle. I believe participants received the following direct and indirect benefits for their participation: (i) women were screened for depression during pregnancy and after birth and those who fulfilled criteria for depression or had thoughts about suicide were excluded from the study and referred to a mental health counsellor at the University of Gondar Specialised Hospital; (ii) participants might value the opportunity to share their views and experiences about perinatal depression with health professionals; (iii) participants might become better informed about how to address their own and their neighbour's problems; and (iv) participants might appreciate having their views incorporated into the research findings.

There are benefits also for the discipline. Mental health issues specific to maternal populations have not been given due attention by the government because of limited research on the area. It is hoped that this research would bring additional insights into mental health issues in perinatal populations in Ethiopia. For the community and country, improving the health status of mothers and children would ultimately have benefits for the general population. The findings of this project would form the basis of the development of interventions focusing on perinatal depression.

3.6.1.1.3. Burden and/or risks

Participant risk in this project might include: (i) feeling burdened by the donation of their time; (ii) experiencing emotional discomfort and distress during the interview process; (iii) being diagnosed as 'depressed' might represent a negative shift in self-perception; (iv) experiencing negative consequences of being identified as having been involved in the study; (v) fearing that they would be deprived of services if they did not agree to participate in the research; and (vi) the risk that their comments might be misrepresented.

3.6.1.1.4. Non-maleficence and justice

The possibility of harms or risks in the study were minimised through the following measures: (i) the survey was specifically designed to contain the minimum number of items to limit their time; (ii) study participants who felt emotional and/or distressed were advised to contact a

nominated mental health counsellor at the University of Gondar Specialised Hospital psychiatry clinic; (iii) participants were reminded before and throughout the study that their involvement remained voluntary and that they may withdraw from the study at any time; (iv) participants fulfilling the criteria for depression were referred to the mental health counsellor; (v) data collectors were educated to be alert to emotional discomfort or distress during interviews and always to deal with participants sensitively and non-judgmentally; and (vi) study participants were told that they had the right to ask for clarity in case they suspected that their information was misinterpreted or wrongly documented. Justice as an ethical principle in this study was ensured by: (i) random selection of study participants; (ii) efforts made so benefits outweighed risks or harms; and (iii) the PC's plan to introduce a project that would benefit the perinatal population.

3.6.2. Ethical approvals granted

The nature of research design and type of study participants needed ethical approval from Ethiopia and Australia. As such, ethical approval was obtained from the Social and Behavioural Research Ethics Committee of the Flinders University, Australia with a reference number 7959, 2018 (Annex 2.8), and the Institutional Review Board of the University of Gondar with a reference number O/V/P/RCS/05/1601, 2018 (Annex 2.9). A support letter from the University of Gondar Research and Community Service Vice President to Gondar Town Health Office and respective kebeles was also secured (Annex 2.10 & 2.11).

Chapter Four: Findings from systematic reviews and meta-analyses

4.1. Introduction

The studies described in this chapter were systematic reviews and meta-analyses of perinatal depression prevalence and its association with adverse birth and infant health outcomes. The reviews examined the extent of the disorder in the global and local contexts and allowed the identification of gaps in the literature. The chapter narratively presents the findings of three systematic reviews that were conducted in alignment with the thesis main objectives. The first umbrella review aimed to determine the global epidemiology of antenatal depression and associated adverse birth outcomes by summarising findings from published systematic reviews and meta-analyses. The second review aimed to pool systematically AND prevalences and their association with the risk of adverse birth outcomes by including primary studies conducted in LMICs. The third review aimed to pool PND prevalences and their association with the risk of adverse infant health outcomes by including primary studies conducted in LMICs. The detailed methods for all systematic reviews were presented in chapter three. This chapter presents the findings of the reviews in three sections: search results, discussion, and conclusion of the first, second and the third reviews separately and sequentially.

4.2. Antenatal depression and its risk on adverse birth outcomes: Umbrella review

This umbrella review provides useful evidence regarding the global burden of antenatal depression and its association with adverse birth outcomes. The review may provide guidance for health policy development and planning. The CINAHL (EBSCO), MEDLINE (via Ovid), PsycINFO, Emcare, PubMed, Psychiatry Online, and Scopus databases were searched for systematic reviews based on observational studies and published between January 1st, 2007 and August 31st, 2018. Assessment of Multiple Systematic Reviews (AMSTAR) checklist scores were used to assess the quality of the included reviews. Vote counting and narrative review were conducted to summarise the global prevalence of antenatal depression and its associated factors. Statistical pooling was conducted for estimating the association of AND with the risk of LBW and preterm birth. The detailed method has been presented in chapter three, section 3.1. This sub-section presents the results, discussion, and conclusion of the review. This scoping review has been published.

https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-020-8293-9.

4.2.1. Umbrella review results

4.2.1.1. Search

The search strategy identified 265 references for all search terms on antenatal depression and its association with adverse birth outcomes. After duplicates removed and abstracts reviewed, 35 references were deemed eligible for full-text review. After full-text review, 17 were excluded for the following reasons: the review included primary studies conducted on restricted populations, only one database was searched, the exposure or outcome differed from the main objective of this review of reviews, or were not identified as systematic reviews. The remaining 10 reviews (306 primary studies with a combined total of 877,246 study participants) on AND prevalence (22, 50, 133, 167, 409-414) and six reviews (39 primary studies with a combined total of 75,451 study participants) focused on the association between antenatal depression and adverse birth outcomes (47, 49, 51, 52, 101, 415) were included in the final analysis (Figure 4.1).

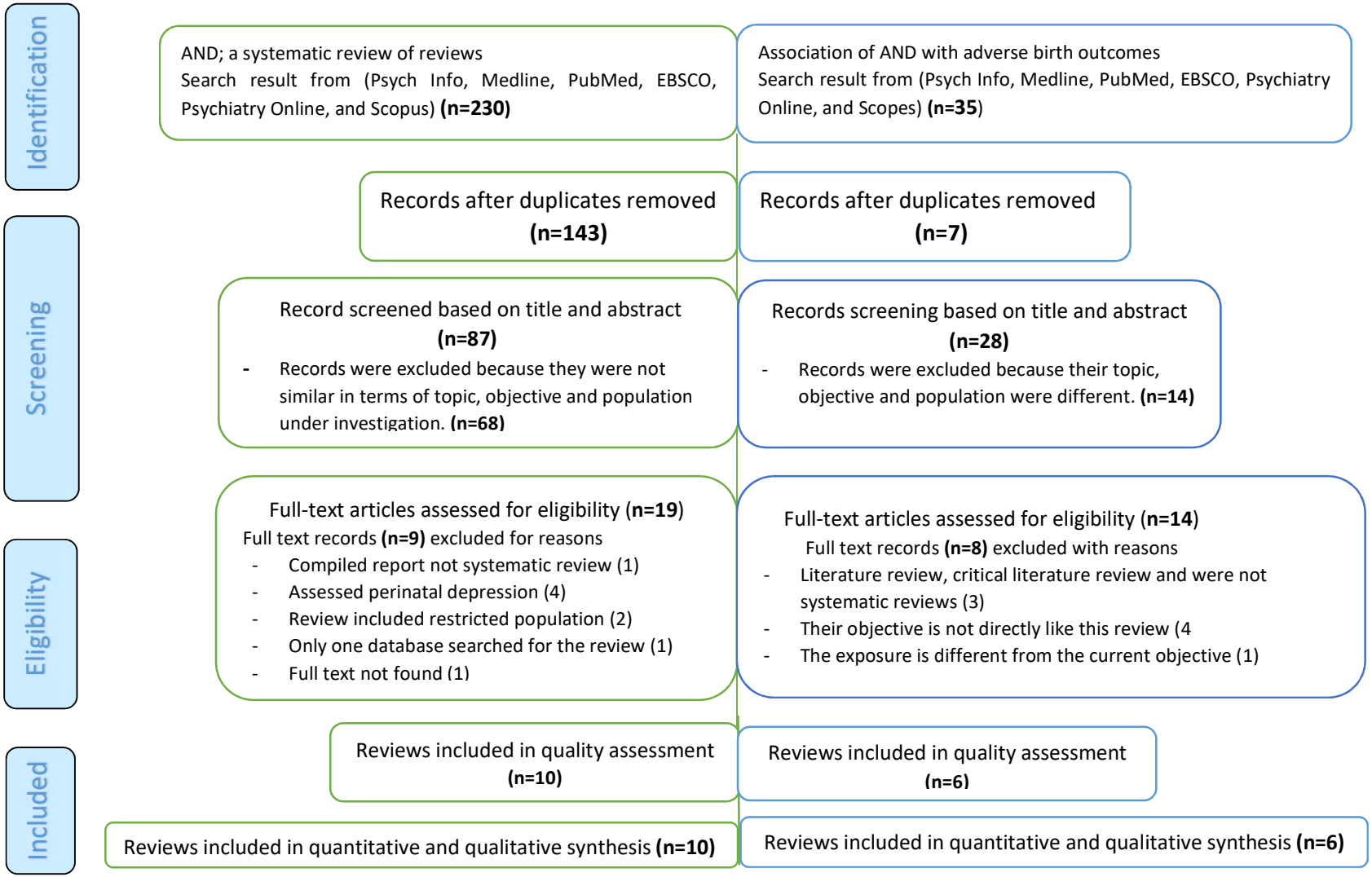


Figure 4.1: PRISMA diagram for a systematic review of reviews conducted on antenatal depression and its effect on adverse birth outcomes, (2007-2018).

4.2.1.2. Global prevalence and factors associated with antenatal depression

The reviews included primary studies that were published from 1968 to 2017 and systematic reviews that were published from 2010 onwards. The number of studies included in the reviews ranged from seven (with a total of 2,161 participants) to 97 (with a total of 1,541,303 participants). The EPDS was the predominant screening tool used across the reviews. PubMed/MEDLINE, Psych INFO, CINAHL and Scopus were the most cited databases for searching primary studies. Four reviews assessed the quality of included studies following the standard assessment method. All reviews reported risk factors associated with AND while only four reported pooled prevalence of AND (Table 4.2). Two systematic reviews achieved the threshold for an upper-quality score while the rest achieved middle-quality scores (Table 4.3).

Across included systematic reviews, global AND prevalence as low as 7% was reported in high-income countries and as high as 65% in low-income countries (410). Current or previous exposure to abuse and violence (in six reviews), lack of social and partner support (in four reviews), and family or personal history of CMDS (in three reviews) were psychosocial factors documented to be associated with AND globally. Unplanned or unwanted pregnancy significantly increased the risk of AND in three reviews involving 36 primary studies. Low economic status or financial difficulty increased the risk of AND in three reviews of 32 primary studies. Having a history of poor obstetric outcomes such as past pregnancy complications (hyperemesis gravidarum, caesarean section, hypertension, diabetes mellitus), adverse birth outcomes (LBW, preterm birth, stillbirth, abortion), and infant loss after birth were associated with an increased risk of AND in four reviews of 33 primary studies. Pregnant women with a history of smoking, alcohol and illicit drug use were significantly more likely to have depression in one review of 29 primary studies. Low educational status was associated with increased risk of AND in two reviews of 22 primary studies. One review investigated the role of diet and nutritional supplementation on antenatal depression and reported inconclusive findings (413) (Table 4.3).

Table 4.1: Summary of systematic reviews conducted on antenatal depression included in the scoping review (N=10, 2007-2018)

Review	Geographic coverage of the review	Prominent tools used	Data base searched	Number of primary studies	Number of participants	Quality assessment	Main findings relevant to the review		AMSTAR score
							AND Prevalence	Risk factors	
Biaggie, 2016 From 2003 to 2015	Developed countries	Not reported	PubMed, Psych INFO, Cochrane Library	97	1,541,303	Not assessed	Not reported	- Lack of partner or social support (in 13 studies) - History of abuse or domestic violence (in 6 studies) - Personal history of mental illness (in 7 studies) - Unplanned or unwanted pregnancy (in 4 studies) - Adverse events in life and high perceived stress (in 3 studies) - Present or past pregnancy complications or loss (in 3 studies)	5
Gelaye et al. 2016 From 1998 to 2015	Low- and middle-income countries	EPDS (22 studies)	PubMed, Embase, CINAHL, BIOSIS Online	51	48,904	Not assessed quality of the primary studies	25.3% (95% CI: 21.4, 29.6)	- Early life abuse (child maltreatment, a severe early life stressor, includes all forms of physical, sexual and psychological maltreatment that pose harm to a child's health, development or dignity) in 2 studies - Adult abuse (intimate partner violence (IPV), encompassing physical, psychological and sexual abuse in five studies - Maternal low educational attainment in two studies - Maternal low economic status in three studies - Lack of social support in one study - History of mental illness in one study	7

Halim et al. 2017 From 1990 to 2017	Low- and lower middle-income countries	EPDS in ten studies	PubMed, Web of Science, Scopus, Psyc Info, Applied Social Science Index and Abstracts (ASSIA)	24	13,490	Quality assessed but standard criteria not used	15—65%	- Intimate partner violence during pregnancy in 24 studies	7
Mitchel et al. 2017 From 1980 to 2015	Developed countries	BDI in six studies	PubMed, MEDLINE, EMBASE and Psych INFO	12	4,751	NOS criteria	Not reported	- Hyperemesis gravidarum in 12 studies	7
Roomruang wong et al. 2011 From 1968 to 2010	Asian countries	BDI in six studies	MEDLINE (PubMed), Psych INFO and SCOPUS	25	9,126	Quality of primary studies not assessed	20%	- Having a history of premenstrual symptoms (in 3 studies) - Poor marital relationship (in 3 studies) - Unplanned/unwanted pregnancy especially during premarital period (in 8 studies) - Poor obstetric history (complication before or in current pregnancy) (in 5 studies) - Financial difficulties (in 4 studies) - Lack of support from partner or relatives (in 7 studies)	4

Sparling et al. 2017 From 2008 to 2015	All included studies were from developed countries except one from India	EPDS in 21 studies	PubMed, EMBASE and CINAHL	35	88,051	Quality in Prognostic Studies tool, Cochrane Collaboration tool	Not reported	- 173 studies, including three polyunsaturated fatty acids (PUFA) supplementation trials, found no evidence of an association between polyunsaturated fatty acid and depression - 22 studies showed protective effects from depression of healthy dietary patterns, multivitamin supplementation, fish and PUFA intake, calcium, Vitamin D, zinc and possibly selenium - Given the methodological limitations of existing studies and inconsistencies in findings across studies, the evidence on whether nutritional factors influence the risk of perinatal depression is still inconclusive	7
Underwood et al. 2016 From 2000 to 2015	Developed countries	EPDS in 13 studies	EMBASE, PsycINFO, MEDLINE and Cochrane Reviews	16	35,419	List of criteria	17%	- Previous depression history was found as a predictor of a current depression during pregnancy in five studies	7
Wosu et al. 2015 From 1999 to 2014	Developed countries	CES-D/ in three studies	PubMed, EMBASE, PsycINFO, CINAHL, Web of Science, BIOSIS, and Science Direct	7	2161	Newcastle–Ottawa Scale (NOS)	Not reported	- Childhood sexual abuse is strongly associated with antenatal depression (six studies)	8
Lancaster et al. 2010 From 1980 to 2008	Developed countries	CES- D in 49 studies	PubMed, CINAHL, SCOPUS, PsycINFO, Sociological Abstracts, ISI	57	36,257	Quality assessment tool adapted from methods used by US	Not reported	- Life stress (in 18 studies), - Lack of social support (in 24 studies), - Domestic violence (in seven studies) - Unwanted pregnancy (in six studies) - Low income (in 11 studies)	7

			Proceedings, ProQuest			Preventive Services Task Force		- Unemployment (in 14 studies) - Lower education (in 20 studies) - Smoking (in 11 studies) - Alcohol use (in 10 studies) - Illicit drug use (in 8 studies) - Nulliparity (in 18 studies) - Poor obstetric history (in 10 studies)	
Howard et al. 2013 From 2000 to 2012	All continents except Africa	EPDS in 35 studies	Medline, EMBASE, and PsycINFO, and hand searches	67	171,465	Yes, quality appraisal checklist	Not reported	- Lifetime domestic violence (in 11 studies) [Pooled Odds Ratio (POR)=3.04: 95%CI: 2.31,4.01, I^2=51.1%] - Any past year partner violence in five studies, [POR=2.82: 95%CI:1.52, 5.28, I^2=75.3%] - Partner violence during pregnancy in seven studies, [POR=5.00: 95%CI: 4.94, 6.17, I^2=23.7%]	8

Table 4.2: Summary of risk factors associated with antenatal depression (N=10, 2007-2018)

Risk factors	Number of reviews in which the risk factor was reported	Number of primary studies in which the risk factor was reported	Total participants
History of abuse (childhood or current sexual, physical or psychological) or domestic violence or intimate partner violence	6	73	293,621
Lack of partner or social support and poor marital relationship	4	47	226,078
Personal or family history of any mental disorders or stress	3	34	177,014
Unplanned or unwanted pregnancy especially during premarital condition or nulliparity	3	36	70,296
History of bad obstetric condition including current or past pregnancy complications such as hyperemesis gravidarum, adverse birth outcomes (LBW, preterm, stillbirth or infant lose after delivery), previous caesarean section delivery	4	33	56, 916
Maternal low economic status or unemployment or financial difficulties	3	32	20,239
Maternal lifestyle risk factors such as smoking, alcohol use, illicit drug use	1	29	18,444
Maternal low educational status	2	22	14,638
Total	10 reviews	306 primary studies	877,246 participants

Table 4.3: AMSTAR score of included reviews on antenatal depression and associated factors (N=10, 2007-2018)

AMSTAR criteria	Name of the reviews									
	Biaggie, 2016	Gelaye, 2016	Halim, 2017	Mitchel,2017	Roomruangwong, 2011	Sparling, 2017	Underwood, 2016	Wosu, 2015	Lancaster, 2010	Howard, 2013
1. Was an *a priori* design provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was there duplicate study selection and data extraction?	No	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes
3. Was a comprehensive literature search performed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Was status of publication (e.g. grey literature) used as an inclusion criterion?	Yes	Yes	Yes	No	No	No	No	Yes	No	No
5. Was a list of studies (included and excluded) provided?	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer	Can't answer
6. Were the characteristics of included studies provided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

7. Was the scientific quality of the included studies assessed and reported?	No	No	Can't answer	Yes	No	Yes	Yes	Yes	Yes	Yes
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	No	No	Can't answer	No	No	No	No	No	Yes	No
9. Were the methods used to combine the findings of studies appropriate?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Was the likelihood of publication bias assessed?	Not applicable	Yes	Not applicable	No	Not applicable	Not applicable	Not applicable	Yes	Not applicable	Yes
11. Was conflict of interest stated?	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Total AMSTAR score	5 (middle)	7(middle)	7(middle)	7(middle)	4(middle)	7(middle)	7(middle)	8(upper)	7(middle)	8 (upper)

4.2.1.3. Association of antenatal depression with adverse birth outcomes in the global context

Six reviews that investigated the association of AND with adverse birth outcomes were identified. Preterm birth and LBW were the main adverse birth outcomes reported to be associated with AND. The primary studies included in the reviews were conducted in the years 1977 to 2015 and all included reviews were conducted from 2010 onwards. All reviews included primary studies conducted in developed countries, except a single primary study from India. The Centre for Epidemiological Depression Scale (CED-S) was the most commonly used screening tool in the primary studies (used by 52 studies). There were 25 and 39 primary studies conducted to investigate the association between antenatal depression and the risk of LBW and preterm births, respectively. Three reviews were published as narrative reviews while the remaining three reviews reported pooled estimates of preterm birth and LBW. Four systematic reviews fulfilled the criteria for upper-quality category while the remainder were scored as middle-quality (Table 4.4).

Four systematic reviews (47, 49, 52, 415) reported an increased risk of LBW among women exposed to AND, and the other review reported a lack of significant association (101). Pooling the estimates of these five reviews produced the risk of LBW of 1.39 (95%CI: 1.22, 1.58; I^2=35.2%). This means that the risk of having LBW was 39% higher among pregnant women with AND. From five reviews conducted to test the association between antenatal depression and preterm birth, four reported that AND increased the risk of preterm birth (47, 51, 101, 415) while the result from the remaining review was non-conclusive (52). Meta-analysis of the five included reviews resulted in a pooled risk of preterm birth of 1.49 (95%CI: 1.32, 1.68; I^2=0.0%) among pregnant women with AND relative to non-depressed women (Table 4.5). The test of publication bias confirmed no evidence of missing studies, and the result of sensitivity analysis indicated that no review unduly influenced the pooled estimate.

Table 4.4: Characteristics of studies included in a systematic review of reviews for assessing association between antenatal depression and adverse birth outcomes (N=6, 2007-2018)

Author, year	Geographic coverage of the review	Prominent tools used	Data base searched	Number of studies and number of participants	Quality assessment tool used	Main findings relevant to our review		AMSTAR score
						Preterm birth	LBW	
Ascort et al. 2014 Included studies conducted from 1977 to 2013	USA, Europe, Asia	CES-D (19 studies)	PubMed and PsycINFO	- PTB=50 studies with sample size of 286,043 - LBW=33 studies with sample size of 43,534	NOS	- Considering the methodological quality of studies, research on depression and preterm birth is inconclusive - Was a systematic review because pooling was not conducted	- It was found that about more than half (53 %) of published LBW findings reported statistically significant associations with AND and LBW - Was a systematic review because pooling was not conducted	8
Araujo et al. 2010 Included studies conducted from 1996 to 2007	United States, Norway, Canada, Denmark, India, England, United Kingdom	Not found	PubMed, SciELO, and ISIWEB	10 studies with sample size of 231,201	Downs & Black quality assessment check list		- Depression during pregnancy was associated with LBW in seven studies - Was a systematic review because pooling was not conducted	5

Grigoriadis et al. 2013 Included studies conducted from 1992 to 2010	Most studies were from USA with a few from Australia, China, Europe	CES-D with different cut-off values in 11 studies	MEDLINE, EMBASE, CINAHL, Scopes and PsycINFO	- PTB=15 studies with sample size of 23,754 - LBW=6 studies with sample size of 14,090	Systematic Assessment of Quality in Observational Research (SAQOR) and NOS	- Preterm birth (PAOR=1.37; 95% CI, 1.04, 1.81) I^2=61% - No evidence of publication bias	- LBW was not significantly associated with AND (POR =1.21; 95% CI, 0.91, 1.60) I^2=0.0% - No evidence of publication bias	10
Grote et al. 2010 Included studies conducted from 1980 to 2009	Most of the studies were from USA with others from Europe, Asia, Brazil	CES-D in 10 studies	MEDLINE, PsycINFO, CINAHL, Social Work Abstracts, Social Services Abstracts, and Dissertation Abstracts	- PTB=20 studies with sample of 29,295 - LBW=11 studies with sample size of 13,544	Developed by modifying the instrument of Downs and Black	- Preterm birth was associated with AND; PRR=1.39 [1.19–1.61] - The association between AND and risk of preterm birth was found to be higher among women of lower socio-economic status in the United States. - I^2=61% - Publication bias checked and corrected	- Low Birth Weight was associated with depression during pregnancy; PRR=1.49 [1.25–1.77] - The association between AND and risk of LBW was found to be higher in developing countries compared with USA (RR=2.05; 95% CI, 1.43, 2.93) - I^2=70%	7

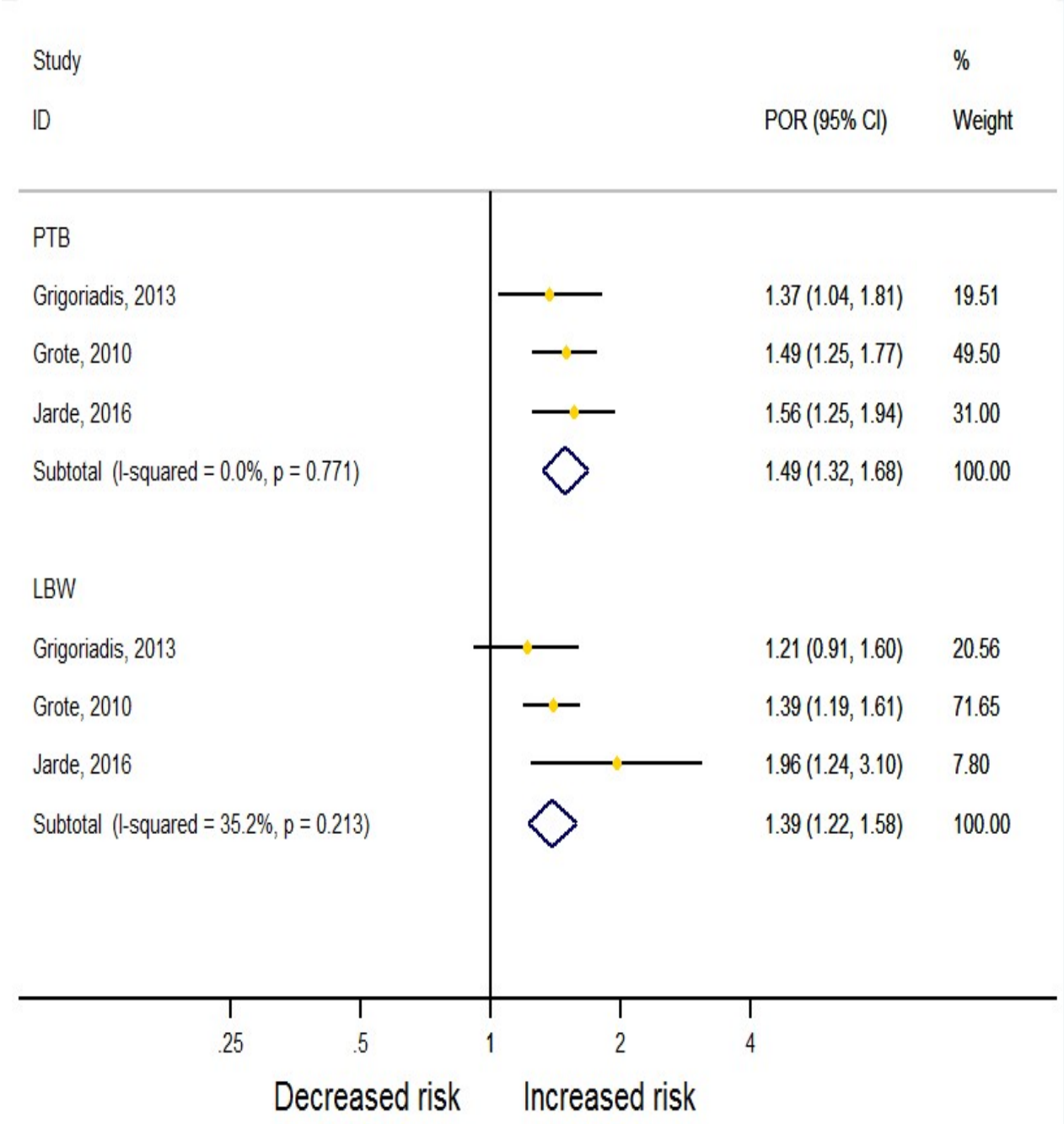
							- Publication bias checked and corrected	
Jarde et al. 2016 Included studies conducted from 1992 to 2015	Most studies were from USA and other developed countries	DSM-IV (nine studies) and CES-D (six studies)	MEDLINE, EMBASE, PsycINFO, Cumulative Index to Nursing and Allied Health, Cochrane Central Register of Controlled Trials, and Web of Science.	- PTB=14 studies - LBW=8 studies with sample size of 25,663	Newcastle–Ottawa Scale	AND was associated with an increased risk of preterm birth (POR, 1.56; 95% CI, 1.25, 1.94) I^2=39%	AND was associated with an increased risk of LBW (POR, 1.96; 95% CI, 1.24, 3.10) I^2=48%	10
Staneva et al. 2015 Included studies conducted from 1992 to 2015	USA, Europe, Brazil, Canada, UK, Norway, and China	CES-D in six studies	MEDLINE, CINAHL, PsycInfo, and Cochrane databases and manual searches	- 14 studies investigated the association between AND and PTB - Sample size not clear	Checklist developed by a knowledge synthesis group for the specific purpose of review of the evidence	- Preterm birth was independently and significantly predicted by AND - Was a systematic review because pooling was not conducted		7

Note: PTB: Preterm birth; LBW: Low birth weight; PRR: Pooled Relative Risk; POR: Pooled Odds Ratio; NOS: Newcastle–Ottawa Scale; CES-D: Centre for Epidemiologic Studies Depression Scale

Table 4.5: Summary of reviews conducted to assess the effect of antenatal depression on birth outcomes (N=6, 2007-2018)

Type of outcome	Number of primary studies	Sample size	Estimates from the reviews	Pooled estimates, I^2
LBW	6	14,090	POR=1.21 (95%CI: 0.91, 1.60)	PAOR=1.39 (95%CI: 1.22, 1.58) I^2=35.2% (P=0.213)
	11	13,544	PRR=1.39 (95%CI: 1.19, 1.61)	
	8	25,663	POR=1.96 (95%CI: 1.24, 3.10)	
Total	25	53,297		
Preterm birth	15	23,754	POR=1.37 (95%CI: 1.04, 1.81)	PAOR=1.49 (95%CI: 1.32, 1.68) I^2=0.0% (P=0.771)
	20	29,295	PRR=1.49 (95%CI: 1.25, 1.77)	
	14		POR=1.56 (95%CI: 1.25, 1.94)	
Total	39	75,451		

Note: PAOR: Pooled Adjusted Odds Ratio PRR: Pooled Relative Risk POR: Pooled Odds Ratio



***Note**: LBW: Low Birth Weight, PTB: Preterm Birth, POR: Pooled Odds Ratio*

Figure 4.2: Association between antenatal depression, LBW and preterm birth in a systematic review of reviews (N=6, 2007-2018).

4.2.2. Scoping review discussion

The scoping review found a substantial burden of AND in LMICs and developed countries, indicating that it is becoming a major global public health concern. This finding supports prior evidence documenting that depressive disorders are a significant cause of disease burden globally (416, 417). Many studies have found that depression varies with gender, with women being more vulnerable than men because of a range of genetic, hormonal, cultural and economic disparities (54, 418-421). The risk of acquiring depression is two times higher during a female's reproductive ages (422) because of changes in female sex hormones, physical and other burdens of pregnancy, childbirth, and parenting (423-426). Antenatal depression has significant child developmental implications because women, especially those in lower-income countries, tend to take the main child-caring role (427). Because of the intergenerational effect of depression, female children of women affected by depression have twice the risk of acquiring depression in their future pregnancies relative to females born to non-depressed women (428, 429). Supplementing this, a prospective study found that 38% of children of depressed women developed signs of depression by the age of 20 and 65% developed signs by 35 years of age (430). It has been suggested that this intergenerational phenomenon may be at least partly explained by foetal programming (431) and in a major way by environmental-related factors that affect temperament, cognitive development, coping ability, and reactivity to stress (432). There is currently no internationally approved treatment for AND, however, developed countries have started screening pregnant women for depression and providing safe interventions such as psychotherapy (116, 418, 433).

This scoping review identified maternal history of abuse or violence as the number one risk factor for AND. This is a new finding which has not been noted in previous systematic reviews (167, 412). Possible direct biological mechanisms include: (i) individuals with lifetime abuse tended to have altered brain morphology and function (434, 435); (ii) corticotropin-releasing hormone and cortisol production were found to be high in women with exposure to early life adversity (436, 437); and (iii) similar inflammatory and epigenetic pathways were observed in people with depressive symptoms and history of childhood abuse and violence (438, 439). The indirect psychosocial mechanisms include recalling previous depression episodes, lack of social support,

and socio-demographic differences (440-442). This is supported given that personal history of CMDs was also found to be consistently associated with risk of AND in this scoping review.

AND was more prevalent among women who reported poor social or partner support. A buffering role of support from partner, family or friends during pregnancy through enhancing the mother's coping ability and emotional stability has been noted as important in maintaining good mental health (443, 444). On the other hand, lack of social support can give rise to a sense of worthlessness and hopelessness that leads women to experience stress and depression (445). However, the challenge of temporal relationship between social support and antenatal depression should be give due emphasis, one could the cause of the other if direction of association could not be established. Given this, psychological therapy, improving social networks, and providing opportunities for social interaction have been suggested as appropriate interventions to reduce maternal depression (116, 433, 446). However, the quality of such support may largely depend on the quality and duration of relationships and availability of maternal mental health services (176, 447).

Unwanted or unplanned pregnancy and a history of poor obstetric outcomes were found to increase the chance of AND in multiple studies. Disengagement with a current pregnancy might occur because of fear of economic burden or hardship that might increase the likelihood of stress or depression (167). The current scoping review identified a strong link between financial difficulties and antenatal depression. Disengagement with the current pregnancy might also occur because of young age or premarital pregnancy, which may also increase the risk of maternal stress or depression (167, 448). This may be exacerbated in countries in which such pregnancies are outside socio-cultural norms. In relation to this, low education level and risky behavioural practices were also found to increase the odds of AND, because these would create additional layers of stress into women's daily lives. Women with a recent history of adverse pregnancy and birth outcomes might also experience trauma that ultimately affects their psychological functioning (449-452) thus increasing their fear and stress in the current pregnancy (122, 409, 453).

In the current scoping review AND was found to be associated with 49% and 39% increased risk of preterm and LBW, respectively. Various causal pathways have been suggested for the association between antenatal depression and risk of such adverse birth outcomes. (i) Depression may exert an influence on adverse birth outcomes via dysregulation of the hypothalamic–pituitary–adrenocortical axis (16), which stimulates the release of stress hormones such as cortisol, preventing adequate oxygen and nutrient flow to the foetus (44, 454). (ii) Antenatal depression also increases the production of corticotropin-releasing hormone from the placenta, which can lead to premature labour (a situation named 'Placental Clock') (455). In contrast, other studies have reported a lack of correlation between stress hormones and level of cortisol secretion (456, 457), inconclusive findings (458), and an increased level of cortisol hormone secretion in the second and third trimesters of pregnancy (459). However, the evidence that hormonal and psychosocial risk factors play an important role in the cause of LBW and stillbirth remains more convincing than opposing findings. (iii) Depressed women are more likely to have inflammation or infection of the reproductive organs (460, 461) and this might disrupt the maternal immune system, resulting in a greater risk of infections and, potentially, affecting foetal growth (47). (iv) Depressed women may be more likely to consume alcohol and tobacco products, be less likely to attend medical care (57, 462, 463), and have a poor appetite, all of which can impact maternal nutrition and foetal development (464).

To the date of the literature search, this scoping review is the first to summarise the global burden and association of AND with the risk of LBW and preterm births. The evidence was generated from systematic reviews that demonstrated fair to good quality scores on the AMSTAR quality rating scale. Nonetheless, the results of this scoping review have to be interpreted with caution because (i) different screening tools with different cut-off values were used to define AND; (ii) the systematic reviews included primary studies with different study designs; and (iii) reviews from low-income countries were underrepresented. The ecological fallacy might also be an issue to be considered in this review because the associations might not hold across specific countries and at an individual level. These limitations might affect the global generalisability of the findings obtained from this scoping review.

4.2.3. Scoping review conclusions and recommendations

The findings from the current scoping review certainly suggest depression is a major public health problem affecting pregnant women, especially underprivileged women, globally. While the associations between antenatal depression and risk of LBW and preterm birth were relatively modest overall, effects would be more profound in countries with a high burden of antenatal depression and poor mental health care service access and quality. The findings from this scoping review underscore the need for public health and clinical focus on AND, with attention paid to the development of context-specific interventions appropriate to each country.

4.3. Antenatal depression and the risk of adverse birth outcomes: the case of LMICs

This systematic review is an extension of the previous scoping review (presented in section 4.2) and was designed to summarise the burden and association of AND with the risk of adverse birth outcomes tailored to LMICs. CINAHL, MEDLINE, Emcare, PubMed, Psych Info, Psychiatry online, and Scopus databases were systematically searched to identify observational studies conducted on antenatal depression and associated risk factors published between January 1, 2007, and December 31, 2017. The NOS was used for appraising the quality of primary studies to be included in the review. The detailed methodology of this study has been presented in chapter three section 3.2 and this section presents the results, discussion, and conclusions of the findings, which has also been published.

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0227323.

4.3.1. Antenatal depression review results

4.3.1.1. Search

Database searching identified 313 records for antenatal depression and 156 records for its risk on adverse birth outcomes. After excluding 344 duplicates and screening the titles and abstracts of 125 articles, 42 records were excluded. The full text and quality review of the remaining 83 records yielded 73 eligible studies to be included in the systematic review and meta-analysis. From these articles, 64 were on antenatal depression and 9 articles were on the association of AND with adverse birth outcomes (Figure 4.3).

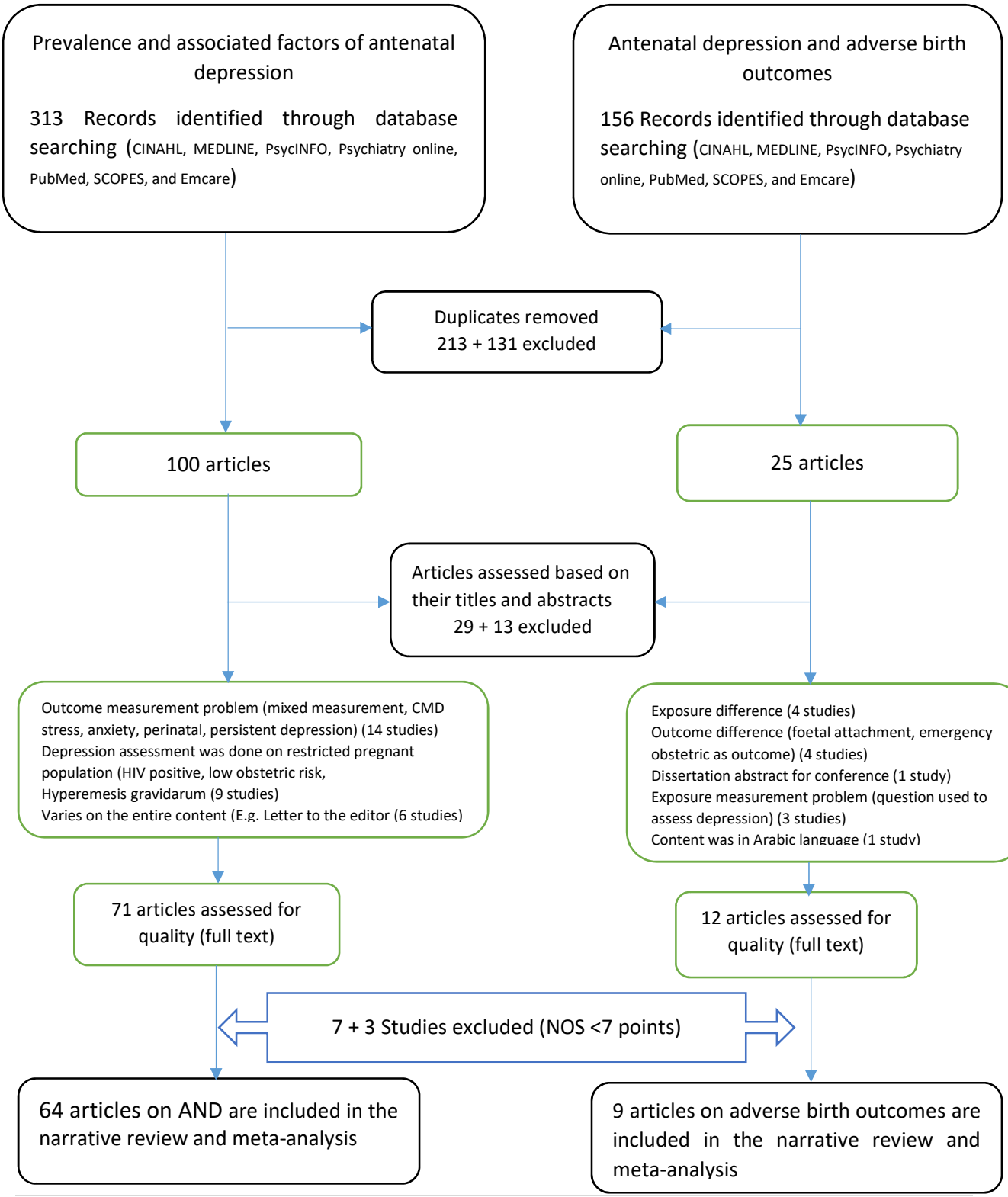

Prevalence and associated factors of antenatal depression
313 Records identified through database searching (CINAHL, MEDLINE, PsycINFO, Psychiatry online, PubMed, SCOPES, and Emcare)
Antenatal depression and adverse birth outcomes
156 Records identified through database searching (CINAHL, MEDLINE, PsycINFO, Psychiatry online, PubMed, SCOPES, and Emcare)
Duplicates removed
213 + 131 excluded
100 articles
25 articles
Articles assessed based on their titles and abstracts
29 + 13 excluded
Outcome measurement problem (mixed measurement, CMD stress, anxiety, perinatal, persistent depression) (14 studies)
Depression assessment was done on restricted pregnant population (HIV positive, low obstetric risk,
Hyperemesis gravidarum (9 studies)
Varies on the entire content (E.g. Letter to the editor (6 studies)
Exposure difference (4 studies)
Outcome difference (foetal attachment, emergency obstetric as outcome) (4 studies)
Dissertation abstract for conference (1 study)
Exposure measurement problem (question used to assess depression) (3 studies)
Content was in Arabic language (1 study)
71 articles assessed for quality (full text)
12 articles assessed for quality (full text)
7 + 3 Studies excluded (NOS <7 points)
64 articles on AND are included in the narrative review and meta-analysis
9 articles on adverse birth outcomes are included in the narrative review and meta-analysis

Figure 4.3: Flow chart of study inclusion for systematic review and meta-analysis of antenatal depression and its effect on birth outcomes in LMICs, (2007-2017).

4.3.1.2. Antenatal depression prevalence and associated factors in LMICS

Of 64 articles (44,035 study participants) included in a meta-analysis of AND, 49 (77%) were found in middle-income countries and 46 (72%) were health institution-based studies. About 20 (31%) studies investigated AND during the last trimester of pregnancy. About 34 (53%) studies used EPDS for screening for AND. A relatively large number of studies, 20 (31%), were published in the year 2015–2016 (Table 4.6).

Pooling all included prevalence studies was impossible because of the high heterogeneity index (I^2=96.7%, P<0.001). As such, pooled estimate from sub-analysis was reported based on the following characteristics: year of publication, income group, study setting, sample size, tools used for screening, and time of pregnancy at which the screening was conducted. The pooled estimate from sub-analysis was adjusted for publication bias because the bias found by Egger's test was significant (P<0.001). The pooled odds ratio was not affected when individual studies were omitted during sensitivity analysis.

Table 4.6: Summary of studies conducted on antenatal depression in LMICs, (N=64, 2007–2017)

	Author, P. year	Country by income	Study setting	Sample size	Trimester screened	Tool used for screening	Prevalence
1.	Adewuya et al. 2007 (465)	Middle	HI	180	3	DSM-IV	8.3%
2.	Esimai et al. 2008 (466)	Middle	HI	195	1,2,3	HADS	10.8%
3.	Gausia et al. 2009 (467)	Middle	Community	361	3	EPDS	33%
4.	Luna Matos et al. 2009 (468)	Middle	HI	222	1,2,3	EPDS	40.1%
5.	Mitsuhiro et al. 2009 (469)	Middle	HI	1000	1,2,3	CESD-10	12.9%
6.	Pereira et al. 2009 (470)	Middle	HI	331	3	CESD-10	14.2%
7.	Pottinger et al. 2009 (471)	Middle	HI	452	1,2,3	EPDS	25%
8.	Golbasi et al. 2010 (472)	Middle	Community	258	1,2,3	EPDS	27.5%
9.	Silva et al. 2009 (473)	Middle	HI	1264	1,2,3	EPDS	21.1%
10.	Kaaya et al. 2010 (474)	Low	HI	560	2	HSC	39.5%
11.	Mohammad et al. 2011 (475)	Low	HI	353	1,2,3	EPDS	67.2%
12.	Nasreen et al. 2011 (476)	Low	Community	720	3	EPDS	18.3%
13.	Li et al. 2011 (25)	Middle	HI	454	1,2,3	EPDS	39.0%
14.	Lau et al. 2011 (477)	Middle	HI	1609	2	EPDS	35.9%
15.	Senturk et al. 2011 (478)	Middle	HI	971	3	EPDS	33.1%
16.	Faisal-Cury et al. 2011 (479)	Middle	HI	312	2	BDI	21.1%
17.	Melo Jr et al. 2011 (292)	Middle	HI	600	3	EPDS	24.3%
18.	Hartley et al. 2011 (480)	Middle	Community	1062	1,2,3	EPDS	39.0%
19.	Rochat et al. 2011 (481)	Middle	HI	109	2	DSM-IV	47%
20.	Ajinkya et al. 2012 (482)	Middle	HI	185	1,2,3	BDI	9.2%
21.	Fisher et al. 2012 (34)	Middle	Community	419	1	EPDS	22.4%
22.	Fisher et al. 2012 (34)	Middle	Community	419	3	EPDS	10.7%

23.	Fisher et al. 2012 (34)	Middle	Community	419	1,2,3	EPDS	17.4%
24.	Silva et al. 2012 (483)	Middle	Community	1264	1,2,3	EPDS	20.5%
25.	Lara et al. 2012 (484)	Middle	Community	250	1,2,3	CESD-10	16.2%
26.	Manikkam et al. 2012 (35)	Middle	HI	387	3	EPDS	38.5%
27.	Fadzil et al. 2013 (175)	Middle	HI	175	1,2,3	HADS	10.3%
28.	Jiong et al. 2013 (176)	Middle	Community	1262	1,2,3	EPDS	20.2%
29.	Bindt et al. 2013 (312)	Middle	HI	719	3	PHQ	28.9%
30.	Dibaba et al. 2013 (187)	Low	Community	627	3	EPDS	19.9%
31.	Gemta et al. 2013 (188)	Low	HI	660	1,2,3	EPDS	25.6%
32.	Guo et al. 2013 (328)	Middle	HI	654	3	PHQ	26.3%
33.	Guo et al. 2013 (327)	Middle	HI	654	3	PHQ	28.3%
34.	Dmitrovic et al. 2014 (178)	Middle	HI	212	3	EPDS	21.7%
35.	Abujilban et al. 2014 (30)	Low	HI	218	3	EPDS	57%
36.	Actas et al. 2014 (289)	Middle	HI	266	1,2,3	BDI	18.8%
37.	Stewart et al. 2014 (485)	Low	HI	583	2	SRQ	21.1%
38.	Weobong et al. 2014 (250)	Middle	Community	2086	1	SRQ	9.9%
39.	Waqas et al. 2015 (274)	Middle	HI	289	3	HADS	31.8%
40.	Barrios et al. 2015 (273)	Middle	HI	1521	1	PHQ	29.1%
41.	de Oliveira et al. 2015 (141)	Middle	HI	358	3	EPDS	28.2%
42.	Abdelhai et al. 2015 (486)	Middle	HI	376	1,2,3	HADS	10.4%
43.	Mahenge et al. 2015 (261)	Low	HI	1180	1,2,3	HSC	78.2%
44.	Rwakarema et al.; 2015 (37)	Low	HI	397	1,2,3	EPDS	33.8%
45.	Heyningen et al. 2015 (256)	Middle	HI	376	1,2,3	CIS-R	22.0%
46.	Biratu et al. 2015 (127)	Low	HI	393	1,2,3	EPDS	24.9%

47.	Bavle et al. 2016 (26)	Middle	HI	318	1,2,3	EPDS	12.3%
48.	George et al. 2016 (283)	Middle	Community	202	1,2,3	CIS-R	16.3%
49.	Moshki et al. 2016 (31)	Middle	HI	208	3	EPDS	37.0%
50.	Padmapriya et al. 2016 (32)	Middle	Community	1144	1	EPDS	7.3%
51.	Alvarado-Esquivel et al. 2016 (286)	Middle	HI	270	1,2,3	EPDS	37.4%
52.	de Jesus Silva et al. 2016 (281)	Middle	HI	209	1,2,3	HADS	14.8%
53.	de Moraes et al. 2016 (9)	Middle	HI	375	1,2,3	HADS	40.8%
54.	Malqvist et al. 2016 (36)	Middle	Community	1038	3	EPDS	22.7%
55.	Thompson et al. 2016 (38)	Middle	HI	314	1,2,3	EPDS	24.5%
56.	Ayele et al. 2016 (57)	Low	HI	388	1,2,3	BDI	23.0%
57.	Bisetegn et al. 2016 (165)	Low	Community	527	1,2,3	EPDS	11.8%
58.	Bitew et al. 2016 (53)	Low	Community	1311	2	PHQ	29.5%
59.	Gelaye et al. 2017 (75)	Middle	HI	1298	2	PHQ	10.3%
60.	Huanging et al. 2017 (260)	Middle	HI	4210	1,2,3	HADS	12.5%
61.	Shidhaye et al. 2017 (33)	Middle	HI	302	1,2,3	EPDS	16.9%
62.	Coll et al. 2017 (258)	Middle	Community	4130	2	EPDS	16.0%
63.	Mossie et al. 2017 (255)	Low	HI	196	1,2,3	BDI	31.1%
64.	Sahile et al. 2017 (487)	Low	HI	233	3	BDI	31.2%

Note: HSC: Hopkins Symptom Checklist; **CIS-R**: Clinical Interview Schedule–Revise; **HI**: Health Institution; **BDI**: Beck Depression Inventory; **EPDS**: Edinburgh Postnatal Depression Scale; **HADS**: Hospital Anxiety and Depression Scale; **CIS-R**: Clinical Interview Schedule Revised; **SRQ**: Self Reporting Questionnaire; **CESD-10**: Centre for Epidemiological Studies Depression Scale; **DSM-V**: Diagnostic and Stastical Manual of Mental Disorder; **PHQ**: Patient Health Questionnaire

Pooled prevalence (PP) of AND was highest in the year 2011–2012 (PP=28.6%, 95%CI: 22.3, 34.8), followed by the year 2015–2016 (PP=26.8%, 95%CI: 17.8, 35.8). AND was higher in low-income countries (PP=34.1%, 95%CI: 22.7, 45.6) and in health institution-based studies (PP=27.6%, 95%CI: 23, 32.3) compared with middle-income countries and community-based studies, respectively. AND was found to increase over the three trimesters: 17.1% (95%CI: 7.7, 26.5) in the first trimester, 27.1% (95%CI: 19.7, 34.6) in the second trimester, and 28.9% (95%CI: 23.7, 34.1%) in the third trimester. The pooled AND prevalence was high in studies with fewer than 600 participants (PP=25.7%; 95%CI: 22.1, 29.5) and those that used the Hopkins Symptom Checklist for screening depression (PP=58.9%, 95%CI: 21, 96.8) (Table 4.7).

Table 4.7: Sub-analysis of antenatal depression prevalence in LMICs (N=64, 2007–2017), (Random effect model)

Variables of sub-analysis	Number of studies (%)	Sample size	Pooled prevalence; 95%CI
Year of publication			
2007–2008	2 (3.13)	375	9.46 (6.5, 12.5)
2009–2010	8 (12.5)	4,448	26.4 (19.5, 33.4)
2011–2012	16 (25.0)	9,533	28.6 (22.3, 34.8)
2013–2014	12 (18.7)	8,116	23.8 (18.3, 29.3)
2015–2016	20 (31.2)	11,194	26.8 (17.8, 35.8)
2017	6 (9.4)	10,369	18.2 (14.6, 21.8)
Income of the country			
Low income	15 (23.4)	8346	34.1 (22.7, 45.6)
Middle income	49 (76.6)	35,689	22.7 (20.1, 25.2)
Study setting			
Health institution	46 (71.9)	26536	27.6 (22.9, 32.3)
Community based	18 (28.1)	17499	19.8 (16.1, 23.5)
Time of screening			
First trimester	4 (6.2)	5170	17.1 (7.7, 26.5)
Second trimester	8 (12.5)	9912	27.1 (19.7, 34.6)

Third trimester	20 (31.2)	9532	28.9 (23.7, 34.1)
All trimester	32 (50.0)	19421	23.9 (18.2, 29.5)
Median sample size			
<=600	42 (65.6)	13290	25.7 (22.0, 29.5)
>600	22 (34.4)	30745	24.8 (18.9, 30.6)
Tool used for screening depression			
EPDS	34 (53.1)	23,612	27.2 (23.5, 30.8)
CIS-R	2 (3.1)	578	19.3 (13.8, 24.9)
PHQ-9	6 (9.4)	6157	25.4 (17.3, 33.4)
SRQ-20	2 (3.1)	2669	15.4 (4.4, 26.4)
Hopkins symptom checklist	2 (3.1)	1740	58.9 (20.9, 96.8)
BDI	6 (9.4)	1580	22.2 (15.7, 28.6)
HADS	7 (10.9)	5829	18.6 (11.8, 25.4)
DSM-IV	2 (3.1)	289	27.4 (10.5, 65.3)
CESD-10	3 (4.7)	1581	13.6 (11.9, 15.3)

Note: BDI: Beck Depression Inventory; EPDS: Edinburgh Postnatal Depression scale; **HADS**: Hospital Anxiety and Depression Scale; **CIS-R**: Clinical Interview Schedule Revised; **SRQ**: Self Reporting Questionnaire; **CESD-10**: Centre for Epidemiological Studies Depression Scale; **DSM-V**: Diagnostic and Stastical Manual of Mental Disorder

Unlike findings in the scoping review presented in section 4.2, poor obstetric history (POR=2.01; 95%CI: 1.67, 2.42) and economic difficulties (POR=2.03; 95%CI: 1.63, 2.53) were the most common risk factors for AND in LMICs. Poor obstetric history was identified in 16 studies and economic difficulties was identified in 14 studies as being significantly associated with risk of AND. Poor social support (POR=1.77 95%CI: 1.49, 2.10) and a history of CMDs (POR=3.27; 95%CI: 2.47, 4.33) were significantly associated with the risk of AND in 13 studies. Moreover, having a history of violence identified in 11 studies (POR=2.99; 95%CI: 2.20, 4.07), unsatisfactory marital relationship in 9 studies (POR=2.18; 95%CI: 1.64, 2.90), and male gender preference in four studies (POR=1.41; 95%CI: 2.97, 6.26) were the remaining risk factors associated with AND (Table 4.8).

Table 4.8: Risk factors significantly associated with antenatal depression, a meta-analysis of studies in LMICs (N=64, 2007–2017), (estimate from random effect model after trim and fill analysis)

Variable of sub-analysis	Number of studies	Sample size	POR, 95%CI	I^2, p-value
Poor obstetric history (*history of adverse birth outcome, unwanted pregnancy, obstetric complications*)	16	13450	2.01 (1.67, 2.42)	81.7%, p=0.137
Economic difficulties	14	11207	2.03 (1.63, 2.53)	74.3%, p=0.001
Poor social support	13	7372	1.77 (1.49, 2.10)	85.7%, p=0.001
History of CMD (*depression, anxiety, stressful life events*)	13	11799	3.27 (2.47, 4.33)	89.9%, p=0.001
History of all forms of violence	11	7428	2.99 (2.20, 4.07)	71.7%, p=0.001
Unsatisfactory marital condition (*Unmarried, divorced, separated, shorter marital duration, polygamous*)	9	7533	2.18 (1.64, 2.90)	73.0%, p=0.001
Male gender preference (the family preferred male to female child)	4	1135	2.97 (1.41, 6.26)	88.2%, p=0.001

4.3.1.3. Association of antenatal depression with the risk of adverse birth outcomes in LMICS

Nine studies investigated the association between antenatal depression and the risk of adverse birth outcomes. Of these, six were in middle-income countries and were conducted in community settings, with half of them using the EPDS to screen depression. Almost all (8, 90%) of the studies were prospective cohort design with a combined sample size of 5,540. Antenatal depression was significantly associated with LBW in five of seven studies. Similarly, half of the studies reported significant associations between antenatal depression and preterm birth (Table 4.9).

The results from a meta-analysis showed that the risk of having adverse birth outcomes (LBW or preterm birth) was 1.59 times (95%CI: 1.34, 2.92) higher among antenatally depressed women relative to those without depression. Compared with LBW, the risk of preterm birth was significantly higher in pregnant women with signs of depression (PRR=2.41; 95%CI: 1.47, 3.56) (Figure 4.4). The pooled relative risk was adjusted for publication bias (P<0.001) using Tweedie and Duval's trim and fill analysis in the random effect model (Figures 4.5 & 4.6).

Table 4.9: Summary of studies conducted on the effect of antenatal depression on adverse birth outcome in LMICs, (N=9, 2007–2017)

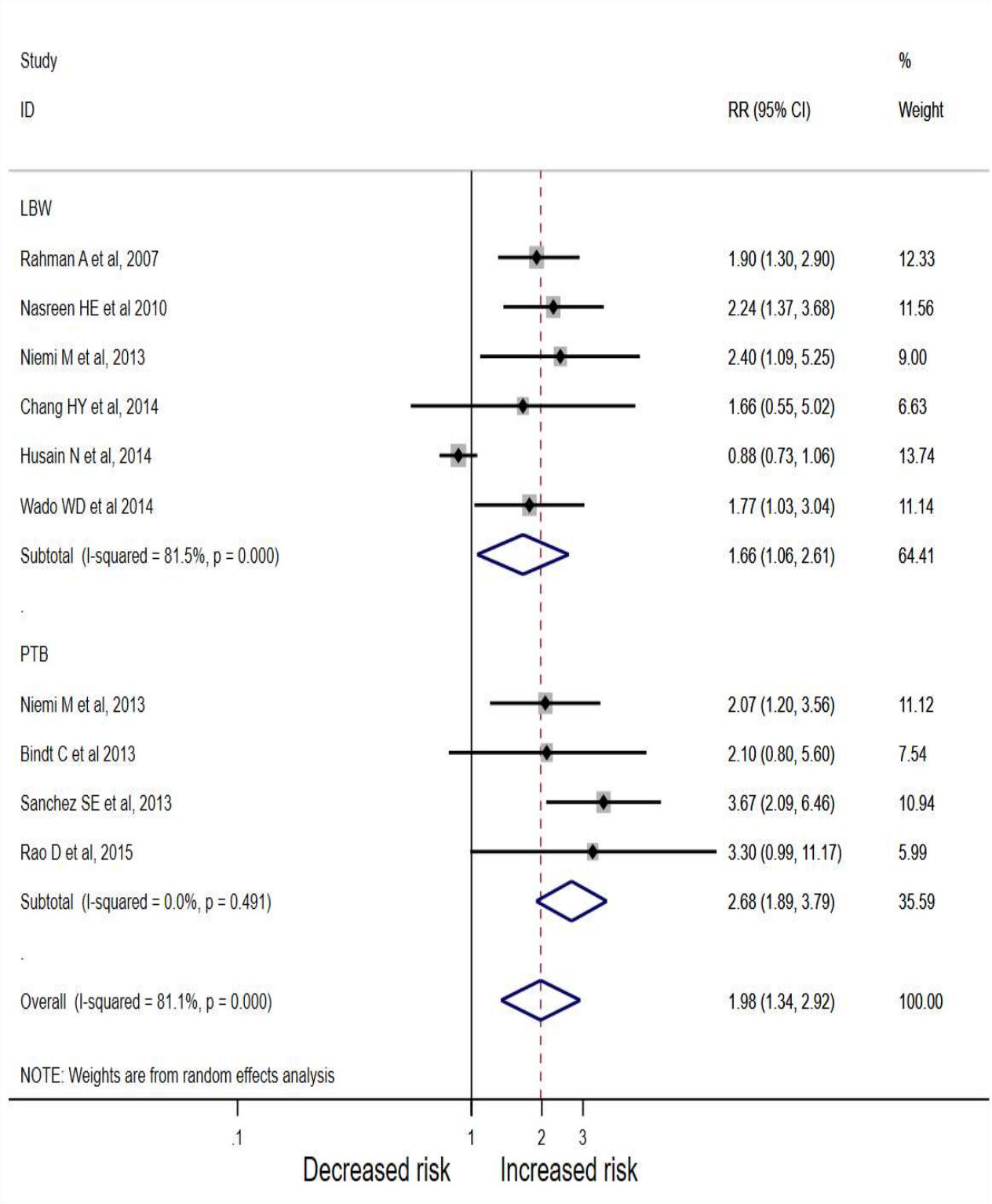
Author, Year	Country, income	Study setting	Study design	Sample size	Follow up start time	Tool used for screening	LBW (<2500gm) RR/OR; 95%CI	PB(<37weeks), OR/RR: 95%CI
Rahman et al. 2007 (488)	Pakistan, Low	Community	Prospective cohort	290	3rd	ICD-10	1.9; 1.3, 2.9	
Nasreen et al. 2010 (489)	Bangladesh, Middle	Community	Prospective cohort	720	2nd and 3rd	EPDS>=10	2.24; 1.37, 3.68	
Niemi et al. 2013 (301)	Vietnam, Middle	Community	Prospective cohort	334	3rd	EPDS >=3	2.40;1.09, 5.25	2.07, 1.2, 3.56
Sanchez et al. 2013 (319)	Peru, Middle	HI	Case control	959	3rd	PHQ-9>=10		3.67, 2.09, 6.46
Chang et al. 2014 (310)	Korea, Low	HI	Prospective cohort	691	3rd	CESD-10>=10	1.66; 0.55, 5.02	
Husain et al. 2014 (308)	Pakistan, Low	Community	Prospective cohort	763	3rd	EPDS >=12	0. 88; 0.73, 1.06	
Rao et al. 2015 (318)	India, Middle	HI	Prospective cohort	150	2nd & 3rd	PHQ-9>=5		3.3, 0.99, 11.17
Bindt et al. 2013 (312)	Ghana, Middle	HI	Longitudinal, birth cohort	719	3rd	PHQ-9 >=10	β=52.2; 18.2, 122.6	2.1, 0.8, 5.6
Wado et al. 2014 (55)	Ethiopia, Low	Community	Longitudinal, birth cohort	537	2nd & 3rd	EPDS>=13	1.77; 1.03, 3.04	

LBW: Low Birth weight; **PB**: preterm birth **HI**: Health Institution; **ICD-10**: International Classification of Disease 10th; **EPDS**: Edinburgh Postnatal Depression Scale; **SRQ**: Self Reporting Questionnaire; **CESD-10**: Centre for Epidemiological Studies Depression Scale; **PHQ**: Patient Health Questionnaire

As the test for heterogeneity (I^2=81.1%, p=0.0) was significant, the final estimate was stratified by variables deemed responsible for the heterogeneity. As such, the risk of adverse birth outcomes was high in middle-income countries (PRR=2.51; 95%CI: 1.92, 3.28), in health institution-based studies (PRR=2.92; 95%CI: 1.92, 4.43), and when depression commenced in the second trimester (PRR=2.47; 95%CI: 1.76, 3.46). The association between antenatal depression and adverse birth outcomes did not differ between studies in which pregnant women were clinically diagnosed with depression and those who were identified based on a self-reported scale (Table 4.10). The sensitivity analysis showed that removing any study from a meta-analysis did not alter the estimates of the pooled relative risk of adverse birth outcomes (Figure 4.7).

Table 4.10: Sub-analysis of the effect of antenatal depression on adverse birth outcomes in LMICs (N=9, 2007-2017), (random effect model, I^2=81.1%)

Variable of sub-analysis	Number of studies (%)	Sample size	Pooled RR; 95%CI	I^2, p-value
Income of the country				
Low income	4	2324	1.42 (0.85, 2.38)	81.3%, p=0.029
Middle income	5	3216	2.51 (1.92, 3.28)	0.0%, p=0.736
Study setting				
Health institution	4	2519	2.92 (1.92, 4.43)	0.0%, p=0.607
Community-based	5	3021	1.72 (1.11, 2.67)	83.6%, p=0.002
Time follow up started				
2nd and 3rd trimester	3	2366	2.47 (1.76, 3.46)	19.3%, p=0.454
Third trimester	6	3174	1.66 (1.04, 2.66)	78.9%%, p=0.026
Tool used for screening depression				
EPDS	4	2688	1.70 (1.01, 2.83)	84.1%, p=0.01
PHQ-9	3	1828	3.20 (2.04, 5.04)	0.0%, p=0.633
ICD-10	1	290	1.90 (1.30, 2.90)	
Type of adverse birth outcomes				
Low birth weight	6	3712	1.66 (1.06, 2.61)	81.5%%, p=0.008
Preterm birth	4	2496	2.41 (1.47, 3.56)	0.0%, p=0.620
Sample size				
<350	3	1151	2.07 (1.55, 2.77)	0.0%, p=0.83
>=350	6	4389	1.84 (1.05, 3.25)	85.9%, p=0.001



Note: RR: relative risk; PTB: Preterm birth; LBW: Low birth weight

Figure 4.4: Association between antenatal depression and adverse birth outcomes (N=9, 2007–2017) in LMICs sub-analysed by type of outcomes.

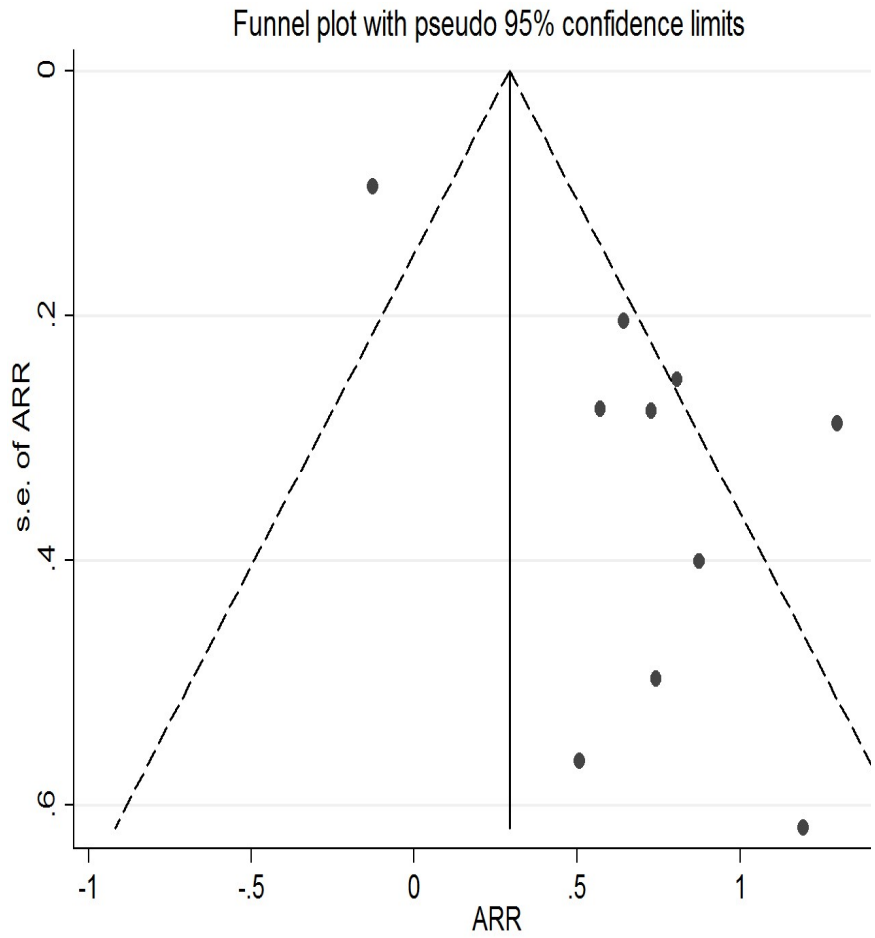


Figure 4.5: Funnel plot before Tweedie and Duval's trim and fill analysis

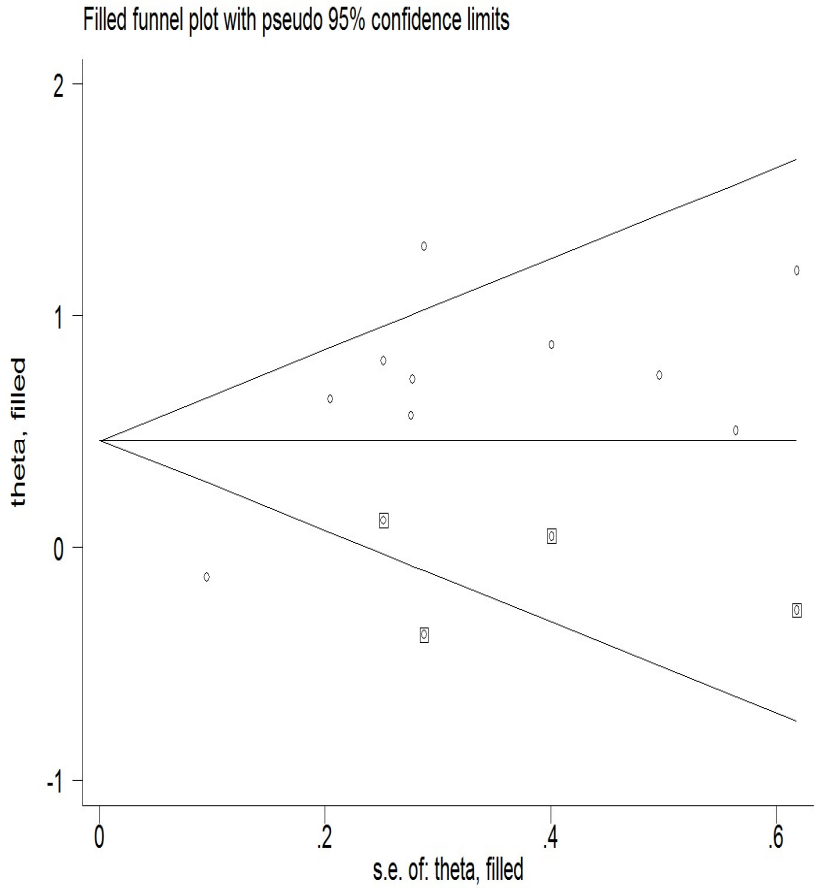
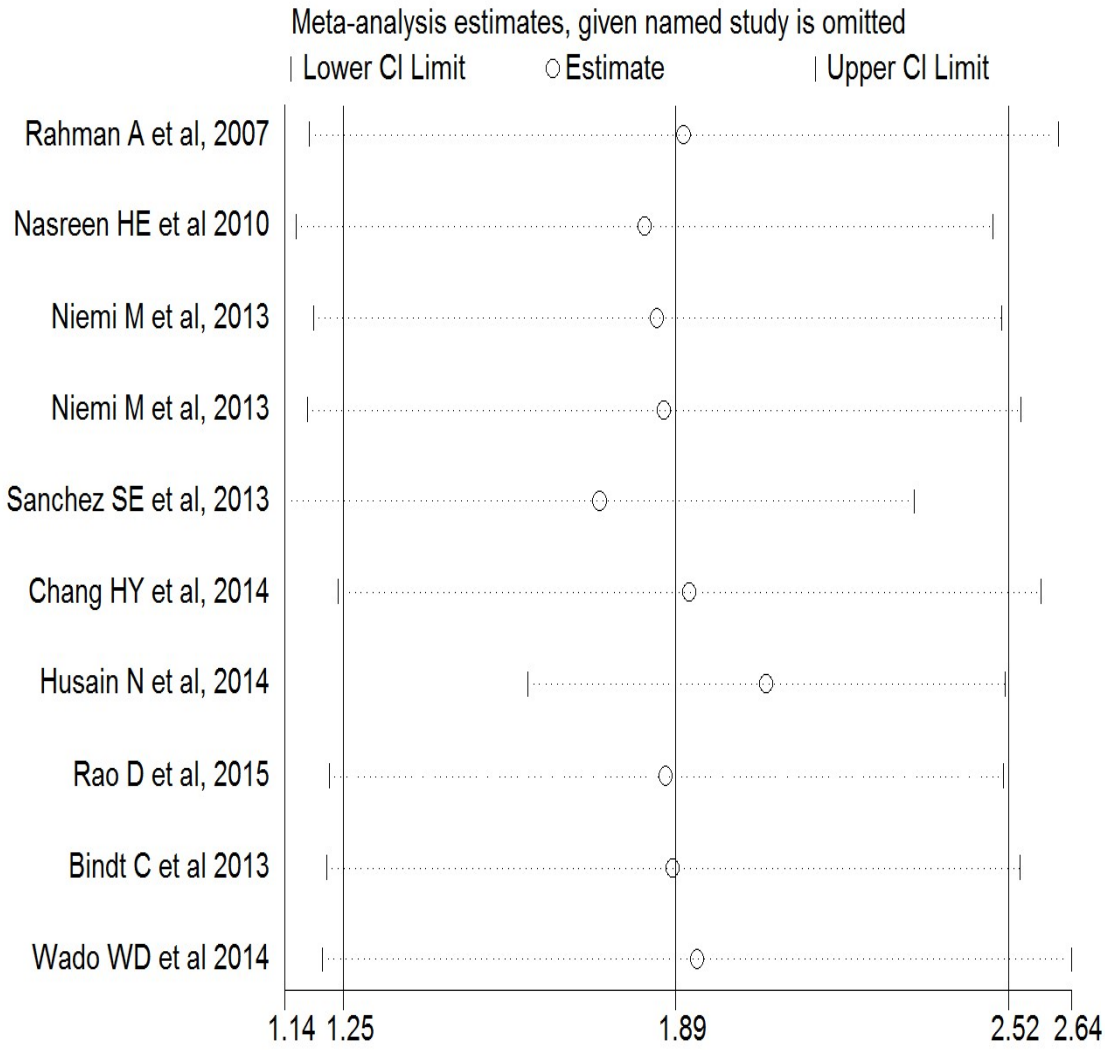


Figure 4.6: Funnel plot after Tweedie and Duval's trim and fill analysis (filled by four studies)



Note: CI: confidence interval

Figure 4.7: Sensitivity analysis for studies on antenatal depression and its association with adverse birth outcomes (N=9, 2007–2017) in LMICs

4.3.2. Antenatal depression review discussion

This systematic review provided concise estimates about the epidemiology of antenatal depression and its association with the risk of adverse birth outcomes in LMICs. The pooled prevalence of AND found in LMICs was in the range of the global estimate of AND reported in section 4.2. This review found that the prevalence of AND has increased over time (from 9.5% in 2007 to 18.2% in 2017). The increase might support predictions that depression will become the third leading cause of disease burden in low-income countries by 2030 or might be due to the symptom scales picking up transient distress in response to ongoing social adversities (12, 490). Consistent with previous reviews (50, 491), this review found significantly higher AND prevalence in low-income countries relative to middle-income countries. Depression has not previously been prioritised as an area for intervention relative to other problems during pregnancy in low-income countries (491). Risk factors of such CMDs are also thought to be more common in low-income countries relative to middle-income countries (50). The review identified that AND increases from the first to the third trimester of pregnancy, which contrasts with the quadratic pattern (increase during the first and third trimesters of pregnancy) reported elsewhere (20). An increased pattern of depression from the first to the second trimester because of increases or persistent manifestation of risk factors during the whole pregnancy was also reported elsewhere (492). Further studies could assist in identifying the appropriate timing and frequency of screening and risk factors that are common in each trimester of pregnancy to employ targeted interventions.

Unlike the finding from the scoping review (presented in section 4.2), poor obstetric history (such as unwanted pregnancy, multiparity, history of miscarriage, stillbirth, and preterm birth) was the primary risk factor for AND in this study. This is the most plausible explanation of the association in this region because maternal and obstetric health services are not well developed and a substantial number of pregnancies end in mortality (493). Bearing larger numbers of children resulting from unplanned pregnancies might create considerable economic impacts that lead to stress (491). History of miscarriage, stillbirth and preterm birth (defined here as a negative pregnancy history) may be associated with trauma and fear about the current pregnancy's outcomes (409). Other complications such as hypertension, diabetes mellitus, and hyperemesis gravidarum could also pose additional stress (494). The familial and recurrent nature of

depression and other mental health morbidities was reported by Shyn and Hamilton (138). Consistent with this finding, a history of CMDs was found to predict a high prevalence of AND in the current review.

Consistent with the current review, a meta-analysis of randomised controlled studies of psychological treatment for CMDs in low-income countries identified social support as an effective intervention (495). Good social support (496) could positively affect the maternal stress coping ability by playing a buffering role in the causal paths between stressors and depression (50, 413, 496). This was also noted in the scoping review presented in section 4.2. Exposure to sexual, physical, and emotional violence before or during pregnancy, including a history of childhood abuse, was identified as the most important risk factor for AND globally (section 4.2). Because this relationship was not consistent across LMICs, further research might require understanding the reasons for these differences. However, as proposed in the previous section, contributing factors may include the disruption of neurobiological and stress response system through changing brain structure and function (497-499) leading to the overproduction of stress hormone. Reduced relationship satisfaction was reported as a risk factor for depression symptoms. The risk for depression was also higher in the context of a family preference for a male child. Family gender preference could directly affect partner relationships in a way that ultimately affects maternal support (50, 167).

Consistent with the scoping review findings (section 4.2), a history of AND was associated with a 59% increased risk of adverse birth outcomes. A similar finding was noted in previous systematic reviews (50, 52), however, Szegda et al. (44) reported no association between antenatal depression and adverse birth outcomes. An increased risk for preterm birth and LBW among women with depression history was consistent with meta-analyses published by Grigoriadis (101) and Grote (47). More importantly, this review found that the association of AND with adverse birth outcomes was found to be similar across diagnostic and screening-based studies. The causal mechanisms suggested between antenatal depression and risk of adverse birth outcomes have been discussed in section 4.2.2. The review included all available high-quality studies on antenatal depression and its effect on adverse birth outcomes in LMICs, however, the estimations

may still be subject to measurement bias. For instance, the way depression is measured plays an important role in variation in estimates and its effects. The estimates from EPDS were consistent with previous reviews but there was greater variation among estimates from studies using other tools (50, 156, 500). Nonetheless, the applied analytical approach that most addressed the heterogeneity provides some confidence that this evidence shows the true burden and consequences of AND in LMICs. The issue of ecological fallacy might also hold true because the associations might not hold across specific countries and at an individual level.

4.3.3. Antenatal depression review conclusions and recommendations

This systematic review found that AND is highly prevalent in and increases through pregnancy, as well as increasing over the last ten years in LMICs. The identified risk factors for AND in LMICs are similar to those reported globally but with some variability. For instance, abuse and violence were the primary risk factors in the global context while poor obstetric history was the primary risk factor in LMICs. Other risk factors, such as lack of social support, previous episode of CMDs, and financial difficulties, are commonly reported in both contexts. Similarly, an association between antenatal depression and risk of adverse birth outcomes was also noted in both reviews. Importantly, the association between antenatal depression and risk of adverse birth outcomes was similar across diagnostic and screening-based studies. Thus, the suggested intervention methods in both reviews are clear and specific: early detection of depression during pregnancy through screening and providing appropriate interventions.

4.4. Postnatal depression and its association with the risk of adverse infant health outcomes in LMICs

While the impact of PND on motherhood and newborn in developed countries is well described, its epidemiology and health consequences in infants are not well known in LMICs. The objective of this review was to determine the burden and association of PND with adverse infant health outcomes in LMICs. A search for observational studies written in the English language and conducted in LMICs between December 1st, 2007, and December 31st, 2017 was conducted in the CINAHL, MEDLINE, Emcare, PubMed, Psych Info, and Scopus databases. The NOS was used for appraising the quality of primary studies to be included in the review. The detailed methodology of this study has been presented in chapter three section 3.3 and this section presents the results, discussion, and conclusions of the findings. The review described in this section has been published https://bmcpregnancychildbirth.biomedcentral.com/articles/10.1186/s12884-020-03092-7.

4.4.1. Postnatal depression review results

4.4.1.1. Search

The database search retrieved 832 records on prevalence and factors associated with PND and 459 records for the effect of PND on adverse infant health outcomes. After excluding duplicates and reviewing titles and abstracts, 1,142 records were excluded. Full-text review of 149 records excluded 67 records. The quality assessment of the remaining 84 records yielded 75 eligible studies for including in quantitative analysis. From these articles, 58 were on PND (57, 95, 191, 195, 200-203, 205, 207-209, 212-217, 220-223, 226, 228, 230-232, 243, 259, 266, 270, 271, 280, 292, 321, 322, 327-331, 334, 338, 501-513). Seventeen articles investigated the association between PND and risk of adverse infant health outcomes (92, 95, 321-324, 326-332, 505, 514-516) (Figure 4.8).

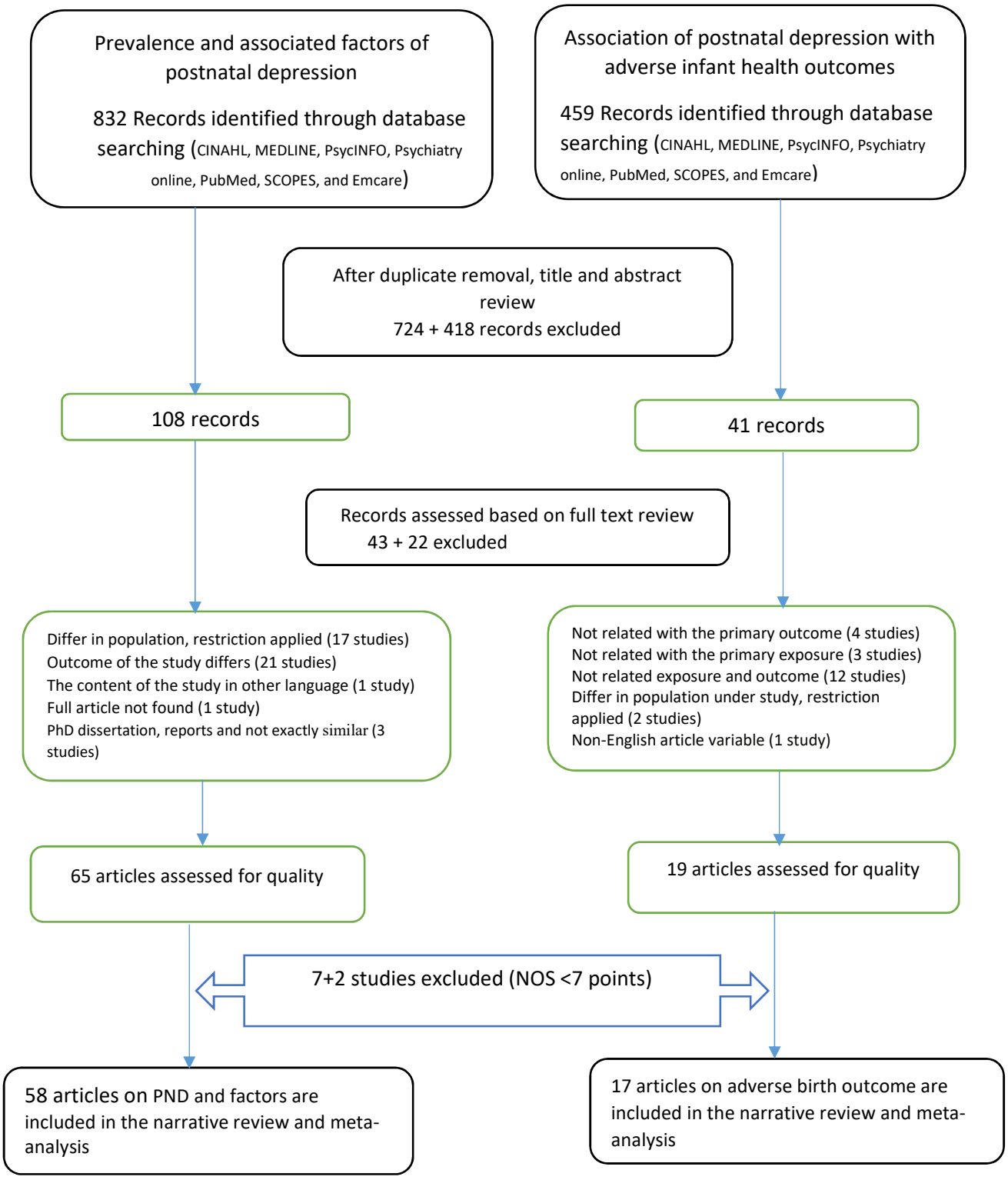


Figure 4.8: Flow chart of study inclusion for systematic review and meta-analysis of postnatal depression and its effect on adverse infant health outcomes in LMICs, 2007–2017.

4.4.1.2. Postnatal depression prevalence in LMICs

In total, 58 studies published between 2007 and 2017 were included, with sample sizes ranging between 87 and 16,560 participants. Of the 58 studies (total 63,293 population), 47 (81%) were conducted in middle-income countries, 38 (66%) were institution-based studies, and 41 (70%) used EPDS for screening depression. Fourteen studies were conducted in Africa, 13 in countries from North and South America, and 31 in Asia. A wide range of PND prevalence was reported across the studies (3.5% in Ghana to 58.8% in Iran). The evidence from Cochran Q (I^2=99.0%), visual inspection of forest plot, and Higgins test (p=0.001) showed significant heterogeneity. As a result, sub-analysis was done while the estimate from DerSimonian and Laird's random-effect model was used to calculate the pooled PND prevalence. Further, because of a significant small study effect (Egger's test, P<0.01), the final estimates in the sub-group analysis were obtained after the trim and fill analysis. A sensitivity analysis showed a PND prevalence ranging between 18.8% and 25.0% (Table 4.11).

Table 4.11: Summary of studies conducted on postnatal depression and associated factors in LMICs (2007–2017), (N=58)

	Author, P. year	Year	Country, income	Study setting	Sample size	Time of assessment	Tool used	Prevalence
1.	Dindar et al. 2007	2007	Middle	HI	679	birth to 48 weeks	EPDS	25.6%
2.	Ege et al. 2008	2008	Middle	Community	364	6 to 48 weeks	EPDS	33.2%
3.	Flores-Quijano et al. 2008	2008	Middle	HI	163	2 to 12 weeks	EPDS	24.5%
4.	Hasselmann et al. 2008	2008	Middle	HI	429	birth to 8weeks	EPDS	35.8%
5.	Tannous et al. 2008	2008	Middle	Community	271	6 to 8 weeks	EPDS	20.7%
6.	Durat et al. 2009	2009	Middle	HI	126	birth to 48 weeks	EPDS	23.8%
7.	Yagmur et al. 2010	2010	Middle	Community	730	birth to 48 weeks	EPDS	21.0%
8.	Botino et al. 2012	2012	Middle	HI	811	birth to 20 weeks	EPDS	24.3%
9.	Goker et al. 2012	2012	Middle	HI	318	4 to 48 weeks	EPDS	31.4%
10.	Pocan et al. 2013	2013	Middle	HI	187	4 to 6 weeks	EPDS	28.9%
11.	Melo Jr. et al. 2012	2012	Middle	HI	555	4 to 6 weeks	EPDS	10.8%
12.	Mathisen et al. 2013	2013	Middle	HI	87	4 to 6 weeks	EPDS	37.2%
13.	Serhan et al. 2012	2012	Middle	Community	110	8 to 24 weeks	EPDS	9.1%
14.	De Castro et al. 2014	2014	Middle	HI	604	birth to 36 weeks	EPDS	10.6%
15.	Lara et al. 2014	2014	Middle	HI	210	24 weeks	SCID-I	13.4%
16.	Corrêa et al. 2016	2016	Middle	HI	3060	birth to 48 weeks	EPDS	19.5%
17.	Robert et al. 2016	2016	Middle	HI	194	birth to 6 weeks	EPDS	40.2%
18.	Ho-Yen et al. 2007	2007	Low	Community	426	4 to five weeks	EPDS	4.9%
19.	Baghianimoghadam et al. 2007	2007	Middle	HI	120	1 to 16 weeks	BDI	58.8%
20.	Gao et al. 2008	2008	Middle	HI	130	6 to 8 weeks	EPDS	13.8%
21.	Kadir et al. 2009	2009	Middle	HI	293	4 to 6 weeks	EPDS	27.3%

22.	Wan et al. 2009	2009	Middle	HI	342	6 to 8 weeks	EPDS	15.5%
23.	Petrosyan et al. 2011	2011	Middle	HI	437	3 months	EPDS	14.4%
24.	Ahmed et al. 2012	2012	Middle	HI	1000	6 to 8 weeks	EPDS	28.4%
25.	Hegde et al. 2012	2012	Middle	HI	150	6 to 14 weeks	EPDS	15.5%
26.	Zainal et al. 2012	2012	Middle	HI	411	6 to 8 weeks	MINI	6.8%
27.	Swapan et al. 2013	2013	Middle	HI	202	6 weeks	PRIME MD	15.8%
28.	Panyayong et al. 2013	2013	Middle	Community	1731	6 to 8 weeks	EPDS	8.4%
29.	Abdollahi et al. 2014	2014	Middle	HI	1801	8 to 12 weeks	EPDS	4.5%
30.	Deng et al. 2014	2014	Middle	Community	1823	4 weeks	EPDS	27.4%
31.	El-Hachem et al. 2014	2014	Middle	HI	228	4 weeks	EPDS	12.0%
32.	Giri et al. 2015	2015	Low	HI	346	6 to 10 weeks	EPDS	30.0%
33.	Yusuff et al. 2015	2015	Middle	HI	2072	4 to 24 weeks	EPDS	14.3%
34.	Murray et al. 2015	2015	Middle	HI	431	4 to 24 weeks	EPDS	18.1%
35.	Shivalli et al. 2015	2015	Middle	HI	102	4 to 6 weeks	EPDS	31.4%
36.	Abdollahi et al. 2014	2014	Middle	HI	1910	12 weeks	EPDS	19.0%
37.	Safadi et al. 2016	2016	Low	HI	315	12 weeks	PHQ-9	25.0%
38.	Iranpour et al. 2017	2017	Middle	Community	360	12 weeks	EPDS	34.8%
39.	Liu et al. 2017	2017	Middle	Community	882	4 weeks	EPDS	6.7%
40.	Ramchandani et al. 2008	2008	Middle	Community	1035	24 weeks	PDQ	16.4%
41.	Stewart et al. 2009	2009	Middle	HI	501	36 weeks	DSM-IV	13.9%
42.	Hassanein et al. 2014	2014	Low	Hi	290	12 weeks	EPDS	39.0%
43.	Mohammed et al. 2014	2014	Low	Community	200	56 weeks	EPDS	49.5%
44.	Khalifa et al. 2015	2015	Low	HI	300	12 weeks	EPDS	9.2%
45.	Stellenberg et al. 2016	2016	Middle	Community	159	6 to 14 weeks	EPDS	50.3%

46.	Weobong et al. 2013	2016	Middle	Community	13, 360	4 weeks	PHQ-9	3.8%
47.	Shamu et al. 2016	2016	Low	HI	842	6 weeks	CES-D	21.4%
48.	Azale et al. 2016	2016	Low	Community	385	24 weeks	PHQ_9	12.1%
49.	Surkan et al. 2009	2009	Middle	HI	595	24 to 48 weeks	CES-D	56.0%
50.	Machado et al. 2014	2014	Middle	HI	168	4 to 12 weeks	EPDS	16.1%
51.	Gausia et al. 2010	2010	Low	Community	318	6 to 8 weeks	EPDS	20.1%
52.	Upadhyay et al. 2016	2016	Middle	Community	1833	20 to 84 weeks	SRQ-20	29.8%
53.	Islam et al. 2016	2016	Low	Community	426	24 weeks	EPDS	35.2%
54.	Saeed et al. 2016	2016	Low	Community	325	96 weeks	AKUADS	40.0%
55.	Ndokera et al. 2008	2008	Middle	community	278	8 to 48 weeks	SRQ-20	9.7%
56.	Guo et al. 2013	2013	Middle	HI	654	12 weeks	PHQ_9	8.9%
57.	Guo et al. 2013	2013	Middle	HI	654	12 weeks	PHQ_9	11.8%
58.	Weobong et al. 2015	2017	Middle	Community	16,560	4 to 12 weeks	DSM-IV	3.5%

Note: **HI**: Health Institution; **PDQ**: Pitt Depression Questionnaire; **AKUADS**: Aga Khan University Anxiety and Depression Scale; **EPDS**: Edinburgh Postnatal Depression Scale; **BDI**: Beck Depression Inventory; **CED**: Centre for Epidemiological studies Depression Scale; **SCID-I**: Structured Clinical Interview for the DSM-IV depression module; **MINI**: Mini International Neuropsychiatric Interview; **PHQ-9**: Patient Health Questionnaire; **SRQ-20**: Self Reporting Questionnaire

Postnatal depression prevalence increased from 18.2% (95%CI: 12.8, 23.5) in 2010–2012 to 25.6% (95%CI: 19.9, 27.2) in 2016–17. The prevalence of PND was higher in low-income countries (Pooled Prevalence (PP)=25.8%; 95%CI: 17.9, 33.8) and in health institution-based studies (PP=22.1%; 95%CI: 18.8, 25.3). The prevalence of PND increased from the earliest weeks of birth (PP=17.6%; 95%CI: 7.7, 27.5) to the end of the second year after the birth (PP=25.2%; 95%CI: 19.9, 30.5). Among screening tools, PND estimated using the diagnostic test (DSM-IV) was the lowest (PP=8.6%; 95%CI: 1.6, 18.8) relative to other screening tools (Table 4.12).

Table 4.12: Sub-analysis of postnatal depression prevalence in LMICs (N=58, 2007–2017), (random effect model, result after trim and fill analysis)

Variable of sub-analysis	Number of studies	Sample size	Pooled prevalence; 95%CI
Year of publication			
2007–2009	15	5,752	25.1 (18.1, 32.2)
2010–2012	10	4,840	18.2 (12.8, 23.5)
2013–2015	20	14,000	19.6 (15.8, 23.5)
2016–2017 (two years)	13	38,701	25.6 (19.9, 27.2)
Income of the country			
Low income	11	4,173	25.8 (17.9, 33.8)
Middle income	47	59,120	20.7 (18.4, 23.1)
Study setting			
Health institution	38	21,717	22.1 (18.8, 25.3)
Community based	20	41,576	20.9 (17.9, 23.9)
Time of screening			
Birth to 4 weeks	5	16,487	17.6 (7.8, 27.5)
5 weeks to 10 weeks	22	26,599	21.9 (18.0, 25.7)
11 weeks to 16 weeks	12	7,683	17.9 (14.1, 21.8)
17 weeks to 96 weeks	19	12,524	25.2 (19.9, 30.5)
Tool used for depression screening			

EPDS	41	25,013	22.6 (19.6, 25.7)
PHQ-9 and SRQ-20	7	17,479	14.4 (6.2, 22.6)
DSM-IV	2	17,061	8.6 (1.6, 18.8)
Other/BDI, CED, SCID-I, MINI/	8	3,740	28.3 (16.9, 39.8)
Sample size			
<=1091	49	19,143	23.4 (20.2, 26.5)
>1091	9	44,150	14.4 (10.6, 18.1)

Note: EPDS: Edinburgh Postnatal Depression Scale; **BDI**: Beck Depression Inventory; **CED**: Centre for Epidemiological studies Depression scale; **SCID-I**: Structured Clinical Interview for the DSM-IV depression module; **MINI**: Mini International Neuropsychiatric Interview; **DSM-IV**: Diagnostic and Statistical manual, 5th edition; **PHQ-9**: Patient Health Questionnaire; **SRQ-20**: Self Reporting Questionnaire

Poor obstetric history in 18 studies (POR=1.98; 95%CI: 1.66, 2.36), history of CMDs in 13 studies (POR=3.30; 95%CI: 1.88, 5.80), and poor social support during the postnatal period in 12 studies (POR=2.44; 95%CI: 1.92, 3.09) were identified as the most common risk factors for PND. Maternal low economic status (POR=2.05; 95%CI: 1.66, 2.54) and concomitant maternal and newborn health issues (POR=3.16; 95%CI: 1.96, 5.08) were reported as risk factors for PND in 12 and 11 studies, respectively. The odds of PND were also found to be higher among postnatal mothers with a history of any form of violence (POR=2.61; 95%CI: 2.16, 3.15) and those who had low educational status (POR=2.06; 95%CI: 1.56, 2.73), in seven studies each (Table 4.13).

Table 4.13: Summary of risk factors significantly associated with postnatal depression in LMICs (N=58, 2007–2017), (random effect model, result after trim and fill analysis)

Variable of sub-analysis	Number of studies	Sample size	POR, 95%CI	I^2, p-value
Poor obstetric history (*unplanned pregnancy, GDM, GHP, labor complication, history of emesis, multiparty*)	18	28,766	1.98 (1.66, 2.36)	64.5%, p=0.001
History of CMD (*depression during pregnancy, family psychiatric illness, stressful life event*)	13	10,074	3.30 (1.88, 5.80)	99.2%, p=0.001
Poor social support	12	11,206	2.44 (1.92, 3.09)	73.8%, p=0.001
Low economic status	12	7,671	2.05 (1.66, 2.54)	96.2%, p=0.001
Concomitant maternal and newborn health issues	11	5,954	3.16 (1.96, 5.08)	91.7%, p=0.001
Exposure to any forms of violence (*physical, emotional, sexual*)	7	5,730	2.61 (2.16, 3.15)	0%, p=0.867
Low maternal educational status	7	5,549	2.06 (1.56, 2.73)	48.2%, P=0.07

CMD: common mental disorder**, GDM:** gestational diabetes mellitus**, GHP:** gestational hypertension

4.4.1.3. Association between postnatal depression and risk of adverse infant health outcomes in LMICs

Seventeen studies (with 33 estimates), with a total of 31,454 postnatal women participants, were included in this analysis. Nine studies were from Africa, eight from Asia, and four were from countries in North America. Fifteen studies represented middle-income countries and five studies represented low-income countries. Twelve (57%) studies were longitudinal and 12 (57%) were community-based, with sample sizes ranging from 166 to 16,560 participants. Centre for Epidemiological Studies Depression scale (CED) and EPDS screening tools were used in 7 (33%) and 5 (23.8%) of the studies, respectively. Of the 33 estimates, 19 were in relation to malnutrition, ten in relation to common infant illness, and four studied non-exclusive breastfeeding. Seventeen estimates reported relative risks (RR), 13 reported odds ratios (OR)

while the remaining three estimated hazard ratios (HR). The associations between PND and malnutrition (underweight, wasting, stunting, short stature), PND and common infant illness (diarrhea, febrile illnesses, cough), and PND and non-exclusive breastfeeding were significant in 12, eight, and three studies, respectively (Table 4.14). The final estimate was adjusted for publication bias by trim and fill analyses in the random effect model (Figures 4.9 & 4.10). As such, PND was associated with 1.31 times increased risk of adverse infant health outcomes (95%CI: 1.17, 1.48). The relative risks for malnutrition, common infant illnesses, and non-exclusive breastfeeding were 1.39 (95%CI: 1.21, 1.61), 1.55 (95%CI; 1.39, 1.74) and 2.55 (95%CI; 1.41, 4.61), respectively. (Figure 4.11).

A final analysis of the association between PND and adverse infant health outcomes was stratified by different characteristics of the studies, which helped to reveal the consistency of association. As such, (i) the pooled estimate for OR (POR=2.62; 95%CI: 2.03, 3.38) was larger than for RR (PRR=1.24; 95%CI: 1.10, 1.41) and HR (PHR=1.44; 95%CI: 1.21, 1.70), this might be odds ratio overestimate the strength of association for common outcomes; (ii) the risk was consistent across studies using EPDS (PRR=2.44; 95%CI: 1.51, 3.81) and PHQ (PRR=1.43; 95%CI: 1.20, 1.72) compared with studies using clinically diagnosed depression (DSM/MINI) (PRR=1.87; 95%CI: 1.61, 2.16); (iii) the RR of adverse infant health outcomes decreased as the age of the infant increased, from 1.75 (95%CI: 1.51, 2.03) up to the age of six months to 1.28 (95%CI: 1.06, 1.54) at the age of 12 months and above; (iv) the risk of adverse infant health outcomes was lower in low-income countries (PRR=1.40; 95%CI: 1.37, 1.74) compared with middle-income countries (PRR=1.59; 95%CI: 1.40, 1.81); and (v) as sample sizes increased, the association between PND and adverse infant health outcomes decreased; from 1.98 (95%CI; 1.63, 2.40) for those included a sample size less than 1500 to 1.27 (95%CI; 1.10, 1.46) for studies with larger sample sizes. The pooled estimate of the association between PND and adverse infant health outcomes was not affected when individual studies were omitted during the sensitivity analysis.

Table 4.14: summary of studies conducted on the effect of postnatal depression on adverse infant health outcomes in LMICs, (2007–2017) (N=17)

	Author, P. year	Country, income	Study setting	Study design	Sample size	weeks	Screening tool used	Infant adverse health outcome	Estimate (RR/OR)	LCI	UCI
1.	Hasselmann et al. 2008	Brazil, Middle	HI	cohort	429	4 to 8 weeks	EPDS	Non-exclusive breastfeeding	1.21	1.02	1.45
2.	Surkan et al. 2009	Brazil, Middle	HI	cross-sectional	595	6 to 12 months	CES	Short stature	1.8	1.1	2.9
3.	Machado et al. 2014	Brazil, Middle	HI	longitudinal	168	1 to 3 months	EPDS	Non-exclusive breastfeeding	1.61	1.19	2.19
4.	Gausia et al. 2010	Bangladesh, Low	Community	longitudinal	318	6 to 8 weeks	EPDS	Diarrhea	1.74	1.25	3.42
5.	Rahman et al. 2016	Pakistan, Low	Community	cohort	279	6 months	DSM-IV	Non-exclusive breast feeding	1.42	0.98	2.06
6.	Upadhyay et al. 2016	India, Middle	Community	longitudinal	1833	5 to 21 months	SRQ-20	Stunting	1.53	1.21	1.92
7.	Islam et al. 2016	Bangladesh, Low	Community	cross sectional	426	6 months	EPDS	Non-exclusive breast feeding	5	2.27	11.11
8.	Saeed et al. 2016	Pakistan, Low	Community	cross sectional	325	2 years	AKUADS	Stunting	3.15	1.91	5.18
								Under weight	3.26	1.99	5.34
9.	Adewuya et al. 2007	Nigeria, Middle	HI	case control	242	6 to 12 weeks	SCID-NP	Poor weight	3.41	1.3	8.52
								Poor height	3.28	1.03	10.47
10.	Guo et al. 2013	Ghana, Middle	HI	follow up	654	3 months	PHQ	Febrile illnesses	1.32	1.01	1.74

	Guo et al. 2013	Cote D'Ivoire Middle						Febrile illnesses	1.57	1.20	2.07
11.	Ashaba et al. 2013	Uganda, low	HI	case control	166	1 -5 years	MINI	Malnutrition	2.4	1.11	5.18
12.	Weobong et al. 2017	Ghana, Middle	Community	longitudinal	16,560	4 to 12 weeks	DSM-IV	Diarrhea	1.8	1.45	2.14
								Cough	1.49	1.28	1.7
								Fever	1.8	1.49	2.11
								Vomiting	1.98	1.26	2.71
13.	Madeghe et al. 2016	Kenya, Middle	HI	cross sectional	200	6 to 14 weeks	EPDS	Non-breastfeeding	6.14	2.45	13.36
								Under weight	4.4	1.91	11.93
14.	Wemakor et al. 2016	Ghana, Middle	HI	cross sectional	384	0-59 months	CED	Stunting	2.48	1.29	4.77
15.	Ndokera et al. 2008	Zambia, Middle	Community	cross sectional	278	2-12 months	CED	Serious illness	1.64	0.51	5.24
								Diarrhea	1.32	0.71	2.48
								Underweight	1.48	0.35	6.22
16.	Maureen M Black et al. 2009	Bangladesh, Low	Community	cross sectional	221	6-12 months	CED	Stunting	2.17	1.24	3.81
17.	Benett et al. 2015	India, Middle	Community	longitudinal	1930	12 months	CED	Stunting	1.18	1.03	1.35
								Underweight	1.11	0.97	1.26
		Ethiopia, Low			1885			Stunting	0.91	0.81	1.02
								Underweight	1.01	0.89	1.15
		Peru, Low			1946			Stunting	1.06	0.93	1.22
								Underweight	0.85	0.6	1.19
		Vietnam Low			1961			Stunting	0.91	0.81	1.02
								Underweight	1.29	1.03	1.62

Note: **HI**: Health Institution; **EPDS**: Edinburgh Postnatal Depression Scale; **CED**: Centre for Epidemiological studies Depression Scale; **MINI**: Mini International Neuropsychiatric Interview, **DSM-IV**: Diagnostic and Statistical manual, 5th edition; **SCID-NP**: Structured Clinical Interview for DSM-IV Axis I Disorders; **PHQ**: Patient Health Questionnaire; **SRQ-20**=Self Reporting Questionnaire; **AKUAD**: Aga Khan University Anxiety and Depression Scale; **LCI**: lower confidence interval, **UCI**: upper confidence interval

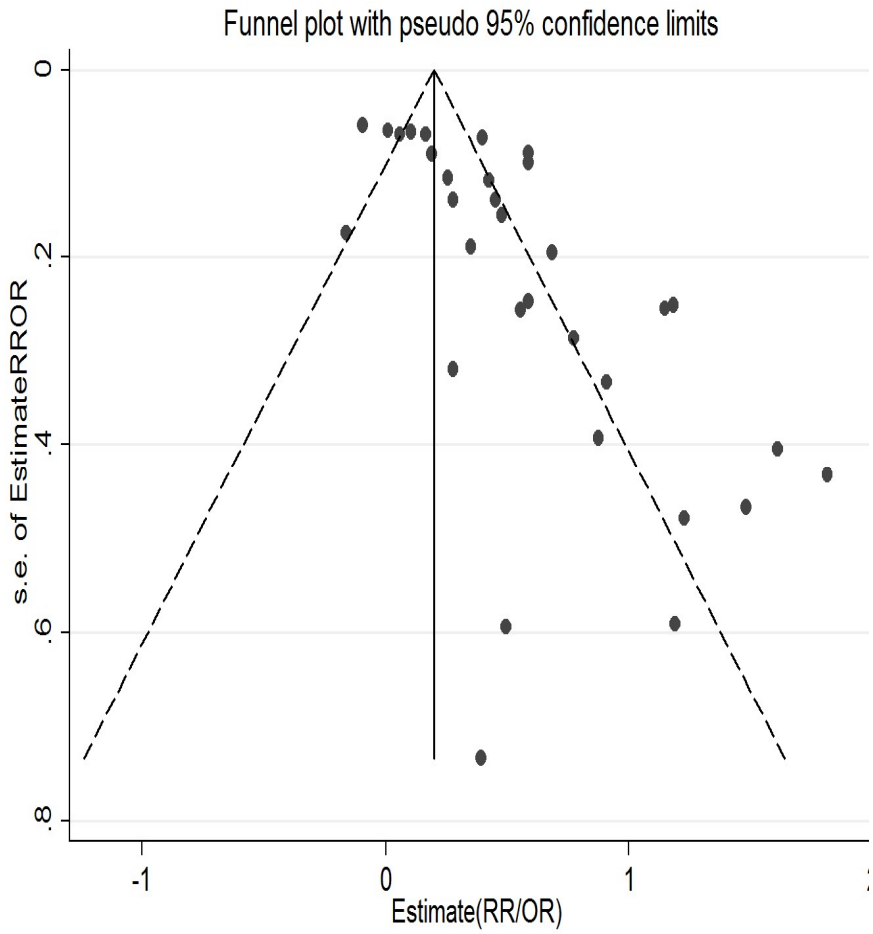


Figure 4.9: Funnel plot before Tweedie and Duval's trim and fill analysis for testing publication bias

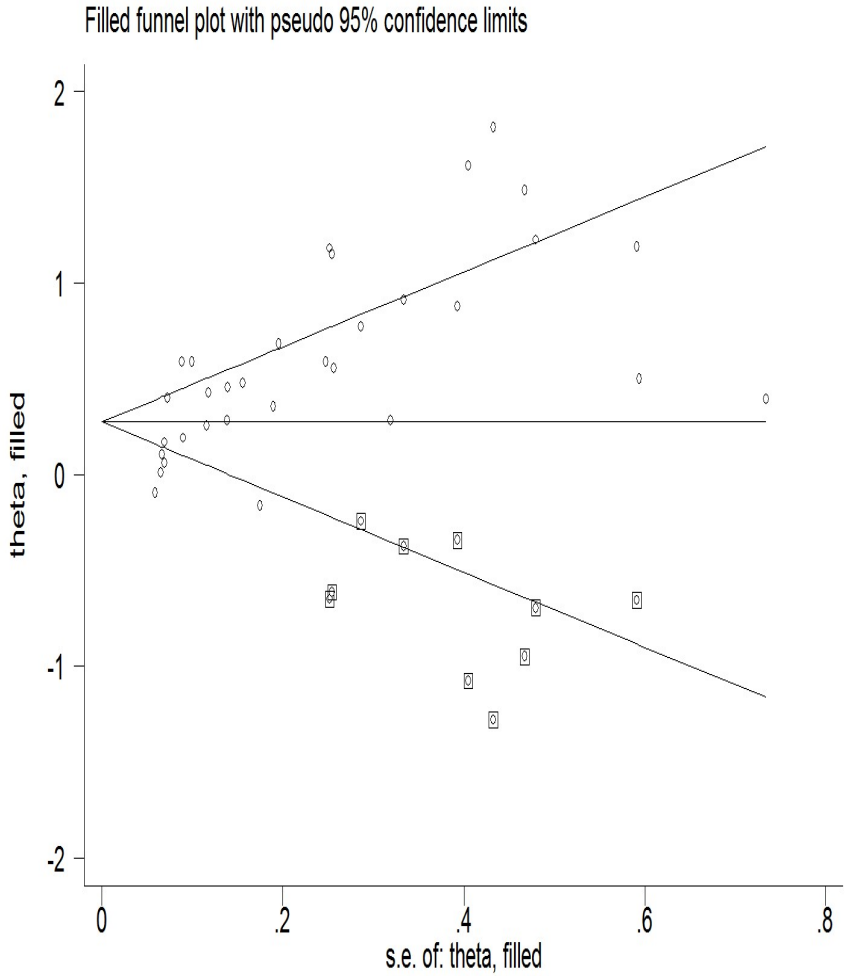


Figure 4. 10: Funnel plot after Tweedie and Duval's trim and fill analysis (10 unpublished studies found on the topic)

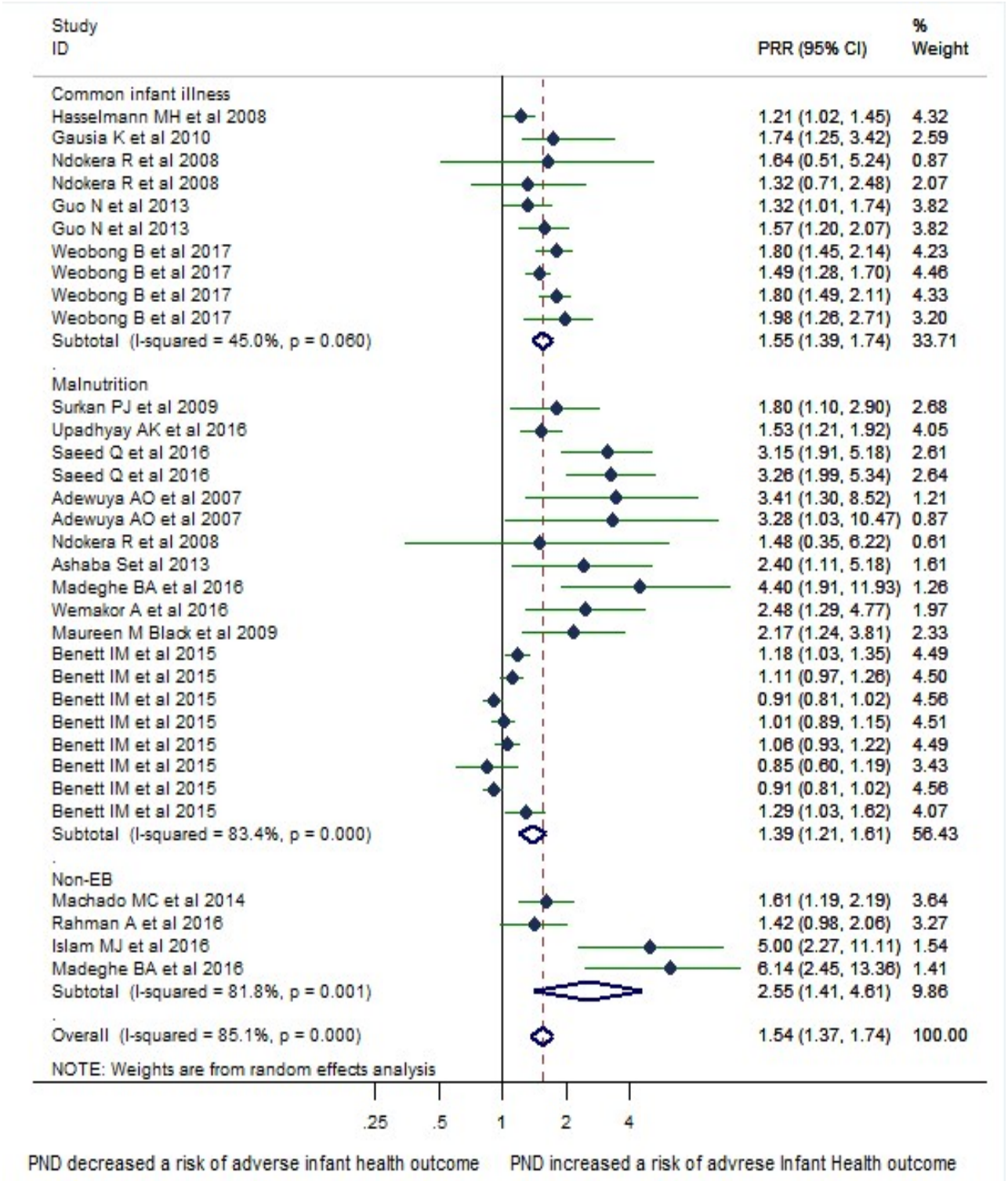


Figure 4.11: Forest plot of the effect of perinatal depression on adverse infant health outcomes (N=17) in LMICs sub analysed by the type of adverse infant health outcome

4.4.2. Postnatal depression review discussion

The current systematic review and meta-analyses included 58 primary studies on PND and 17 studies (with 33 estimates) that dealt with the association of PND with adverse infant health outcomes. The evidence from the meta-analysis showed that one in four women in low-income countries and one in five women in middle-income countries experienced PND. These findings were consistent with findings of a systematic review in LMICs conducted by Gelaye (50) and slightly higher than in reviews conducted in Africa (76, 234). It has been suggested that the rapid decline in reproductive hormone (estrogen) following childbirth, further exacerbated by psychosocial and socioeconomic factors, is the cause of PND (517). PND prevalence has increased from 18% to 25% in the last seven years, supporting the WHO prediction that depression will be the third global leading cause of morbidity by 2030 (12, 490). Postnatal depression was found to increase in the first 10 weeks, slightly decrease from 11 to 16 weeks, and steadily increase again from 17 to 96 weeks after birth. The trend for the first 16 weeks has also been noted in other studies conducted in developed countries (84, 518). However, the interpretation of these estimates should take into consideration the window of measurement, because a wider window predicts larger estimates. Community-based studies, studies using diagnostic tools (DSM-IV) for identifying depression, and studies with larger samples predicted relatively smaller PND prevalences. The PND estimate is relatively consistent with the global estimate of AND (section 4.2) and the AND prevalence estimated in LMICs (section 4.3), suggesting the magnitude of the problem is similar across the perinatal period.

Consistent with AND risk factors (section 4.3), poor obstetric history (unwanted or unplanned pregnancy, multiparity, history of emesis) was an important predictor of PND. Similar to AND, PND could be linked to economic hardship and trauma caused by prior birth and parenting experiences (76, 107). The effect of unwanted or unplanned pregnancies on AND would also continue to be an important predictor of depression during the postnatal period because it does not change. Its effect is generally linked to emotional and instrumental support that women might expect from their partners and families (519). A history of CMDs, poor social support and exposure to violence were identified as significant predictors of AND (section 4.3). Because these factors are mostly unchanged over the perinatal period, it is not surprising that their influence would also support the emergence of PND. These findings are consistent

with previously published systematic reviews (50, 76, 84, 411). Poor social support could aggravate maternal stress and depression symptoms because it may affect self-confidence and efficacy (519, 520), as was also discussed in section 4.3. Pregnant women with existing depression or a history of CMDs were more likely to develop PND. It has been suggested that such individuals may develop diminished positive affect (521) and may have more negative cognitive responses to life events, and such effects may be exacerbated during the perinatal period (522, 523). The effects of childhood abuse and maternal violence on PND are likely to be similar to those of AND, as described in sections 4.2 and 4.3.

Low economic status and poor maternal and newborn health were found to predict PND. Economic adversity was also identified as a risk factor for AND in sections 4.2 and 4.3. This is unsurprising given that economic adversity is unlikely to be resolved in the short time represented by the perinatal period. Women living in low-income countries face challenges in accessing adequate housing, health services and nutrition, and may, therefore, have reduced capacity to provide appropriate care for their newborn, which may increase their stress (474, 524). The existence of mental health problems may affect mother–infant interactions and, potentially, hygiene practices in food preparation and storage. Inadequate care may then predispose the newborn to various neonatal and infant illnesses. Further, feeling unable to care for their infants might increase maternal feelings of guilt, worthlessness and, ultimately, lead to depression (250, 329).

The findings indicate that PND in LMICs remains largely untreated and there is also growing evidence that untreated PND results in adverse infant health outcomes (50, 99-101). The current systematic review and meta-analysis was also able to demonstrate the positive link between PND and infant health and growth. PND increased the risk of malnutrition (stunting, wasting, short stature), common infant illnesses, and non-exclusive breastfeeding. The meta-analysis estimated that 23.7% (7,442) of infant suffering from adverse health outcomes in the study population (31,454) could be attributed to PND. Potentially, these adverse infant outcomes might have been prevented if PND could have been treated. Further stratified analyses also confirmed the strong link between PND and risk for adverse infant health outcomes. PND as a risk for adverse infant health outcomes was consistently found regardless of depression measures, in both institution- and community-based studies, high- and low-income countries, and irrespective of the study sample size. The relationship between PND

and adverse infant outcomes was also seen across all infant age groups, although the risk decreased as the age of the infant increased.

The positive links between PND and malnutrition (99, 321) and infant morbidity (102) were also reported in previous systematic reviews (234, 525). Both biological (genetic and neuro-regulatory system impairment) and environmental pathways could explain the link between PND symptoms and adverse infant health outcomes (99, 526). The endocrine dysregulation associated with PND is thought to compromise psychosocial functioning, which may affect the mother–infant interaction (527). In LMICs, because of patriarchal society, women tend to be more responsible for caring, feeding, and nurturing their newborn through being at home (528). However, they are also more likely to have inadequate incomes, reduced access to quality water, poor sanitation and limited knowledge of common newborn illnesses and their prevention (77). These conditions might exacerbate depression symptoms, and depressed women might not be able to provide the expected level of care for their infants, predisposing the newborn to various health and nutritional problems. High incidence of non-exclusive breastfeeding among postnatally depressed women has been indicated in previous systematic reviews (1, 529). This may be because of the effect of PND on self-efficacy and intention to breastfeed, as explained in the breastfeeding self-efficacy theory (530, 531). As stated, women with self-efficacy are more likely to initiate breastfeeding early, stay breastfeeding for longer, and more easily overcome challenges of breastfeeding.

Methods and timing of depression measurement and other methodological and cultural heterogeneities may have affected the estimations, although the use of analytical methods is likely to have minimised such problems. Overall, this review was able to provide comprehensive evidence about the burden and consequences of PND on infant morbidity, malnutrition, and early breastfeeding cessation in LMICs. The findings further strengthen the available evidence indicating that PND is a major public health threat for birthing women and their infants. It should also be noted, however, that there remains the issue of ecological fallacy as the associations might not hold across specific countries and at an individual level.

4.4.3. Postnatal depression review conclusions and recommendations

The review suggested that 25% of postnatal women in low-income countries and 20% in middle-income countries are affected by PND. Postnatal women who are more likely to report

PND symptoms include those with poor obstetric histories, low social support, histories of CMDs, low economic status, and those who had exposure to any form of childhood violence or concomitant maternal or newborn health problems. Infants of women with PND were also at higher risk of illness, malnourishment and being non-exclusively breastfed relative to infants of women who did not have depression symptoms. Importantly, this effect was similar between studies that diagnosed depression clinically and those using self-reporting scales. Screening pregnant and postnatal women at an early stage and establishing prompt intervention could reduce the burden of depression and the incidence of maternal and infant morbidity, mortality, disability, and future developmental consequences.

4.4.4. Summary of the chapter

Genetic and epidemiological data have demonstrated that depression is a major disorder of the perinatal period worldwide and particularly in LMICs. The scoping and systematic reviews detailed in this chapter were also able to demonstrate depression as a common and important concern of women's perinatal life. Childhood abuse and maternal violence were found to be the leading risk factors for AND in the global context while poor obstetric conditions were the leading risk factor in LMICs. Nonetheless, both factors are common in LMICs, which indicates the need for strong intervention. In order of descending importance, the other identified risk factors were history of CMDs, lack of social or partner support, and low socioeconomic status. Antenatal and postnatal depression were associated with the risk of LBW, preterm birth, and adverse infant health conditions such as diarrhea, acute respiratory infection, and malnutrition, respectively. Low-income countries such as Ethiopia are substantially under-represented in the pooled estimates of antenatal and postnatal depression and associated adverse birth and infant health consequences because limited studies were available. Furthermore, primarily due to ecological fallacy, it would be difficult to apply evidence generated in this geographic area to the context of Ethiopia. The current thesis was undertaken to address this information gap and the results of this work are presented in the next three chapters.

Chapter Five: Antenatal depression and its association with adverse birth outcomes

5.1. Introduction

The studies in this chapter aimed to investigate AND, its causal mechanisms, and its association with risk of adverse birth outcomes such as LBW, stillbirth, and preterm birth in Gondar town. The chapter has two main sub-chapters. The first sub-chapter elucidates the prevalence of antenatal depression and its associated factors by further showing its potential causal mechanisms. The second sub-chapter presents the findings on the association between antenatal depression and risk of LBW, stillbirth, and preterm birth. The sub-chapters start by summarising methods used, continue by describing the main results and discussions, and end by concluding and recommending further actions.

5.2. Antenatal depression and its potential causal mechanisms

This sub-chapter, which focused on elucidating the potential causal mechanisms of AND has been published. https://bmcpregnancychildbirth.biomedcentral.Com/articles/10.1186/s12884-020-02859-2.

5.2.1. Method summary

A total of 960 pregnant women living in six randomly selected kebeles were initially contacted. Fifteen women declined to participate, and five were unavailable after three further attempts to contact. Finally, 940 agreed to participate and were screened for AND. Among the 940 study participants screened, 24 with EPDS ≥ 17 were excluded because of the high likelihood of their having depression and the associated potential limitation to provide informed consent. A total of 916 participants was ultimately included in this analysis (Figure 3.6).

A Structural Equation Modelling (SEM) analysis under a stress process model framework was fitted to explore the direct and indirect causal relationships between the independent (stressors) and the dependent (AND) variables, and to test the hypothesised causal paths (532, 533). The theoretical reasons for using SEM in this analysis were two: the latent nature of the outcome variable (AND) and the theoretical model used to explain the stress process of AND. The SEM has two main components: (i) the measurement model that shows the relationships between the latent outcome variable (AND) and its indicators; and (ii) the

structural model that shows potential causal relationships between the outcome latent variable and its predictors. To fit the final SEM, depression scales were parcelled into three categories using the random-based parcelling algorithm. Parcelling is a way of recategorising unidimensional latent variables with multiple constructs to get better model fit and convergence (534, 535). The first parcel (Depre1) contained the EPDS 1, 4, and 9. The second parcel (Depre2) contained the EPDS 6, 7, and 8. The third parcel (Depre3) contained the EPDS 2, 3, 5, and 10.

Before fitting the structural model, confirmatory factor analysis was conducted to test the model fitness of a measurement model, the EPDS score. Indicators used to evaluate the model fitness were Sartorra–Bentler chi-squared test of fit ($P > 0.05$), Comparative Fit Index ($CFI \geq 0.90$), Tucker–Lewis Index ($TLI \geq 0.90$), Root Mean Square Error of Approximation ($RMSEA \leq 0.08$), Standardised Root Mean Square Residual ($SRMR \leq 0.08$), and coefficient of determination (R^2) (536). The potential stressors and their hypothesised causal paths were selected based on prior subject knowledge (which informed the questionnaire). Further, a multivariate mixed effect regression analysis was performed to help determine variables suitable for inclusion in the SEM. This was conducted after conditioning the model for socio-demographic, obstetric and psychosocial factors, which were significantly associated ($P<0.05$) in bivariate mixed effects regression. The model identified stressors such as income, attitude to the current pregnancy, history of CMDs, and a fear of giving birth. The potential mediators the model identified for the association included social support, marital agreement, and stress coping.

Model fit was assessed for the hypothesised model, and an iterative approach was used to modify the model through adding and removing paths until a theoretically supported and a statistically fitted model was obtained. As the outcome data had evidence of non-normality and a few covariate variables were missing, the Satorra–Bentler robust maximum likelihood estimator was used in building the model (537). A model that was over identified, recursive, simple, theoretically meaningful and the best fit for the data was retained and interpreted (538). The identified causal paths were further checked using the modification indices (337, 338). The standardised beta coefficients of the direct, indirect, and total effects of significant covariates on AND were reported.

5.2.2. Results

5.2.2.1. Socio-demographic characteristics of the participants

Table 5.1. illustrates study participants' socio-demographic characteristics. About two-thirds (561, 61.2%) of participants were in the age category 25–34 years. The mean (±SD) monthly income of participants was 3,496.5 (±2,962.3) Birr and there is an association between income and antenatal depression (p=0.008). About one-third of participants (347, 37.8%) attained a formal education level between grades 9 and 12, and 654 (71.4%) were engaged in non-paid domestic duties. Nearly half of the study participants (441, 49.2%) reported discussing and agreeing on things with their partners most of the time. Almost all study participants (878, 95.8%), reported poor access to food for their family in the last three months. Associations were found between participants' marital situation (p=0.001), food access (p<0.001) and antenatal depression.

Table 5.1: Socio-demographic characteristics of participants included in the study (N=916), Gondar town, Northwest Ethiopia, 2018 (N=916).

Variable/category	Risk of depression			
	Had depression (n=63), n (%)	No depression (n=853), n (%)	Total n (%)	P-value
Mothers' age in years				
18–24	20 (31.8)	271 (31.8)	291 (31.8)	0.707
25–34	37 (58.7)	524 (61.4)	561 (61.2)	
>=35	6 (9.5)	58 (6.8)	64 (7.0)	
Household monthly income				
Low	40 (63.5)	409 (48.0)	449 (49.0)	0.057
Medium	19 (30.2)	355 (41.6)	374 (40.8)	
High	4 (6.3)	89 (10.4)	93 (10.2)	
Mothers' education				
No formal education	12 (19.1)	106 (12.4)	118 (12.9)	0.024
Grades 1–8	13 (20.6)	221 (25.9)	234 (25.6)	
Grades 9–12	31 (49.2)	316 (37.1)	347 (37.8)	
Diploma and above	7 (11.1)	210 (24.6)	217 (23.7)	
Mothers' occupation				
Domestic duties	42 (66.7)	612 (71.7)	654 (71.4)	

Student	2 (3.2)	13 (1.5)	15 (1.6)	0.016
Government employee	4 (6.3)	125 (14.7)	129(14.1)	
Self employed	15 (23.8)	103 (12.1)	118 (12.9)	
Mothers' marital status				
Single	5 (7.9)	11 (1.3)	16 (1.8)	0.001
Partnered	54 (85.7)	826 (96.8)	880 (96.1)	
Separated	4 (6.4)	16 (1.9)	22 (2.1)	
How often partner discuss and agree on things from their own perspectives				
Most of the time	13 (22.8)	428 (51.0)	441 (49.2)	0.001
Sometimes	25 (43.9)	352 (42.0)	377 (42.1)	
Rarely	15 (26.3)	52 (6.2)	67 (7.5)	
Never	4 (7.0)	7 (0.8)	11 (1.2)	
Difficult to access food for their family in the last three months				
Yes	13 (20.6)	25 (2.9)	38 (4.2)	0.001
No	50 (79.4)	828 (97.1)	878 (95.8)	

Note: p-value was calculated based on chi-squared test statistics

5.2.2.2. Obstetric characteristics of participants

Table 5.2 shows the participants' obstetric characteristics. The majority of pregnancies (777, 84.8%) were planned and an association was found between pregnancy intention and antenatal depression (p=0.001). Around two-thirds of the participants (63.0%) were in their third trimester of pregnancy, and the mean (±SD) duration of pregnancy was 27.8 (±6.7) weeks. Approximately one-third (349, 38.1%) were first pregnancies and the mean (±SD) parity was 2.1 (±1.2). Among participants who had two or more children, 547 (96.5%) had no history of LBW and 530 (93.5%) had no history of preterm birth. Participants with signs of depression were more likely to have a preterm history (p=0.001). The majority of participants (721, 78.7%) were afraid of giving birth in the current pregnancy and 130 (14.2%) were underweight. Associations were found between antenatal depression and fear of giving birth (p=0.001), cigarette smoking (p=0.003), and undertaking physical activity (p=0.009).

Table 5.2: Maternal and obstetric characteristics of study participants (N=916), Gondar town, Northwest Ethiopia, 2018 (N=916)

Variable/category	Risk of depression		Total n (%)	P-value
	Had depression (n=63), n (%)	No depression (n=853), n (%)		
Pregnancy condition				
Planned	31 (49.2)	746 (87.5)	777 (84.8)	0.010
Unplanned	32 (50.8)	107 (12.5)	139 (15.2)	
Pregnancy trimester				
2nd trimester	16 (37.9)	323 (25.4)	339 (37.0)	0.048
3rd trimester	47 (62.1)	530 (74.6)	577 (63.0)	
Difficult to conceive in the current pregnancy				
Yes	9 (14.3)	66 (7.7)	75 (8.2)	0.067
No	54 (85.7)	787 (92.3)	841 (91.8)	
Parity of the mother				
1	24 (38.1)	325 (38.1)	349 (38.1)	0.450
2	16 (25.4)	272 (31.9)	288 (31.4)	
3–8	23 (36.5)	256 (30.0)	279 (30.5)	
Preterm history				
Yes	8 (20.5)	29 (5.5)	37 (6.5)	0.001
No	31 (79.5)	499 (94.5)	530 (93.5)	
Low birth history				
Yes	3 (7.7)	17 (3.2)	20 (3.5)	0.144
No	36 (92.3)	511 (96.8)	547 (96.5)	
History of cesarean section				
Yes	5 (12.8)	67 (12.7)	72 (12.7)	0.981
No	34 (87.2)	461 (87.3)	495 (87.3)	
Antenatal care service uptake (at least one)				
Yes	57 (90.5)	815 (95.5)	872 (95.2)	0.069
No	6 (9.5)	38 (4.5)	44 (4.8)	
Had fear of giving birth				
Yes	37 (58.7)	158 (18.5)	195 (21.3)	0.001
No	26 (41.3)	695 (81.5)	721 (78.7)	
Did physical activity				

Yes	59 (93.7)	839 (98.4)	898 (98.0)	0.009
No	4 (6.3)	14 (1.6)	18 (2.0)	
Exposure to cigarette				
Yes	14 (22.2)	86 (10.1)	100 (10.9)	0.003
No	49 (77.8)	767 (89.9)	816 (89.1)	
Exposure to coffee				
Daily	29 (46.0)	351 (41.1)	380 (41.5)	0.078
Sometimes	26 (41.3)	287 (33.7)	313 (34.2)	
Never	8 (12.7)	215 (25.2)	223 (24.3)	
Nutritional status of the mother				
Normal	54 (85.8)	732 (85.7)	786 (85.8)	0.982
Underweight	9 (14.2)	121 (14.3)	130 (14.2)	

Note: p-value was calculated based on chi-squared test statistics

5.2.2.3. Psychosocial characteristics of participants

The psychosocial characteristics are presented in Table 5.3. The majority of participants (853, 93.1%) had no history of CMDs. Close to half of the study participants (420, 46.9%) reported receiving support from their partners. The majority of participants (785, 80.2%) reported good social support and more than half (558, 60.1%) reported rarely coping with stress. Associations were found between antenatal depression and a history of CMDs (p=0.001), social and partner support (p=0.001), and stress coping ability (p=0.042).

Table 5.3: Psychosocial characteristics of study participants (N=916), Gondar town, Northwest Ethiopia, 2018 (N=916).

Variable/category	Risk of depression		Total n (%)	P-value
	Had depression (n=63), n (%)	No depression (n=853), n (%)		
History of common mental disorders				
Yes	11 (17.5)	52 (6.1)	63 (6.9)	0.001
No	52 (82.5)	801 (93.9)	853 (93.1)	
Social support				
Good	36 (57.1)	699 (81.9)	785 (80.2)	0.001
Poor	27 (42.9)	154 (18.1)	181 (19.8)	
Internal consistency (α)	0.76 (high reliability)			

Partner support				
Always	17 (29.8)	403 (48.0)	420 (46.9)	0.001
Most of the time	11 (19.3)	254 (30.3)	265 (29.6)	
Some of the time	20 (35.1)	150 (17.9)	170 (19.0)	
Rarely	9 (15.8)	32 (3.8)	41 (4.5)	
Stress copping				
Very rarely	2 (3.2)	5 (0.6)	7 (0.8)	0.042
Rarely	31 (49.2)	527 (61.8)	558 (60.9)	
Sometimes	26 (41.3)	277 (32.5)	303 (33.1)	
Most of the time	4 (6.3)	44 (5.1)	48 (5.2)	
Internal consistency (α)	0.5 (moderate reliability)			
Depression symptoms				
Yes	63 (6.9%; 95%CI: 5.3, 8.7)			
No	853 (93.1%)			
Internal consistency (α)	0.74 (High reliability)			

Note: p-value was calculated based on chi-squared test statistics

5.2.2.4. Antenatal depression prevalence in Gondar town

Sixty-three participants had an EPDS score ≥ 12, indicating an AND prevalence of 6.9% (95%CI: 5.3, 8.7). Sixteen (4.7%) depressed participants were in their second trimester and 47 (8.1%) in their third trimester. The median (IQR) of EPDS score was 4 (0–5), with the tool demonstrating high reliability (α=0.74) for measuring maternal depression status. In the multivariable mixed effect linear regression model, participants with signs of depression most commonly showed the following characteristics: rarely discussed and agreed on things with their partner; reported difficulty accessing food for their family; had unplanned pregnancy; had feared to give birth for the current pregnancy; had a history of CMDs, and had poor social and partner support.

5.2.2.5. A measurement model for depression and social support

According to confirmatory factor analysis, a measurement model gives a good fit (Root Mean Square Error of Approximation (RMSEA)=0.042, Comparative Fit Index (CFI)=0.99, Tucker–Lewis Index (TLI)=0.98, Standardised Root Mean Square Residual (SRMR)=0.016, coefficient

of determination (R^2=0.81). All factor loadings were found to be significant at p<0.001. A standardised factor loading for the structural model is displayed in figure 5.1.

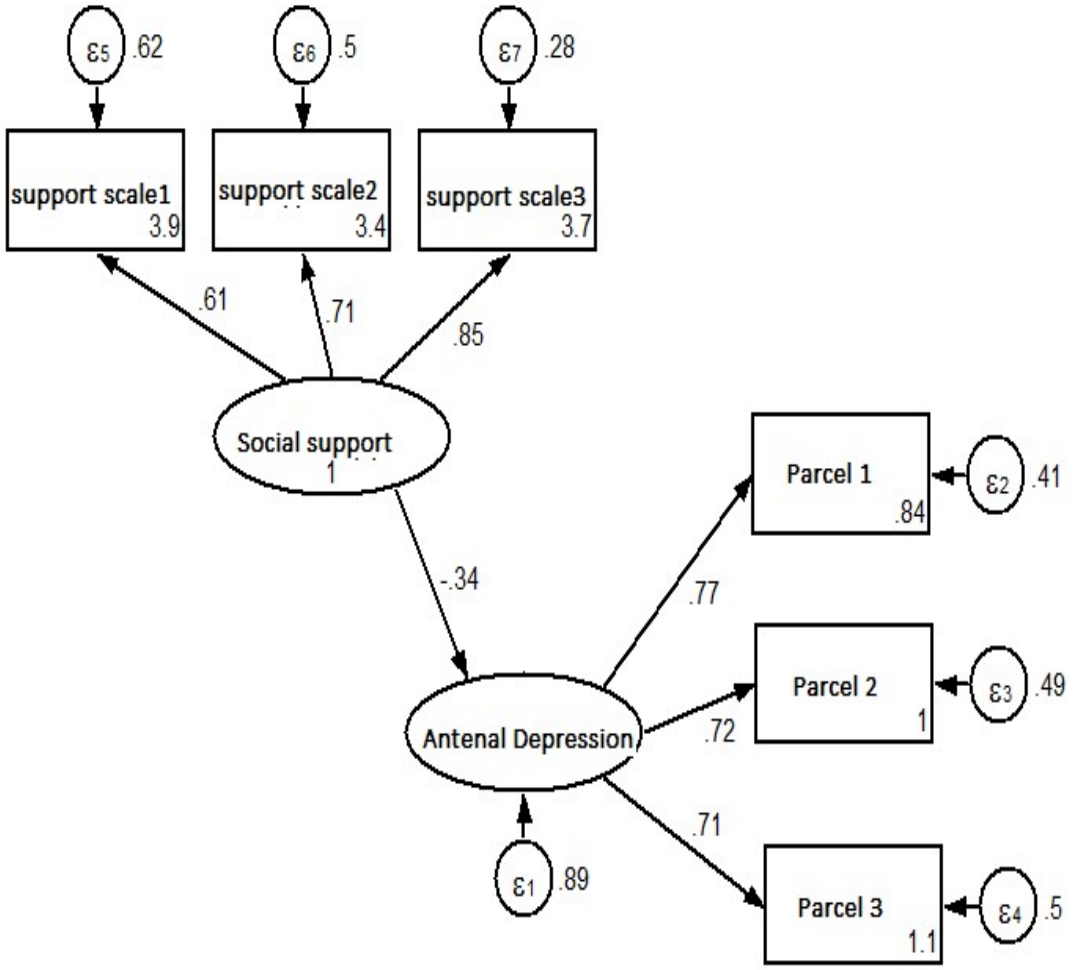


Figure 5.1: Measurement model for social support and antenatal depression (N=916), Gondar town, Northwest Ethiopia, 2018 (N=916).

5.2.2.6. A structural model for elucidating stress process model for antenatal depression

The final structural model is shown in figure 5.2. The final structural model of AND fitted the data well (RMSEA=0.037, CFI=0.98, TLI=0.97, SRMR=0.022, coefficient of determination (R^2=0.35). In the SEM output, in line with the stress process model, stressors and mediators related to participants' depression in the context of Gondar town were identified. Worrying about food for the last three months, a history of CMDs, fear of giving birth for the current pregnancy, and unplanned pregnancy were identified as stressors of AND (p<0.001). Social support, marital situation (satisfaction), and partner support appeared to partially mediate

the effect of stressors on AND ($p<0.001$). The coefficient of determination (R^2) result showed that the model explained 35% of the total variation in depression symptoms.

There were direct (β=–0.11), indirect (β=–0.04), and total (total standardised β=–0.15) negative effects of adequate family food access on AND score. As such, the depression score was decreased by 0.15 standard deviations (SDs) for participants who had adequate food access compared with those who had food access issues. There were direct (β=0.15) and indirect (β=0.11) positive effects of unplanned pregnancy on AND score. Women with unplanned pregnancies had 0.26 more SDs of depression scores compared to other participants (total standardised β=0.26). There was a direct positive effect of fear of giving birth (β=0.29) for the current pregnancy on AND score. As such, an increased AND score of 0.30 SDs (total standardised β=0.30) was found among participants who were afraid of giving birth compared with those who had no fear of giving birth. There was a direct positive effect of a history of CMDs on AND (β=0.18), with an increased depression score of 0.17 SDs found among participants with no history of CMDs (total standardised β=0.17) (Table 5.4 & figure 5.2).

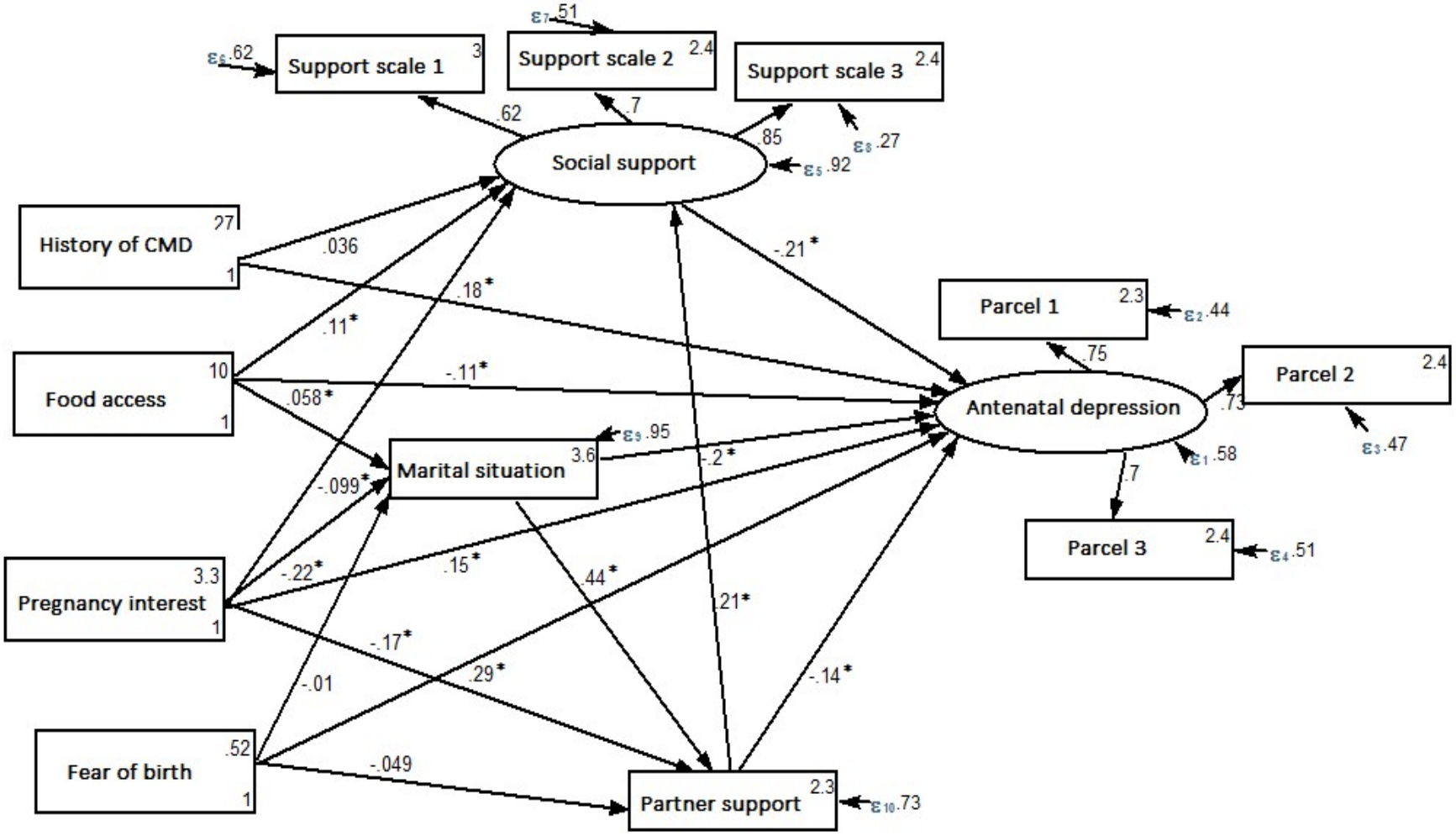


Figure 5.2: Structural equation modelling for a stress process model for antenatal depression (N=916), in Gondar town, Northwest Ethiopia (N=916)

There were direct (β=–0.20) and indirect (β=–0.08) negative effects of marital satisfaction on AND scores. Participant depression score decreased by 0.28 SDs as the level of marital satisfaction increased by one SD (total standardised effect=–0.28). There were direct (β=–0.14) and indirect (β=–0.04) negative effects of partner support on AND score. As partner support increased by one SD, participant depression scores decreased by 0.18 SDs (total standardised effect=–0.18). There was a direct negative relationship between social support and antenatal depression score (β=–0.21). Increasing social support score by one SD would cause a decrease in AND score by 0.21 SDs (total standardised β=–0.21).

Table 5.4: Direct, indirect and total effect of stressors and mediators on antenatal depression score among study participants (N=916), Gondar town, Northwest Ethiopia (N=916)

Pathways	Direct effect β, SE	Indirect effect β, SE	Total effect β, SE
Marital situation (satisfaction) (never (1) ---rarely (2) ---sometimes (3) ---most of the time (4))	–0.20 (0.055) **	–0.08 (0.008) **	–0.28 (0.056) **
Partner support (Never (1) ---rarely (2) ---some of the time (3) ---most of the time (4) ---always (5))	–0.14 (0.041) **	–0.04 (0.009) **	–0.18 (0.041) **
Social support scale (0---14)	–0.21 (0.081) **	-	–0.21 (0.081) **
Adequate food access			
Yes	–0.11 (0.181) **	–0.04 (0.07) *	–0.15 (0.191) **
Intention for the current pregnancy			
Unplanned	0.15 (0.995) **	0.11 (0.05) **	0.26 (0.103) **
Fear of giving birth to the current pregnancy			
Yes	0.29 (0.082) **	0.01 (0.027)	0.30 (0.087) **
History of CMDs			
Yes	0.18 (0.135) **	–0.01(0.032)	0.17 (0.137) **

**≤0.001, *<0.01, β is a standardised estimate

5.2.3. Discussion

A conceptual model developed for pregnant women in Gondar town appears to fit well with the Pearlin stress process theoretical model, thereby revealing potential causal mechanisms of AND (131, 539). The structural model showed that the stressors such as worrying about food, a history of CMDs, fear of giving birth, and unplanned pregnancy, through the partial mediation of social support, marital satisfaction, and partner support, would determine the risk of AND.

Nearly 7% of participants in their second and third trimester had antenatal depression and it was found to be higher among women in their third trimester of pregnancy. This prevalence was slightly lower than a study conducted in Debretabor town (11.8%) (165) and rural areas of Jimma (10.8%) (540). Although the current estimate was also much lower than other estimates reported in Ethiopia (53, 57, 127, 187, 188, 255, 487), it is worth noting the following methodological differences between the current and previous studies: exclusion of participants with a high risk of depression; inclusion of pregnant women only in their second or third trimester; use of different screening tools with different cut-off values; study setting; and use of different data collection approaches. More importantly, risk factors for AND such as low income, unplanned pregnancy, poor social support, and history of pregnancy complications, were more common in previously published studies (413, 491, 494, 496). Despite such discrepancies in prevalence estimates, AND should be considered a major health threat for pregnant women given its documented relationships with adverse birth outcomes such as LBW, preterm birth, and stillbirth (discussed in the next section of this chapter).

Financial difficulty was reported to be the main stressor, with both a direct and indirect effect on AND. The median AND score was significantly lower in participants reporting adequate food access relative to those reporting inadequate food access. Financial stress also had both direct and indirect effects on AND in studies conducted elsewhere (125, 337). Similarly, our recent systematic reviews (documented in chapter four) identified financial problems as a significant predictor of AND. This may be because of the impact of financial stress on maternal self-esteem and social resources of personal coping abilities (166, 541). Having a history of CMDs was another component of stressors that was found to have a direct positive effect on the occurrence of AND.

AND was more common among pregnant women with a personal or family history of mental health morbidities (138) as mental health comorbidities have a familial and recurring nature (182). Some studies have also suggested that pregnant women's recall of previous experiences with depression might increase their chance of developing depressive symptoms in the current pregnancy (542, 543).

A fear of giving birth for the current pregnancy led to a higher positive score for AND in the form of a direct pathway. This may be because fear affects self-esteem, personal coping ability, and psychological preparedness for delivery. The source of the fear might be related to poor obstetric history, lack of experience, and psychosocial problems, all factors which, separately or concomitantly, increase the probability of stress (133, 167, 544). In this causal model, having an unplanned pregnancy was found to increase AND score, directly and indirectly. Unplanned pregnancy is associated with poor personal and social resources which might otherwise buffer the link between such stressors and women's chance of developing depression (15, 16, 545). Similar to other potential stressors, the reasons leading to fear of giving birth should be identified and targeted for intervention at the time of antenatal care visits.

As reported in previous studies (39, 75, 126, 182, 413, 496), satisfaction with the marriage, partner and social support mediated the link between antenatal depression and stressors. In this study, good satisfaction with the marriage and partner support enhanced social support, and their presence synergistically further reduced AND scores. In contrast, lack of partner or social support gave rise to a sense of worthlessness and hopelessness, the worst stage of depression that could end up with maternal suicide or severe psychiatric condition (445). These findings also support the psychosocial stress theory, in which social and partner support are acknowledged as positive mediators of depression and anxiety symptoms (176, 546, 547).

Exclusion of study participants with high depression scores (≥ 17 on EPDS) because of ethical constraints might have resulted in underestimation of AND in the study. The stress process model was based on cross-sectional data, which can make it difficult to establish causality. The omission of variables such as violence and history of abuse, also because of ethical constraints associated with participant burden, and low reliability of the stress coping scale could pose a risk for residual

confounding. Whilst the empirical data best fits the current stress process-model, because of these limitations, it is difficult to rule out a range of other potential alternatives to stress models (548). As such, further studies addressing the limitations above would come up with the best replicable model. Nonetheless, this study is the first to replicate the stress process model developed by Pearlin with a large sample and best fit model in Ethiopia.

5.2.4. Conclusions and recommendations

The estimated prevalence of AND in this study was lower than that estimated in previous studies in Ethiopia. The data suggested and tested a relevant conceptual model that shows potential causal mechanisms of AND in the context of Gondar town. Based on the model, a history of CMDs, unplanned pregnancy, fear of giving birth, and problems with food access were identified as the main stressors of AND. The model also identified marital satisfaction, partner and social support as mediators of a stress process leading to AND. Interventions that can enhance a marital relationship, social and partner support could substantially prevent AND through buffering the effects of other stressors. Screening for depression before and during pregnancy, assessing potential causes of depression, economic interventions to alleviate food insecurity, and providing targeted interventions for women should be considered as necessary steps for prevention. These should be taken as important precautions to reduce the risk of AND on the women and adverse birth outcomes that will be discussed in the following sub-chapter.

5.3. Association of antenatal depression with the risks of LBW, preterm birth, and stillbirth

This sub-chapter, which assessed the risk of AND on LBW, preterm birth, and stillbirth has been published https://journals.plos.org/plosone/article/comments?id=10.1371/journal.pone.0234728.

5.3.1. Method summary

After screening for AND in the second or third trimester (as presented in section 5.2), 916 pregnant women were followed to birth to assess their birth outcomes. During the follow-up, four withdrew from the study, eight were lost to follow-up, and nine were excluded because of their high risk of depression (defined as EPDS >=17). Finally, 895 postnatal women with complete data on birth outcomes were included in this analysis, with a response rate of 97.7% (Figure 3.6).

As occurrences of LBW, preterm birth or stillbirth (collectively referred to here as adverse birth outcomes) were rare, their risk was estimated using a generalised linear model with an identity log and binomial link function (log-binomial) (549). However, because convergence issues were encountered with the use of the log-binomial model (43, 44), a modified Poisson regression (550) was used as a substitute. It has been also suggested that the modified Poisson regression model improves the precision of estimates, is robust to omitted covariates (551, 552), and is efficient for modelling clustered data (553). Risk factors that were significant at $p<0.2$ in the univariate analysis and those assumed to be associated with outcomes were included in the multivariate analysis. The potential moderating effects of assumed variables were tested by including interaction terms into the model (554). The crude and adjusted relative risks with their 95% confidence intervals were presented for variables deemed significant at p-value <0.05.

A Generalised Structural Equation Model (GSEM) was used to investigate the mediation effect of covariates on the causal path between antenatal depression and adverse birth outcomes. The GSEM has the following advantages: (i) it is possible to evaluate potential causal mechanisms with the structural model; (ii) it allows the possibility of exploring direct and indirect effects of multiple interacting variables, simultaneously; and (iii) it has the possibility of choosing different link and distributions appropriate for variables included in the model (555, 556). In this case, a GSEM with logit link function was used for estimating mediating effects as the mediators and outcome variables were binary (557, 558). The direct and indirect paths between the identified covariates and the risk of adverse birth outcomes were reported. The Akaike Information Criteria (AIC) and Bayesian Information Criterion (BIC) were used to refine the initial model suggested by expert knowledge, and lastly, the models with the best fit were retained and interpreted. User-written ldecomp command was used to obtain the coefficients of the direct, indirect and total effects of the mediators and outcome variables (559, 560). Unstandardised beta coefficients, standard errors, and p-values for the direct, indirect, and total effects obtained from the fit model were presented.

5.3.2. Results

5.3.2.1. Socio-demographic characteristics of participants

Table 5.5 shows the socio-demographic characteristics of those participating in the follow-up stage. The mean (±SD) age of participants was 26.5 years (±4.5) and more than half of participants (551, 61.6%) were aged 25–34-years. There was no association between the age of study participants and the risk of adverse birth outcomes (p=0.48). Most participants (714, 79.8%) were Orthodox Christians and 860 (96.1%) were married. There was a significant association between religion and adverse birth outcomes (p=0.012). The majority of participants (639, 71.4%), were engaged in unpaid home duties and 339 (37.9%) had completed secondary education. The mean (±SD) monthly income of participants was 3,516 (±2984) Ethiopian birr. No associations were found between age (p=0.48), income (p=0.52) and risk of adverse birth outcomes.

Table 5.5: Socio-demographic characteristics of study participants included in the follow up (N=895), Gondar town, Northwest Ethiopia, 2018 (N=895)

Variable/category	Adverse birth outcomes			p-value
	Yes (n=163), n (%)	No (n=732), n (%)	Total n (%)	
Mothers' age at enrolment				0.840
18–24 years	51 (31.3)	231 (31.56)	282 (31.5)	
25–34 years	99 (60.7)	452 (61.75)	551 (61.6)	
>=35 years	13 (8.0)	49 (6.7)	62 (6.9)	
Household monthly income				0.760
Low	76 (17.4)	361 (82.6)	437 (48.8)	
Medium	68 (18.6)	297 (81.4)	365 (40.8)	
High	19 (20.4)	74 (79.8)	93 (10.4)	
Mothers' education				0.700
None	17 (10.4)	97 (13.2)	114 (12.7)	
Primary	43 (26.4)	184 (25.1)	227 (25.4)	
High school	66 (40.4)	273 (37.3)	339 (37.9)	
Tertiary	37 (22.7)	178 (24.3)	215 (24.0)	
Mothers' occupation				0.230

Domestic duties	107 (65.6)	532 (72.7)	639 (71.4)	
Student	2 (1.2)	13 (1.8)	15 (1.7)	
Government employee	27 (16.6)	100 (13.7)	127 (14.2)	
Self employed	27 (16.6)	87 (11.9)	114 (12.7)	
Mothers' religion				0.012
Orthodox Christian	117 (71.8)	597 (81.6)	714 (79.8)	
Muslim	45 (27.6)	128 (17.5)	173 (19.3)	
Protestant Christian	1 (0.6)	7 (0.96)	8 (0.89)	
Mothers' marital status				0.430
Single	3 (1.8)	16 (2.2)	19 (2.1)	
Partnered	159 (97.5)	701 (95.8)	860 (96.1)	
Separated	1 (0.61)	15 (2.0)	16 (1.8)	
Difficulty accessing food in the last three months				0.910
Yes	7 (4.3)	30 (4.1)	37 (4.1)	
No	156 (95.7)	702 (95.9)	858 (95.9)	

Note: p-value was calculated based on chi-squared test statistics

5.3.2.2. Obstetric and behavioural characteristics of the participants

Table 5.6 shows the obstetric and behavioural characteristics of study participants. There were 763 (85.2%) planned pregnancies, 341 (38.1%) first pregnancies, and 509 (91.9%) women had no history of adverse birth outcomes. A total of 857 (95.7%) participants attended Antenatal Care (ANC) services, 704 (78.7%) were not fearful about the delivery, and 766 (85.6%) had no nutritional deficits. There were 877 (98.0%) participants who undertook physical exercise at the time of pregnancy. There were 799 (89.3%) participants without tobacco exposure and 369 (41.2%) who consumed coffee daily. Chi-squared test showed that participants with adverse birth outcomes were more likely to report being fearful about the delivery (p=0.018) and had slightly higher mean MUAC measurement (p=0.002).

Table 5.6: Obstetric and behavioural characteristics of study participants included in the study (N=895), Gondar town, Northwest Ethiopia, 2018 (N= 895)

Variable/category	Adverse birth outcomes		Total n (%)	p-value
	Yes (n=163), n (%)	No (n=732), n (%)		
Pregnancy intention				0.570
Planned	141 (86.5)	622 (85.0)	763 (85.2)	
Unplanned	22 (13.5)	110 (15.0)	132 (14.8)	
Parity of the mother				0.680
1	58 (35.6)	283 (38.7)	341 (38.1)	
2	56 (34.4)	228 (31.1)	284 (31.7)	
3–8	49 (30.1)	221 (30.2)	270 (30.2)	
Previous adverse birth history				0.070
Yes	13 (12.4)	32 (7.1)	45 (8.1)	
No	92 (87.6)	417 (92.9)	509 (91.9)	
Antenatal care service uptake (at least one visit)				0.180
Yes	153 (93.9)	704 (96.2)	857 (95.7)	
No	10 (6.1)	28 (3.8)	38 (4.3)	
Fearful about the delivery				0.018
Yes	46 (28.2)	145 (19.8)	191 (21.3)	
No	117 (71.8)	587 (80.2)	704 (78.7)	
Undertook physical activity				0.860
Yes	160 (98.2)	717 (97.9)	877 (98.0)	
No	3 (1.8)	15 (2.0)	18 (2.0)	
Exposure to tobacco				0.89
Yes	17 (10.4)	79 (10.8)	96 (10.7)	
No	146 (89.6)	653 (89.2)	799 (89.3)	
Exposure to coffee				0.5
Daily	66 (40.5)	303 (41.4)	369 (41.2)	
Sometimes	62 (38.0)	247 (33.7)	309 (34.5)	
Never	35 (21.5)	182 (24.9)	217 (24.3)	

Nutritional status of the mother				
Underweight (18–22 cm)	20 (12.3)	109 (14.9)	129 (14.4)	
Normal (22.5–31 cm)	143 (87.7)	623 (85.1)	766 (85.6)	
MUAC mean (±SD)	24.4 (1.6)	23.9 (1.7)		0.002

Note: p-value was calculated based on chi-squared test statistics

5.3.2.3. Psychosocial characteristics of participants

Table 5.7 shows the psychosocial characteristics of participants. The majority (833, 93.1%) of participants had no history of CMDs, 716 (80.0%) reported good social support, and 842 (94.1%) reported good partner support. There were 560 (62.3%) participants who had poor stress coping ability and 58 (6.5%) who had moderate depression symptoms during pregnancy. The chi-squared test showed that poor partner support (p=0.005) and reduced stress coping ability (p=0.049) were associated with the risk of adverse birth outcomes. However, AND was not associated with the risk of adverse birth outcomes (p=0.81).

Table 5.7: Psychosocial characteristics of pregnant mothers included in the study (N=895), Gondar town, Northwest Ethiopia, 2018 (N=895)

Variable/category	Adverse birth outcomes		Total n (%)	p-value
	Yes (n=163), n (%)	No (n=732), n (%)		
History of common mental disorder				0.430
Yes	9 (5.5)	53 (7.2)	62 (6.9)	
No	154 (94.5)	679 (92.8)	833 (93.1)	
Social support				0.440
Good	134 (82.2)	582 (79.5)	716 (80.0)	
Poor	29 (17.8)	150 (20.5)	179 (20.0)	
Internal consistency (α)	0.76 (high reliability)			
Partner support				0.005
Always	95 (58.3)	319 (43.6)	414 (46.3)	
Most of the time	32 (19.6)	230 (31.4)	262 (29.3)	
Some of the time	27 (16.6)	139 (19.0)	166 (18.5)	
Rarely	9 (5.5)	44 (6.0)	53 (5.9)	

Stress coping ability				0.049
Poor	113 (69.3)	447 (61.1)	560 (62.3)	
Good	50 (30.7)	285 (38.9)	335 (37.4)	
Internal consistency (α)	0.5 (moderate reliability)			
Antenatal depression				0.810
Yes	13 (8.0)	45 (6.1)	58 (6.5)	
No	150 (92.0)	687 (93.5)	837 (93.5)	
Internal consistency (α)	0.74 (High reliability)			

Note: p-value was calculated based on chi-squared test statistics

5.3.2.4. Incidence proportion and predictors of adverse birth outcomes

In this study, the incidence proportions for stillbirth, LBW, and preterm births were 1.90% (n=17; 95%CI: 1.11, 3.02), 5.25% (n=47; 95%CI: 3.88, 6.92), and 16.42% (n=147; 95%CI: 14.05, 19.01), respectively. In the multivariate analysis model, religion, occupation, ANC, stress coping ability, partner support, and fear of giving birth were significantly associated with the risk of preterm births. Antenatal depression was not directly associated with the risk of preterm birth. However, an interaction term between partner support and antenatal depression suggested the need for a moderation and mediation analysis. According to the moderation analysis, partner support appeared to moderate the risk of AND on preterm births. As such, study participants who had depression and moderate support were 4.38 (95%CI: 1.25, 15.33) times at higher risk of preterm births, and those who had depression and poor support were 4.99 (95%CI: 1.28, 19.42) times at higher risk of preterm births relative to participants who had no depression and good support.

According to the mediation analysis, there was an indirect effect of AND on preterm birth through partner support (unstandardised β=–0.137, p=0.007). Thus, the effect of AND on preterm birth has been reduced through partner support. Likewise, an indirect effect of AND on preterm birth via the mother's fear of delivery (unstandardised β=0.213, p=0.05) was also seen. This is true because a high level of AND increased fear of delivery and, subsequently, the risk of preterm birth. An indirect effect of AND on preterm birth through stress coping was not significant (Tables 5.8, 5.9, 5.10 & Figure 5.3). The indirect path from AND to preterm birth through the mother's

fear of giving birth was significant although the indirect total effect was non-significant, which might indicate need for further study.

Participants who identified as Muslim were more likely to have preterm birth (ARR: 1.61 95%CI: 1.16, 2.24) compared with their Orthodox counterparts. Likewise, being a Muslim directly (unstandardised β=0.465, p=0.007) and indirectly (unstandardised β=0.125, p=0.017) increased the risk of preterm birth via the mediation effect of maternal stress coping ability and partner support. The risk of preterm birth was 1.46 (ARR=1.46; 95%CI: 1.06, 2.01) times higher among participants who were afraid of giving birth. The direct positive effect of being afraid of giving birth on preterm birth was also suggested in path analysis (unstandardised β=0.535, p=0.013). The risk of preterm birth was higher among participants who were government employees relative to those who performed home duties only (ARR=1.49; 95%CI: 1.01, 2.19). Similarly, the direct positive effect of occupation on preterm birth has been suggested in path analysis (unstandardised β=0.261, p=0.038). Participants who had no ANC were at an increased risk of preterm birth (ARR=1.77, 95%CI: 1.03, 3.03), although this relationship was not observed in path analysis (Tables 5.8 & 5.10, and Figure 5.3).

Table 5. 8: Multivariable analysis of adverse birth outcome predictors in Gondar town, Northwest Ethiopia, 2018 (N=895)

Variables	Preterm birth		Low Birth Weight		Stillbirth	
	CRR, 95%CI	ARR,95%CI	CRR, 95%CI	ARR,95%CI	CRR, 95%CI	ARR,95%CI
Women's religion						
Orthodox	Reference					
Muslim	1.61 (1.17, 2.22)	1.61 (1.16,2.24)*				
Women's occupation						
Domestic duties	Reference					
Government employee	1.32 (0.91, 1.94)	1.49 (1.01,2.19)*				
Self-employee	1.42 (0.95, 2.11)					
Had fear of delivery						
Yes	1.52 (1.11, 2.09)	1.46 (1.06,2.01)*				
No	Reference					
Antenatal care service uptake						
Yes	Reference					
No	1.65 (0.94, 2.86)	1.77 (1.03,3.03)*				
Preterm birth						
Yes			9.86 (5.53,17.56)	9.44 (5.06,17.63)*		
No			Reference			
MUAC measurement of the mother	1.15 (1.06, 1.24)					
Exposure to cigarette smoking						
Yes			1.97 (0.98,3.95)	2.19 (1.10, 4.37)*		
No			Reference			
Symptom of Depression						
No depression	Reference					
Depressed	1.17 (0.67,2.03)		1.72 (0.71,4.18)		3.09 (0.91,10.46)	3.22 (1.04,9.98)*
Try to cope stress						
Poor	Reference					
Good	0.67 (0.48,0.93)				0.36 (0.10,1.24)	0.27 (0.07,0.99)*

The model has been adjusted for age, income, education, marital status, pregnancy intention, previous adverse history, parity, partner and social support.

Note: * significant at p-value <0.05; **CRR**: Crude relative risk; **ARR**: Adjusted relative risk; **95%CI**: 95% confidence interval

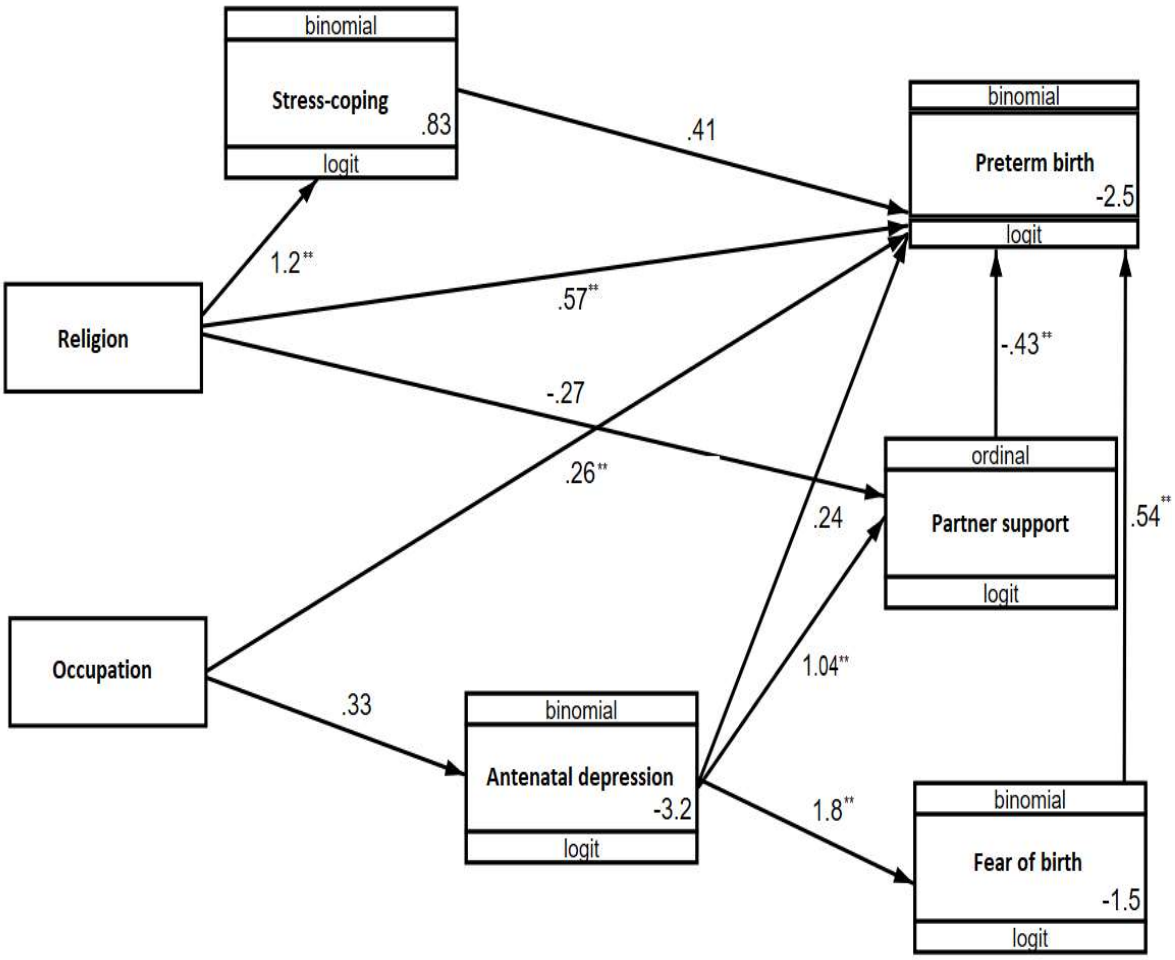


Figure 5.3: A mediation analysis model showing hypothesised causal pathways underlying antenatal depression and preterm birth in Gondar town, Northwest Ethiopia, 2018 (N=895)

The second adverse birth outcome investigated was LBW. After adjusting for confounders, preterm birth and tobacco exposure were found to increase the risk of LBW. Antenatal depression was not directly associated with the risk of LBW. However, further moderation analysis suggested that partner support appeared to moderate the relationship between antenatal depression and the risk of LBW. The risk of LBW was therefore 3.40 times (95%CI: 1.26, 9.17) higher among participants with depression and poor support relative to participants with no depression and good support. However, in a mediation analysis, AND had no direct (unstandardised β=0.341, p=0.460) or indirect total effect (unstandardised β=0.393, p=0.202) on the risk of LBW (Table 5.8, 5.9, 5.10 & Figure 5.4). However, (i) the path between AND → cigarette exposure → LBW; and (ii) the path between AND→partner support→

preterm birth was significant although the indirect total effects were not significant, showing some form of indirect effect that might need further investigation.

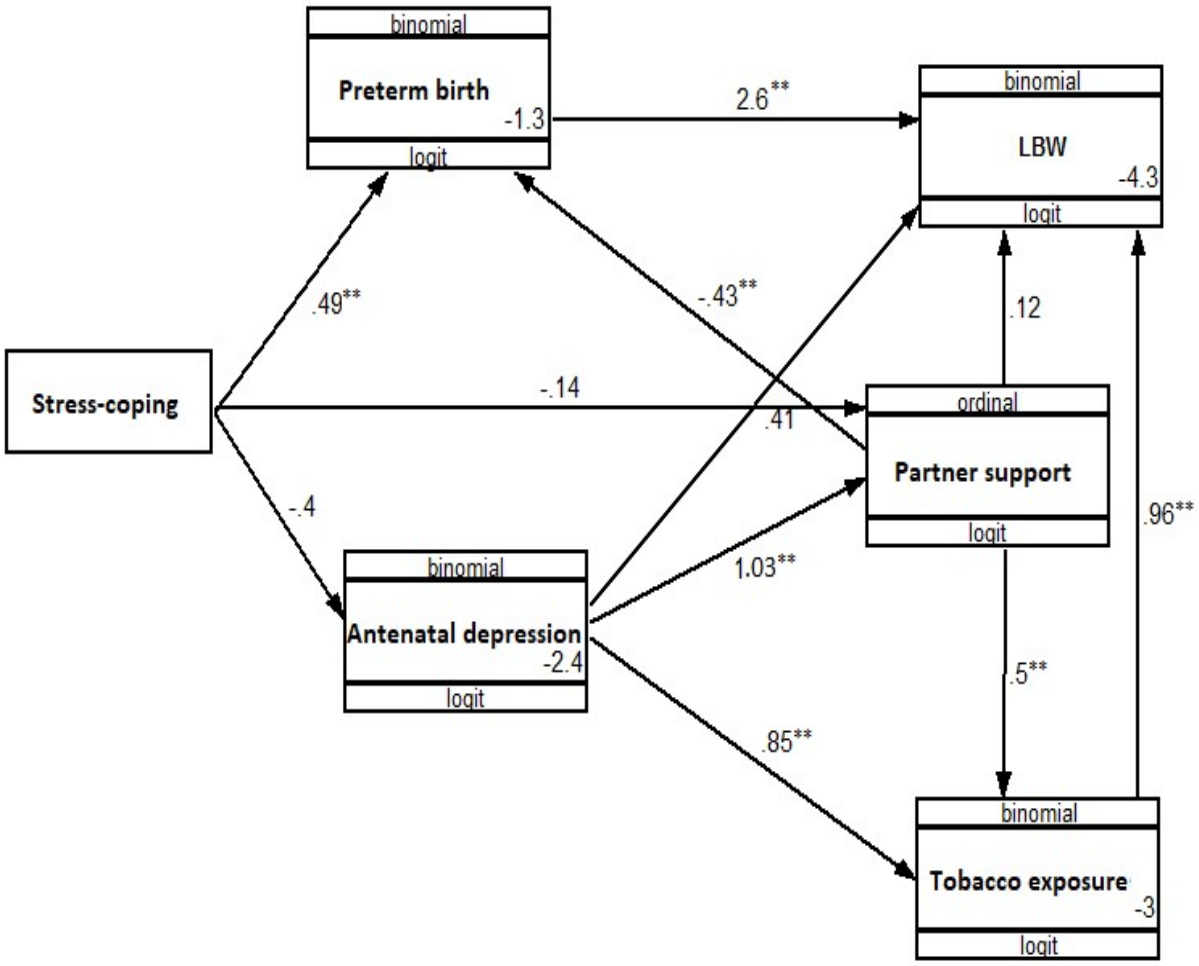


Figure 5.4: A mediation analysis model showing hypothesised causal pathways underlying antenatal depression and low birth weight in Gondar town, Northwest Ethiopia, 2018 (N=895)

Stress coping ability had an indirect effect on LBW (unstandardised β=0.245, p=0.026) through preterm birth (Figure 3 and Table 6). The risk of LBW was 9.44 times (95%CI: 5.06, 17.63) higher among preterm births compared with full term births and preterm birth had also a direct positive effect on the risk of LBW (unstandardised β=2.588, p=0.001) in mediation analysis. Preterm birth also mediated the effect of stress coping ability (unstandardised β=0.245, p=0.026) on the risk of LBW. Tobacco exposure during pregnancy increased the risk of LBW (ARR=2.19; 95%CI: 1.10, 4.37) and its direct effect was also suggested in mediation analysis (unstandardised β=0.961, p=0.03) (Tables 5.8, 5.10 & figure 5.4).

Table 5.9: Relative risk of preterm birth and low birth weight moderated by partner support, in Gondar town, Northwest Ethiopia, 2018 (N=895)

Variables	Preterm birth		LBW	
	Crude RR 95%CI	Adjusted RR 95%CI	Crude RR 95%CI	Adjusted RR 95%CI
No depression and good support	Reference		Reference	
Depressed and good support	1.29(0.69,2.39)	4.38(1.25,15.33)*	not estimatable	not estimatable
Depressed and poor support	0.58(0.09,3.70)	4.99(1.28,19.42)*	2.54(0.39,16.32)	3.40(1.26,9.17)*

*Note: * significant at p<0.05*

The last adverse birth outcome investigated was stillbirth. After adjusting for confounders, the risk of stillbirth was significantly associated with antenatal depression and stress coping ability. The risk of stillbirth was 3.22 (95%CI: 1.04, 9.98) times higher among participants with AND. Nevertheless, this association was attenuated in mediation analysis (unstandardised β=1.265, p=0.054). The risk of stillbirth was decreased by 73% in participants with good stress coping ability (ARR: 0.27; 95%CI: 0.07, 0.99) but was attenuated in mediation analysis (unstandardised β=1.101, p=0.087) (Tables 5.8, 5.10 and Figure 5.5).

Table 5.10: Direct, indirect, and total effect of antenatal depression on adverse birth outcomes in Gondar town, Northwest Ethiopia, 2018 (N=895)

Covariates	**Direct**		**Indirect**		**Total effect**	
	β(SE)	*p-value*	β(SE)	*p-value*	β(SE)	*p-value*
Preterm birth						
Antenatal depression	0.251(0.126)	0.571			0.323(0.40)	0.420
Indirect (partner support)			–0.137(0.051)	0.007		
Indirect (fear of delivery)			0.213(0.109)	0.050		
Fear of delivery	0.535(0.216)	0.013				
Partner support	–0.435(0.169)	0.010				
Religion	0.465(0.198)	0.007	0.125(0.052)	0.017	0.590(0.218)	0.007
Occupation	0.261(0.126)	0.038				
Stress coping ability	0.406(0.208)	0.051				
Low birth weight						
Antenatal depression	0.341(0.341)	0.460	0.393(0.308)	0.202	0.735(0.474)	0.121
Cigarette exposure	0.961(0.441)	0.030				
Preterm birth	2.588(0.339)	0.001				

Partner support	0.255(0.329)	0.439	-0.234(0.131)	0.055	0.021(0.345)	0.951
Stress coping	–0.188(0.303)	0.536	0.245(0.110)	0.026	0.057(0.351)	0.871
Stillbirth						
Antenatal depression (no)	1.265(0.656)	0.054				
Stress coping (poor)	1.101(0.643)	0.087				

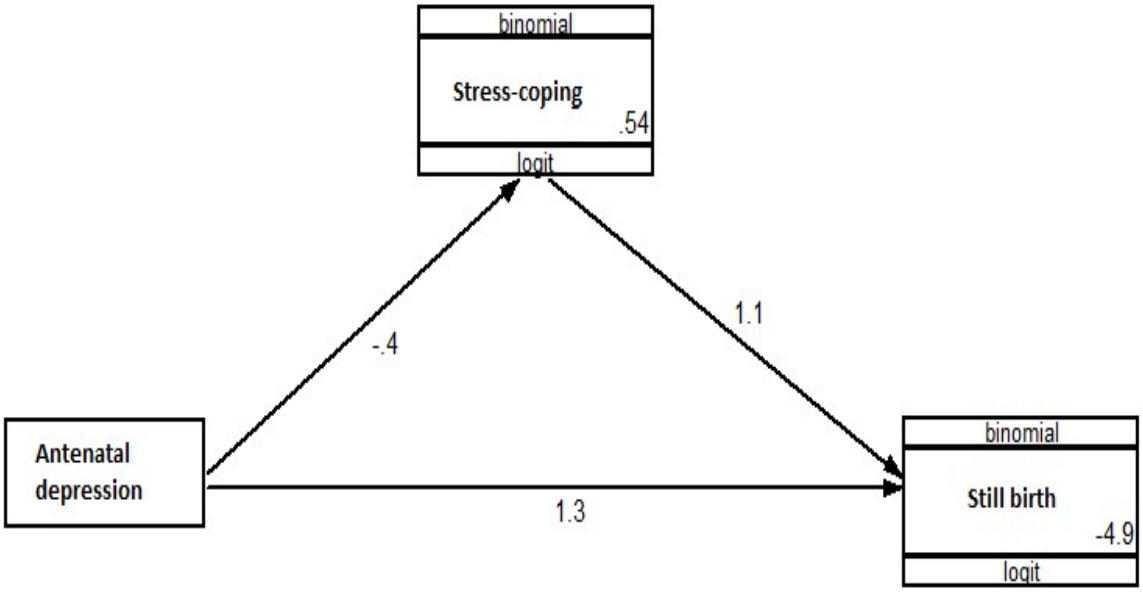


Figure 5.5: A mediation analysis model showing hypothesised causal pathways underlying antenatal depression and stillbirth in Gondar town, Northwest Ethiopia, 2018 (N=895)

5.3.3. Discussion

The incidence proportion of stillbirth was 19 per 1000 live births. This finding was similar to that of a systematic review of studies in Ethiopia (561), Ethiopian Demographic and Health Survey data (EDHS) (562), and with the national estimate for Ethiopia (563). However, the current stillbirth rate is much lower than estimates from the Ethiopian Mini Demographic and Health Survey (EMDHS) in Amhara region (564), a health institution-based cohort study conducted in rural Oromia region (565), and an institution-based study in Gondar town (566). The variation in estimates in previous studies is potentially due to different designs, settings, and study periods. Preventable stillbirth has been identified as a major area for a high return on investment in the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030). This strategy set a target to reduce stillbirth to fewer than 10 per 1000 births in every country (143). However, the number of stillbirths reported in current and previous studies

suggests that more work is required in Ethiopia to achieve the target (71). The under-developed health infrastructure, lack of trained health professionals and government focus (145, 567) and, possibly, healthcare centralisation (overseeing the issue of maternal mental health in the pregnancy continuum of care) might explain such a high burden of stillbirth in Ethiopia.

This study found that AND predicted an increased risk of stillbirth by 3.2 times. This seems to be a strong total effect, however, the direct effect of AND on stillbirth has been limited to a marginal and non-significant effect. As such, the findings suggested that there should be some caution in using this evidence for decision making, suggesting further study in the area. Such equivocal findings have been also reported in previous studies conducted in high-income countries (295, 296) and in Ethiopia (54). However, theoretically, there are suggested biological mechanisms for a causal relationship between antenatal depression and stillbirth. For instance, depressed women are more likely to produce high levels of stress hormone (cortisol), which could affect the proper functioning of the placenta, reducing oxygen supply to the foetus and, ultimately, causing foetal distress or death (43). Furthermore, pregnant women with signs of depression may have low levels of health-seeking behaviour, with untreated pregnancy-related problems or infections leading to stillbirth (128, 568). Stress coping ability was found to reduce the risk of stillbirth by 73% but this association was attenuated in a mediation analysis. The total effect of AND indicated in the current study could be plausible, because stress coping ability was also found to buffer the effect of other stressors on AND as identified in section 5.2 of this thesis. Nonetheless, the equivocal evidence found in this study also suggests the need for further studies with larger sample sizes in Ethiopia.

In Ethiopia, 320,000 (10.0%) births are preterm each year (61) and this study estimated an incidence proportion of 16.4%. This estimate was consistent with previous studies conducted in different regions of Ethiopia (565, 566, 569-572), and all estimates were much higher than the global preterm estimate of 10.6% (573). Preterm birth is a major cause of birth complications, being a direct cause of neonatal death (574) and preterm neonatal death with an estimated 32% in a study conducted in Gondar University Comprehensive Specialised Hospital (575). The level of preterm birth observed in recent studies suggests that the burden of preterm birth persists despite a reduction over the last few years (61).

In contrast to other studies, the risk of preterm birth was not directly affected by AND (576-578). However, when modified by partner support, the relationship was significant and the risk of having preterm birth was more than four times higher among depressed women with moderate or poor partner support. Similarly, in the path analysis, depression had significant indirect effects on preterm birth through partner support and fear of delivery, which both individually had a direct positive effect on preterm birth. Both analytical approaches reached a similar conclusion, suggesting that partner support buffered the link between antenatal depression and risk of preterm birth. This finding was consistent with a review of randomised controlled studies that found offering support for at-risk pregnant women may slightly reduce the number of premature births (579). A positive effect of behavioural therapy during pregnancy on good birth outcomes (576) and a buffering effect of perceived support from a partner (580) was also found in similar cohort studies. Most LBW and preterm births are associated with restricted foetal growth (69, 567, 581) and the biological mechanisms that explain this relationship have been discussed in section 4.2.2. According to other reviews (581, 582) and the current finding, apart from routinely practised clinical and public health service interventions, psychosocial interventions might help to reduce behavioural, mental, and psychological risk factors associated to preterm birth.

The risk of preterm birth was higher among women with no ANC access during pregnancy, which is consistent with other studies (569, 570, 583, 584). It is known that adherence to ANC helps in early identification and treatment of obstetric complications, severe infections and for promoting healthy behaviour during pregnancy (585). The other predictor for increased risk of preterm birth was maternal employment status, with those in paid work at 50% higher risk of preterm birth relative to those who performed home duties only. Government or private employees may have reduced time to care for themselves and their pregnancy and to attend clinical care necessary for a healthy pregnancy outcome. Moreover, in support of this, a slightly higher proportion of employed women reported stress and fear about the delivery than non-employed participants, both of which were found to be important risk factors for preterm birth. Participants identifying as Muslim had a 1.61 times higher preterm birth than those identifying themselves as Orthodox Christian. This is a new finding that may need further exploration. However, in this study, a slightly higher proportion of those identifying as Muslim reported receiving less support from their partner, had poor stress coping ability,

had fewer ANC visits, and depression compared with those identifying as Orthodox Christian, and these factors appeared to increase the risk of preterm birth.

In this study, the incidence of LBW was 5.2% (21.0% in preterm and 2.1% in term births), which was lower than other community (55) and health institution-based studies (565, 566, 569, 583). The current study differed from previous research regarding setting and sample size because the current study was conducted in urban settings with a large sample size compared with previous studies. The previous studies were institution-based and used cross-sectional designs, and they may have over- or under-estimated the true magnitude of LBW in the community. However, based on the multifaceted effects of LBW in the life of the newborn and for the community and country (586), even our lower estimated incidence still has the potential for a large impact on health at the population level.

Inconsistent with other studies (42, 55, 248, 296-305) and systematic reviews discussed in chapter four, section 4.1 & 4.2, AND was not associated with the risk of LBW. However, its indirect effect in mediation analysis via partner support and preterm birth has been observed. Similarly, partner support was found to significantly modify the association between antenatal depression and LBW. The combined effect of antenatal depression and poor partner support on the risk of LBW was 3.4 times higher than the effect when women were depressed but supported by their partners. A similar mediation effect for social support between antenatal depression and LBW was also reported in two prospective cohort studies that included Ethiopia (55, 580). Similar to this study, a lack of direct association between antenatal depression and LBW has been reported in previous reviews (44, 101). A significant indirect effect of stress coping ability and a non-significant indirect effect of partner support on LBW mediated by preterm birth was another important path that needs to be considered, as has also been suggested in previous studies (51, 489, 585). As identified in previous studies (587, 588), intrauterine nutritional conditions reflected in LBW could be affected by maternal mental wellbeing. Furthermore, the biological mechanisms related to the mediation and moderation effect of partner support through the relationship between antenatal depression and preterm birth and LBW could be related to stress process mechanisms undertaken in women's body. Antenatal depression increases the production of stress hormone in the body and affects the normal foetal growth and results in premature labour and birth. Partner support would hamper this mechanism by reducing maternal stress and production of stress

hormone (454, 455). Psychosocial risk factors such as antenatal depression and psychosocial risk modifiers such as partner support and stress coping ability have been found to relate to risk of LBW both directly and indirectly. Based on this finding, strengthening partner support through enhancing male involvement in pregnancy and childbirth continuum of care could be very important for considerably reducing the risk of depression and LBW.

Preterm birth as a main cause of LBW has been well established and this study also found that the risk of LBW was 9.44 times higher among preterm births relative to term births (21.1% among preterm births and 2.1% among term births). In further mediation analysis, preterm birth had a direct positive effect on LBW and preterm birth also mediated the effects of stress coping ability and partner support on the risk of LBW. In the path model of preterm birth, partner support and stress coping ability were found to reduce the risk of preterm birth, which in turn helped to reduce the risk of LBW. An association between LBW and preterm birth was also found in similar studies conducted in Gondar (566) and Dangla hospital (589). In contrast, no association between preterm birth and the risk of LBW was reported elsewhere (590). Although the risk factors for preterm birth and LBW are entirely different, the interventions taken to reduce preterm birth would be equally important in reducing the risk of LBW (591).

Tobacco smoke exposure during pregnancy doubled the risk of LBW and its direct effect was also noted in the path analysis. In studies from developed countries (590, 592, 593) the incidence of LBW was found to be higher in women who had tobacco exposure during pregnancy compared with those who were not exposed. A potential mechanism is that cigarette exposure increases the concentration of cotinine and nicotine in the amniotic fluid of the foetus, leading to nicotine-induced placental vasoconstriction, reduced blood oxygen uptake, reduced level of carboxyhemoglobin, and increased occurrence of placental vascular disease, all of which significantly affect foetal growth (594). In Ethiopia, the prevalence of smoking in women was 1% (595) but the risk of second-hand smoking at home was reported to be 62.5% (579, 596). Similarly, in the current study, 10.7% of pregnant women had active or passive tobacco exposure, which suggests that tobacco is becoming a major public health threat in Ethiopia. More importantly, depression by itself could lead to increased maternal smoking initiation or continued smoking during pregnancy, and this link has been indicated in the path analysis. The effect of tobacco smoking on the overall health of individuals and communities has been well established, and its risk for LBW is also indicated. As such, active

implementation of the tobacco control strategy developed by the WHO and endorsed by the Ethiopian government should be supported (597).

This study presented the incidence of the main adverse birth outcomes (LBW, preterm birth, and stillbirth) and proposed how psychosocial risk factors are very important in predicting such outcomes. Psychological science in pregnancy (598) is an emerging research area aimed at examining the psychosocial risk factors of adverse birth outcomes in developed countries. The current study expanded the concept of this science to low-income countries by investigating the psychosocial risk factors, their interaction, and possible stress process mechanisms underlying the occurrence of adverse birth outcomes. The cohort was community based and the study population was selected using a stratified cluster-based random sampling approach. Our results are, therefore, likely to be representative of the incidence and factors that predict adverse pregnancy outcomes within the region. The sample size was also relatively large, although power was reduced by the low frequency of some outcomes. Further, two different approaches were used in assessing the associations. A regression approach allowed the assessment of the overall independent effects of each risk factor. The path analysis allowed the assessment of both the direct and indirect effects of each risk factor, as well as potential mediators of the indirect effects. Finally, the use of a modified Poisson regression approach increased the precision of these estimates and allowed the reporting of relative risks rather than odds ratios, thereby increasing interpretability.

While it was ethically necessary to exclude women with a high probability of depression from the cohort, this exclusion might have affected the study's ability to determine the effect of AND on the risk of adverse birth outcomes. To prevent overburdening of study participants, data on abuse, pregnancy complications (pre-eclampsia, gestational diabetes), history of infections, and inflammations during pregnancy were not collected. Not adjusting the model for these potential confounding variables might have had a minor effect on the precision of the predictive model. However, it is hoped that the use of modified Poisson regression would reduce this effect because it is theoretically robust enough to omitted covariates. The other limitation is associated with the usual challenges of measuring preterm birth because of the accuracy of the last menstrual cycle date. Despite these limitations, our study was able to identify important potentially modifiable risk factors for poor birth outcomes, knowledge which may guide the development of healthy maternal care policy in the future.

5.3.4. Conclusions and recommendations

The incidence of preterm birth, LBW, and stillbirth was high in Gondar town, suggesting the need for government attention. Antenatal depression was found to increase the risk of stillbirth while stress coping ability reduced the risk of stillbirth. Antenatal depression did not directly increase the risk of both LBW and preterm birth; however, the relationship was considerably moderated by partner support. As such, women who were depressed during pregnancy but reported low partner support tended to deliver preterm and LBW babies. The risk of preterm birth was increased in paid employees, Muslim women, women with low levels of ANC, and those who were afraid of delivery. The risk of LBW was found to be increased in women with preterm birth and who had been exposed to tobacco smoke during pregnancy. Public health and clinical interventions that focus on enhancing partner engagement and participation in antenatal support while working to enhance maternal resilience would potentially help to reduce adverse birth outcomes in Gondar town and other similar settings.

Chapter Six: Perinatal depression and its association with adverse infant health outcomes

6.1. Introduction

The studies described in this chapter aimed to investigate PND, its causal mechanisms, and effects of antenatal and postnatal depression on the risk of adverse infant health outcomes in infants aged to six months. Malnutrition, acute respiratory infection (ARI), and diarrhea were the main adverse infant health outcomes explored in this chapter. The chapter has two main sub-chapters, the first of which elucidates the incidence and prevalence of postnatal depression and its associated factors by further exploring potential causal mechanisms. The second sub-chapter presents the findings on association between antenatal and postnatal depression and risk of ARI, diarrhea and malnutrition. The sub-chapters begin with a summary of the methods used, continue by describing the main results and discussions, and then conclude with recommendations for further actions.

6.2. Postnatal depression and its potential causal mechanisms

This part which explores postnatal depression and its potential causal mechanisms has been published https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7206662/.

6.2.1. Method summary

A total of 916 pregnant women was followed from their pregnancy to six months after birth. During this follow-up period, four women refused to participate and eight were lost from the study giving a lost to follow-up rate of 1.3%. Postnatal depression screening was undertaken in 904 women between two and six weeks after birth and nine women were excluded for having a high risk of depression (EPDS ≥17). Finally, data for 895 postnatal women were included in this analysis to determine PND prevalence and explore its predictors and potential causal mechanisms using a stress process theoretical model. A stage by stage description of the number of study participants included in each stage of the follow up has been presented in figure 3.6.

The main outcome for this analysis was PND, which is latent variable, and mediator predictors were supposed to be categorical, for this reason, the GSEM was used for analysis (599). The theoretical reasons for using the SEM and GSEM and the model fitting procedures have been

discussed in section 5.2.1 and 5.3.1. Prior to fitting the structural model, a confirmatory factor analysis was conducted to test model fitness of a measurement model, EPDS score. Next, each variable was checked at a bi-variable level and those associated with PND at values p<0.2 were further analysed using a multivariable mixed effect linear regression model. A model comparison between linear regression and mixed effect linear regression (because of clustering) was made and the mixed effect linear regression model had a better fit than the ordinary linear model in likelihood ratio test (600) at p-value <0.001. Therefore, variables which were significant at a p-value <0.05 in the multivariable mixed effect linear regression model were used to build the structural model based on a stress process theoretical framework. The Mplus version 8.3 (601) was used to produce a standardised beta estimates of direct, indirect, and total effects for the final estimates of the structural model. The robust Poisson regression model was used to identify predictors of incident PND and the theoretical reasons for using this model have been discussed in section 5.2.1.

6.2.2. Results

6.2.2.1. Socio-demographic characteristics of study participants

The socio-demographic characteristics of the participants are shown in Table 6.1. There were no socio-demographic differences between participants with and without PND except for women's educational status (p=0.015). A high proportion of study participants with depression were in the low education category (33, 39.8%) compared with those without depression (194, 23.9%). The mean age (±SD) of study participants was 26.5 (±0.15). The majority (639, 71.4%) were primarily engaged in domestic duties, most (722, 80.7%) were Orthodox Christians, and 860 (96.1%) were partnered.

Table 6.1: Socio-demographic characteristics of participants included in the study, Gondar town, Northwest Ethiopia, 2018 (N=895).

Variable/category	Postnatal depression		Total n=895, n (%)	p-value
	Yes (n=83), n (%)	No (n=772), n (%)		
Women's age at enrolment				0.495
18–24 years	23 (27.7)	259 (31.9)	282 (31.5)	
25–34 years	52 (62.7)	499 (61.5)	551 (61.6)	
>=35 years	8 (9.6)	54 (6.6)	62 (6.9)	

Mean(±SD)	26.7 (0.53)	26.5 (0.15)	26.5 (0.15)	
Household monthly income				0.08
Low	50 (60.2)	387 (47.7)	437 (48.8)	
Medium	27 (32.5)	338 (41.6)	365 (40.8)	
High	6 (7.3)	87 (10.7)	93 (10.4)	
Monthly income Mean(±SD) ETB	2920.5 (238.6)	3576.9 (107.0)	3516 (99.7)	
Education				0.015
None	10 (12.0)	104 (12.8)	114 (12.7)	
Primary	33 (39.8)	194 (23.9)	227 (25.4)	
High school	26 (31.3)	313 (38.5)	339 (37.9)	
Tertiary	14 (16.9)	201 (24.8)	215 (24.0)	
Occupation				0.224
Domestic duties	62 (74.7)	577 (71.1)	639 (71.4)	
Government employee	8 (9.6)	134 (16.5)	142 (15.9)	
Self employed	13 (15.7)	101 (12.4)	114 (12.7)	
Religion				0.761
Orthodox Christian	68 (81.9)	654 (80.5)	722 (80.7)	
Muslim	15 (18.1)	158 (19.5)	173 (19.3)	
Marital status				0.250
Single	3 (3.6)	16 (2.0)	19 (2.1)	
Partnered	77 (92.8)	783 (96.4)	860 (96.1)	
Separated	3 (3.6)	13 (1.6)	16 (1.8)	
Difficulty accessing food in the last three months				0.360
Yes	5 (6.0)	32 (3.9)	37 (4.1)	
No	78 (94.0)	780 (96.1)	858 (95.9)	

Note: Note: p-value was based on chi-squared test statistics

6.2.2.2. Obstetric and behavioural characteristics of study participants

The obstetric and behavioural characteristics of the study participants are shown in table 6.2. A higher prevalence of PND was observed in study participants who had low PNC service uptake (p=0.036), who had self-reported history of delivery complications (p<0.001), LBW (p<0.001), and stillbirths (p<0.001). Many of the pregnancies were planned (697, 85.2%) and the mean (±SD) number of children per woman was 2.1 (±1.2). Most participants (857, 95.7%)

had had at least one ANC visit, 738 (84.0%) had a vaginal delivery, and 818 (91.4%) reported no nutritional problems. A total of 533 participants (60.7%) initiated breastfeeding within an hour of birth and 16.4% had preterm births.

Table 6.2: Obstetric and behavioural characteristics of participants included in the study, Gondar town, Northwest Ethiopia, 2018 (N=895).

Variable/category	Postnatal depression		Total n=895, n (%)	p-value
	Yes (n=83), n (%)	No (n=772), n (%)		
Pregnancy intention				0.122
Planned	66 (79.5)	697 (85.8)	812 (85.2)	
Unplanned	17 (20.5)	115 (14.2)	83 (14.8)	
Parity (no. of births)				0.88
1	31 (37.4)	310 (38.2)	341 (38.1)	
2	25 (30.1)	259 (31.9)	284 (31.7)	
3–8	27 (32.5)	243 (29.9)	270 (30.2)	
Mean(±SD)	2.2 (1.2)	2.1 (1.2)	2.1(1.2)	
Antenatal care service uptake (at least one visit)				0.78
Yes	79 (95.2)	778 (95.8)	857 (95.7)	
No	4 (4.8)	34 (4.2)	38 (4.3)	
Postnatal care service				0.036
Yes	48(64.9)	624(77.6)	672 (76.5)	
No	26(35.1)	180(22.4)	206 (23.5)	
Mode of delivery				0.58
Vaginal	63 (86.3)	675 (83.8)	738 (84.0)	
Caesarean section	10 (13.7)	130 (16.2)	140 (16.0)	
History of self-reported labour complications				<0.001
Yes	64(77.1)	751(92.6)	815(91.2)	
No	19(22.9)	60(7.4)	79(8.8)	
Early initiation of breast feeding (BF) (≤ one hour of delivery)				0.183
Yes	49(68.1)	484(60.0)	533(60.7)	
No	23(31.9)	322(40.0)	345(39.3)	
Median hours of initiation of BF (±IQR)	1(1–6)	1(1–30)	1(1–30)	
History of LBW				<0.001

Yes	66(79.5)	30(3.7)	47(5.3)	
No	17(20.5)	782(96.3)	848(94.7)	
Postnatal nutritional status				0.95
Underweight (18–22 cm)	7 (8.4)	70 (8.6)	77 (8.6)	
Normal (22.5–31 cm)	76 (91.6)	742 (91.4)	818 (91.4)	
MUAC mean (±SD)	83 (0.08)	812 (0.07)	895 (0.09)	
History of preterm birth				0.671
Yes	68(81.9)	132(16.3)	147 (16.4)	
No	15(18.1)	680(83.7)	748 (83.6)	
History of stillbirth				<0.001
Yes	10(12.1)	7(0.9)	17 (1.9)	
No	73(87.9)	805(99.1)	878 (98.1)	

Note: Note: p-value was based on chi-squared test statistics

6.2.2.3. Psychosocial characteristics of study participants

Table 6.3 shows participants' psychosocial characteristics. There were 76 (8.7%) study participants who reported poor marital relationships, 62 (6.9%) reported a history of CMDs before pregnancy, 179 (20.0%) reported low social support, and 413 (47.1%) reported frequent support from their partners. Study participants with signs of PND more frequently reported having a poor marital situation (p=0.001), a history of CMDs before pregnancy (p<0.001), low partner support (p=0.02), and depression during pregnancy (p<0.001).

Table 6.3: Psychosocial characteristics of study participants included in the study, Gondar town, Northwest Ethiopia, 2018 (N=895).

Variable/category	Postnatal depression		Total n=895, n (%)	p-value
	Yes (n=163), n (%)	No (n=732), n (%)		
Marital relationships (mother's perspective)				0.001
Poor	12(15.1)	64(8.0)	76(8.7)	
Good	61(76.2)	527(66.2)	588(67.1)	
Very good	7(8.7)	205(25.8)	212(24.2)	
History of common mental disorders				<0.001
Yes	14(16.9)	48(5.9)	62(6.9)	
No	69(83.1)	764(94.1)	833(93.1)	

Social support				0.30
Poor	13(15.7)	166(20.4)	179(20.0)	
Good	70(84.3)	646(79.6)	716(80.0)	
Social support scale (Median(±IQR))	11(9–13)	11(9–13)	11(9–13)	
Internal consistency (α)	0.76 (high reliability)			
Partner support				0.02
Always	29(36.3)	384(48.2)	413(47.1)	
Most of the time	22(27.5)	238(29.9)	260(29.7)	
Some of the time	25(31.2)	139(17.5)	164(18.7)	
Rarely	4(5.0)	35(4.4)	39(4.5)	
Symptom of antenatal depression				<0.001
Yes	18(21.7)	40(4.9)	58	
No	65(78.3)	772(95.1)	837	
Depression scale (Median(±IQR))	6(3–11)	4(1–7)	4(2–7)	
Internal consistency (α)	0.74 (High reliability)			

Note: p-value was based on chi-squared test statistics

6.2.2.4. Incidence, prevalence and predictors of postnatal depression

Of 895 women screened, 83 (9.27%) screened positive for PND (95%CI: 7.45, 11.36). Sixty-five women who were free of depression during pregnancy tested positive in postnatal period, indicating an incidence proportion of 7.77% (95%CI: 6.04, 9.79). Eighteen women (2.1%) had depression during pregnancy and the postnatal period. Furthermore, 105 women had depression on at least one of the screening times (pregnancy or postnatal) giving a perinatal depression prevalence of 11.7%.

Table 6.4 shows predictors of incidence of PND from a multivariable modified Poisson regression model. In the multivariable model, PNC service, history of CMDs before pregnancy, and depression score during pregnancy predicted the incidence of PND. The incidence risk of PND was 1.8 times higher (Adjusted Relative Risk (ARR), 95%CI: 1.0, 3.2) among study participants who did not have PNC service. An increase of one in EPDS score during pregnancy increased the risk of PND 1.6 times (ARR, 95%CI: 1.4, 1.7). The third risk factor that appeared to increase the incidence of PND was a history of CMDs before pregnancy, with women having

this attribute being at 2.4 times higher (ARR, 95%CI: 1.4, 4.3) risk than those who did not have a history of CMDs.

Table 6.4: Bi-variable and multivariable modified Poisson regression model predicting the incidence of postnatal depression in Gondar town, Northwest Ethiopia, 2018 (N=895).

Variable	Postnatal depression (N=895)		CRR,95%CI	ARR, 95%CI
	Yes, N (%)	No, N (%)		
Postnatal care service (No)	17 (8.9)	174 (91.1)	1.2 (0.7, 2.0)	1.8 (1.0, 3.2)
Depression before pregnancy (Yes)	12 (23.1)	40 (76.9)	3.4 (1.9, 5.9)	2.4 (1.4, 4.3)
Antenatal EPDS score (median, IQR)	5 (2,7)	3 (1, 6)	1.4 (1.3, 1.5)	1.6 (1.4, 1.7)

Note: Adjusted for educational status, monthly income, LBW, stillbirth, self-reported labor complication, pregnancy intention, early initiation of breast feeding, marital agreement and husband support during pregnancy. **CRR**: crude relative risk; **ARR**: adjusted relative risk.

6.2.2.5. A structural model showing potential causal mechanisms of postnatal depression

Results of the standardised model factor loadings for each scale of the EPDS are shown in figure 6.1. The fitness of measurement model was found to be satisfactory (Comparative Fit Index (CFI)=0.78, Tucker–Lewis Index (TLI)=0.71, Standardised Root Mean Square Residual (SRMR)=0.06, coefficient of determination (R^2) =0.80). All factor loadings of the measurement model were significant at p<0.001. After adjusting for potential known confounders, the following factors were identified in a multivariable mixed effect linear regression and used for fitting the structural model: self-reported labour complications, PNC services, early initiation of breastfeeding, LBW, symptoms of CMDs before pregnancy, and symptoms of depression during pregnancy. As such, study participants with a PND were more likely to have self-reported labour complications (standardised β=0.86, p=0.004), LBW (standardised β=0.85, p=0.043), early initiated breastfeeding (standardised β=0.82, p<0.001), not attended PNC service (standardised β=0.67, p=0.005), symptoms of CMDs before pregnancy (standardised β=0.74, p=0.013), and depression symptoms during pregnancy (β=2.78, p<0.001).

The structural model from the GSEM fits the data fairly well (RMSEA=0.062, CFI=0.815, TLI=0.772). Figure 6.2 shows selected candidate structural model illustrating potential causal mechanisms of PND following a stress process theoretical model. AND had a direct (standardised β=0.29), indirect (standardised β=0.07), and total effect (standardised β=0.36)

on PND. This means that having AND increased the score of PND by 0.29 standard deviations but in the presence of labour complications the score further increased to 0.36 standard deviations. An indirect effect of AND was through self-reported labour complications i.e. AND had a direct effect on self-reported labour complications (standardised β=0.17) which in turn also affected PND (standardised β=0.09). Table 6.5 shows beta coefficients of direct, indirect, and total effects of stressors and mediators of PND.

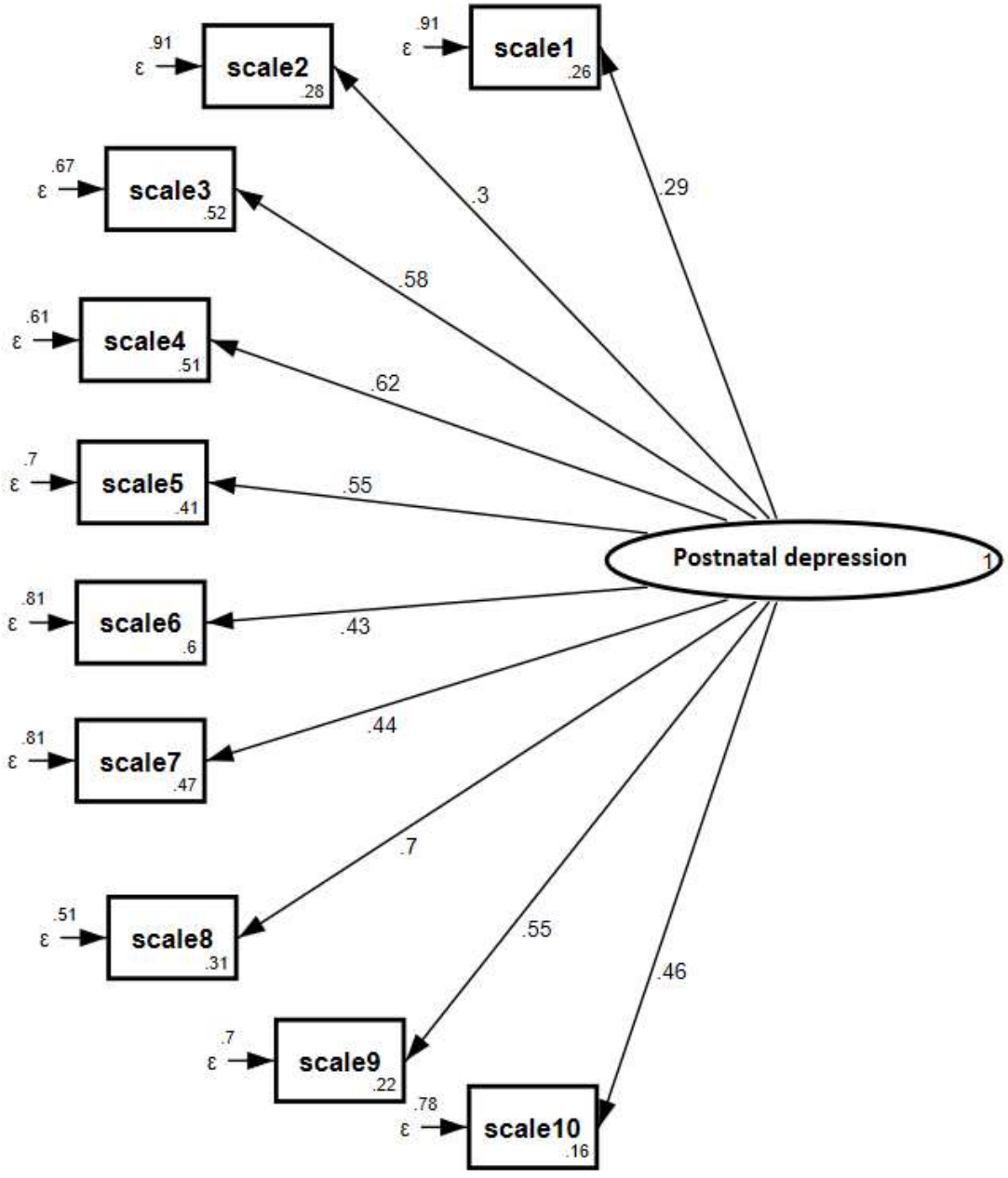


Figure 6.1: Results of standardised factor loadings of a measurement model (items of EPDS) (N=895), Gondar town, Northwest Ethiopia, 2018 (N=895)

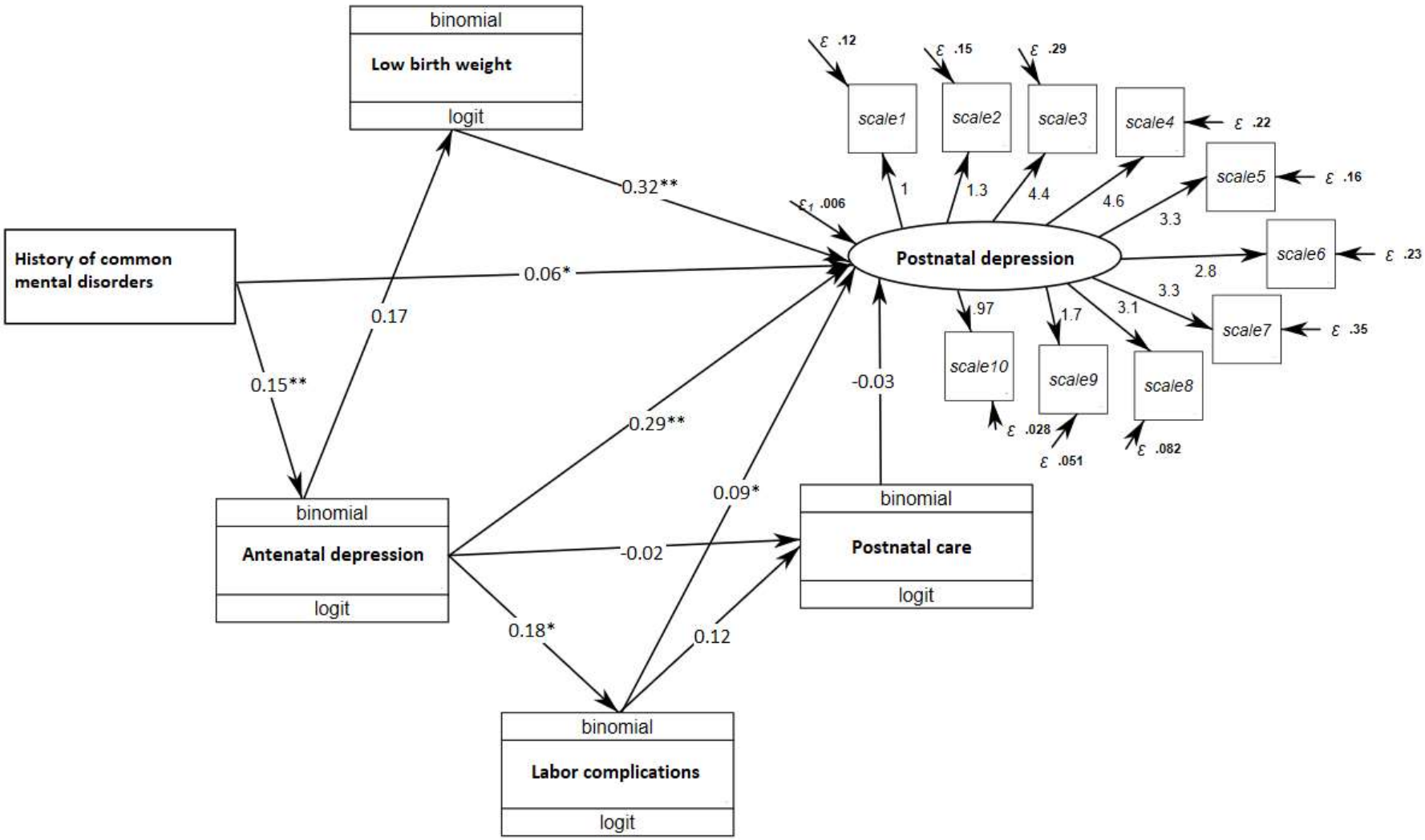


Figure 6.2: Stress process model framework for postnatal depression based on a GSEM model, Northwest Ethiopia, 2018 (N=895). *Note: **≤0.001, *≤0.05, β is standardised estimate*

Symptoms of CMDs before pregnancy had a direct (standardised β=0.06), indirect (standardised β=0.05), and total positive (standardised β=0.11) effect on PND. The two significant indirect paths through which a history of CMDs led to PND were through antenatal depression and self-reported labour complications. Thus, having a history of CMDs overall increased the score of PND by 0.11 standard deviations. In summary, women who had no symptoms of CMDs before pregnancy had reduced chances of depression during pregnancy and self-reported labour complications, which all reduced the score of PND. Low birth weight (standardised β=0.32) and self-reported labour complications (standardised β=0.09) had a direct positive effect on PND. Having LBW and self-reported labour complications increased the score of PND by 0.32 and 0.09 standard deviations, respectively.

Table 6.5: Direct, indirect and total effect of stressors and mediators on postnatal depression among study participants (N=895), Gondar town, Northwest Ethiopia, 2018 (N=895)

Risk factors	Direct effect (β, SE)	Indirect effect (β, SE)	Total effect (β, SE)
Antenatal depression			
Yes	0.29 (0.062) **	0.07 (0.036) *	0.36 (0.053) **
No	refer		
Low birth weight			
Yes	0.32 (0.064) **		0.32 (0.064) **
No	refer		
Self-reported labour complications			
Yes	0.09 (0.37) *	–0.004 (0.016)	0.087 (0.043) *
No	refer		
Postnatal care service			
Yes	–0.03 (0.089)		–0.03 (0.089)
No	refer		
History of CMD before pregnancy			
Yes	0.06 (0.032) *	0.05 (0.02) **	0.11 (0.03) **
No	refer		

Note: **≤0.001, *<0.01, β is standardised estimate

6.2.3. Discussion

PND is one of the most under-investigated and discounted CMDs in low-income countries despite being a threat to the wellbeing of mothers and their newborn babies. Postnatal depression has been neglected, and its complications and manifestations are usually misrepresented as postnatal blues or psychosis (602, 603). In Ethiopia, in addition to the lack of government priority, PND is not well recognised or studied as a part of the perinatal continuum of care. In this community-based cohort study, pregnant women were screened before and after child delivery to explore the extent of depression during the perinatal period and to identify risk factors of PND. The stress process model was used as a theoretical framework of analysis to test and identify the most likely source of stressors and how they interrelated to lead to PND.

In this study, 11.7% and 9.3% of postnatal women reported symptoms of perinatal depression and PND, respectively. The prevalence of PND found in the current study was much lower than that in a community-based cohort study conducted in Sodo district (22.1%) (79). Similarly, the current finding was lower than the community-based cross-sectional studies conducted in Mizan Aman town (22.4%) (82) and Sodo district (12.7%) (78), and the health institution-based cross-sectional studies in urban areas (236, 238, 240). Moreover, this prevalence was also far lower than the pooled prevalence of PND in low-income countries calculated in section 4.4, and in Africa (234). However, previous studies differ from the current study in terms of tools used for screening depression, study design, and setting. The community-based studies used PHQ or SRQ to measure PND and sensitivity and specificity of these tools are different to those of EPDS used in the current study. On the other hand, except for the two studies conducted in Sodo district, the published studies included postnatal women irrespective of weeks after delivery. This might have created a risk of over-estimation because mild depression and mood swings, often referred to as the 'baby blues', are very common (604-606) in the first two weeks following delivery. The other differences were in study setup and design, the studies conducted in Addis Ababa and southwest Ethiopia used institution-based cross-section designs while the current study used a community-based cohort.

The provision of PNC in Ethiopia is very low (607) and mothers who access it might have better awareness or be experiencing severe health conditions that require medical consultation. Therefore, when depression is assessed at health facilities there is more chance of including postnatal women with higher stress levels or who might select negative responses on a screening tool. Similarly, studies conducted in rural settings found higher prevalence of PND than the current study. This may be because of differential distribution of environmental determinants of the development of depression in urban and rural areas (78). However, the current estimate is slightly higher than rural studies conducted in Ethiopia (4.6%) (367) and Ghana (3.8%) (266). Factors contributing to the variation in prevalence might include time of investigation, tools used for screening, and the settings. Nonetheless, this finding is consistent with a study conducted in Sudan (9.2%) (232).

In this follow-up study, new cases of PND occurred in 7.8% of participants and 2.1% of these also had depression during pregnancy, suggesting persistent depression. The figures for incidence and persistent depression in the current study were much lower than those found in a prospective community-based study conducted in a rural area of Ethiopia (79), which reported 15.4% incidence and 11.1% persistence of depression. The study setting (being rural) and use of different tools than the current study might explain the variation in estimates. However, a review of longitudinal studies revealed that, on average, 7% of women reporting depressive symptoms in pregnancy continue to report them during the postnatal period (608). In the current study, women at higher risk of antenatal and postnatal depression were excluded for ethical reasons. It is therefore reasonable to hypothesise that the inclusion of these women in the analysis would have led to a similar estimate to previous studies. Our finding was, however, higher than the incidence (2.4%) and persistence (2.5%) of CMDs found in Butajira (367). In the current study, depression prevalence during pregnancy was lower than in the postnatal period. Although it differed from the previous rural cohort studies in Ethiopia (79, 367), this finding was consistent with the review of longitudinal studies on perinatal depression (608). In conclusion, a number of studies conducted in different areas with various designs demonstrate that a significant proportion of women suffer from perinatal depression in Ethiopia. Based on its impact on infant

health and developmental consequences (609-611), PNC services should routinely address the issue of PND.

Symptoms of CMDs before pregnancy and depression during pregnancy predicted both the incidence and prevalence of PND symptoms. The risk of PND increased by 2.4 times for women who had had CMDs before pregnancy and 1.6 times for women with depression during pregnancy. Similarly, in the path analysis, CMDs before pregnancy and depression during pregnancy had both direct and indirect positive effects on PND. In addition, AND mediated the link between CMDs before pregnancy and PND. The strong effect of previous depression symptoms on PND has been frequently reported in studies conducted in low- (82, 266) and high-income countries and in systematic reviews (75, 191, 604, 608). This was also seen in the systematic review of PND described in section 4.4. This highlights how depression could persist or re-occur during the perinatal period, and its complex interaction or interconnection with episodes occurring before pregnancy. Early screening and intervention are vital to prevent such courses of depression, its poor obstetric and perinatal outcomes, and its long- and short-term effects on newborn health and developmental consequences (54, 612).

There are both biological and environmental causal explanations for depression during the perinatal period. Psycho-social and economic stressors, and the anticipation of a new turn of life before and after pregnancy, affect the normal functioning of hypothalamic–pituitary–adrenal axis and these effects persist throughout the perinatal period (613). Moreover, hormonal changes during pregnancy and increased levels of placental cortisol hormone production can results in persistent symptoms of depression during pregnancy. As well, a sharp reduction in cortisol hormone production following birth may contribute to continued depression symptoms or to the development of new depressive episodes (614-616) postnatally. Whilst hormonal variations during pregnancy are normal, possible environmental stressors that could further raise hormonal production needs to be considered through early identification and management. Public health and clinical interventions should include screening and treating depression symptoms during pregnancy and, if possible, during pre-pregnancy preparation (617).

Having a PNC visit decreased the risk of incident PND, which was increased by 80% in women who had no PNC service. PNC attendance was also positively correlated with PND score in a mixed effect linear regression model, although was non-significant in a path analysis. Previous studies conducted on PND in Ethiopia (78-82, 367) and in other African countries (228-230, 232, 246, 271, 272) were not adjusted for PNC and it was not possible to see whether the current finding was supported by earlier work. PNC attendance was also not identified as an important risk factor in the systematic review conducted in LMICs included in section 4.4 of this thesis. However, immediate contact with health care professionals after delivery is believed to resolve obstetric and psychosocial incidents that most cause psychological morbidities (618). Hence, PNC could help to reduce the incidence of PND, directly or indirectly. One explanation for the non-significant direct relationship between PNC and prevalence of PND in the path analysis could be the inclusion of postnatal women who had depression during pregnancy. It is possible that PNC services could directly prevent incident PND but might not be fully effective in alleviating previous depressive symptoms. Thus, PNC services that address the emotional health of women could prevent new occurrence of depression following birth.

LBW had a direct positive effect on PND in a path analysis. Although previous studies from Ethiopia and elsewhere in Africa did not consider LBW as a risk factor for PND (78-82, 367), studies in other settings have reported the relationship between LBW and PND. For example, a Chinese study using a path analysis reported an indirect effect of LBW on PND (338). Very LBW as a risk factor for PND or psychological distress was further reported in primary studies in developed countries (273, 619). Similarly, studies included in a systematic review by Vigod et al. (108) indicated that mothers of LBW or preterm infants showed sustained depressive symptoms for one year postpartum compared with mothers of normal birthweight infants. This association was also seen in the systematic review conducted in LMICs included in section 4.4. It is well acknowledged that babies born with low weight pose challenges to mothers by interfering with early adaptation to parenthood, parental roles, and generating stress by negatively affecting maternal caring practice (620).

Intention to breastfeed LBW infants and being unable to do so was a significant predictor of PND in the Avon Longitudinal Study of Parents and Children (621). Moreover, an experimental study

conducted in postnatal women with LBW infants in Iran revealed that breastfeeding self-efficacy training can significantly improve maternal stress or depression (622). The results from the current study were inconsistent because early initiation of breastfeeding was associated with increased PND scores in regression analysis, but the association was not significant in the path analysis. In support of this, a study reported that the effect of breastfeeding on PND is extremely heterogeneous and mediated by both breastfeeding intention and maternal mental wellbeing during pregnancy (621). One explanation could be that postnatal women who reported delivery complications or gave birth to LBW or preterm infants were more likely to stay longer in hospitals, where mothers are encouraged to initiate breastfeeding early. On the other hand, inexperienced postnatal women who initiate breastfeeding early might experience pain because of poor technique, which might then increase their tension or stress when contemplating breastfeeding. Further exploration is needed to identify why early initiation of breastfeeding might be correlated with increased PND score and if this effect also persists with normal breastfeeding activity.

Similar to the study from the Sodo district of Ethiopia (78), self-reported delivery complications had a significant but small direct effect on PND. This finding was replicated in studies from India (222) and Nepal (219), and in a systematic review Weobong (266) reporting elevated labour pain and duration as risk factors for PND (107). This was further confirmed in the systematic review and meta-analysis of risk factors associated with PND described in section 4.4. It is possible that childbirth experiences might trigger previous painful memories, because women who experienced difficult deliveries or complicated pregnancies had a higher likelihood of developing Post-Traumatic Stress Disorders (623). Furthermore, because of high maternal mortality in Ethiopia, such complications are more likely to be perceived as life threating and this could also potentially affect the mental wellbeing of postnatal women (624). Thus, immediate psychological therapy as a component of the PNC package would be required for women with history of delivery complications, in order to maintain their emotional state.

To our knowledge, this is the first study to use a follow-up approach to explore the trajectories of perinatal depression and apply a stress process theoretical framework to conceptualise the occurrence of PND in an urban setting in Ethiopia. Through a SEM frame of analysis, a potential causal mechanism of PND was developed using a reasonable sample size and low attrition rate.

However, there are some limitations: (i) assessment of delivery complications was based on participants' perceptions that may not have been completely accurate; (ii) use of a screening tool to measure depression may have led to misclassification of women with and without depression; (iii) excluding women with high possibility of depression may have led to an underestimate of the true burden of the problem in the community; and (iv) out of a desire to minimise the burden and/or potential distress to participants, important risk factors such as childhood abuse and violence were not examined. Thus, it was not possible to adjust for these factors to minimise bias associated with unmeasured covariates.

Although the prevalence of PND in the study was relatively low, its impact on the economy, women and child development is highly significant. This effect would be more pronounced in countries with large populations and low incomes. For example, an economic analysis of perinatal depression in Australia in 2013 showed that not treating perinatal depression cost the country $AUD 538 million (625). Ethiopia is a country with four times the population size and nearly three times the fertility rate of Australia, thus the total cost could be expected to approach $AUD 4 billion or more. Moreover, a recent study on health expenditure in rural Ethiopia found high out-of-pocket payments at the point of service was associated with depression and this is expected to be much higher when it comes to urban areas (626). Thus, failing to intervene to manage perinatal depression could impose a significant economic burden on the country.

In these analyses and in the systematic reviews described in chapter four, it has been well established that depression symptoms before and during pregnancy had a significant direct effect on PND. Hence, early screening for and treatment of depression and its risk factors during pregnancy as a component of the ANC package would significantly reduce the burden and its consequences on birth and post-delivery (627). This finding has policy and practical implications for health professionals, health ministries, the public, and researchers. However, strong government commitment and support is crucial for development and implementation of health interventions targeting perinatal depression. This should start by acknowledging perinatal depression as a public health threat at the policy level in order to set directions and endorse guidelines and working manuals for the broad implementation of appropriate interventions.

6.2.4. Conclusions and recommendations

The incidence and prevalence of PND found in this study was lower than previously published findings from cross-sectional studies in Ethiopia. Mental health disorders before pregnancy and depression during pregnancy were found to be important predictors of incident PND. Both also had direct and indirect effects on PND. Depression during pregnancy mediated the causal link between CMDs before pregnancy and PND. Accessing PNC services predicted incident PND. Self-reported delivery complications and LBW had direct effects on PND, while self-reported delivery complications mediated the link between antenatal and postnatal depression. Early detection and management of depression before and during pregnancy could prevent associated maternal complications and PND.

6.3. Association of antenatal and postnatal depression with risk of adverse infant health outcomes

This sub-chapter focused on identifying effects of antenatal and postnatal depression on adverse infant health outcomes such as diarrhea, malnutrition, and ARI in Gondar town, and an article has been submitted for publication.

6.3.1. Method summary

From 895 women screened for PND, 16 women with stillbirth were excluded and 878 mother–infant dyads were followed up for six months after delivery. At the end of the follow-up period, two women declined continued participation and ten women were lost to follow-up, leading to a 1.3% non-response rate. There was no evidence showing that the loss to follow-up was related to the exposure or the outcome of interest. A complete data set for 866 mother–infant dyads was analysed to address this research question.

The Targeted Maximum Likelihood Estimation (TMLE) was used to investigate the causal effect of antenatal and postnatal depression on risk of infant diarrhea, ARI and malnutrition. The Average Treatment Effect (ATE) of antenatal and postnatal depression, which was reported as a risk difference (RD), was estimated (113, 628). The ATE estimates the average difference in outcome between participants had they been exposed and had they not been exposed, adjusting for potential confounders (629). The TMLE applies G-computation and propensity score methods

that involve both exposure and outcome mechanisms (630, 631). The TMLE is a doubly robust and a substitution estimator that provides unbiased estimates if either the exposure or the outcome are miss-specified (632) and in the presence of outliers, unmeasured confounders, sparsity, and other modelling challenges (633).

The incidence proportions of diarrhea, ARI and malnutrition varied significantly between districts and demonstrated a clustering effect. As a result, the Generalised Estimating Equation (GEE) Poisson with a non-robust standard error estimator and exchangeable correlation was used to estimate the incidence rate ratios as a comparison model (553, 634). Before fitting the model, potential confounding variables were identified using the modified disjunctive cause criterion. Covariates were considered to be potential confounders and adjusted in the multivariable model if: (i) they had significant associations with the exposure, the outcomes or both; (ii) they were not instrumental variables; and (iii) they were not likely to be on the causal pathways between the exposure and the outcomes (635, 636). Multicollinearity was checked using correlation coefficient and Variance Inflation Factor (VIF) with cut-off values of ≥80% and ≥10, respectively (637). The interaction was tested by including an interaction term of antenatal or postnatal depression with social support, partner support, and stress coping ability. Mediation analysis was done using the Generalised Structural Equation Modelling (GSEM) (638).

6.3.2. Results

6.3.2.1. Socio-demographic characteristics

The socio-demographic characteristics of the study participants are described in Table 6.6. The mean ages (±SD) of mothers and infants were 26.5 (±4.5) years and 4.8 (±1.3) months, respectively. There was a significant age difference for infants with and without diarrhea ($p=0.024$) and malnutrition ($p=<0.001$). Nearly half (422, 48.7%) of participants reported being in the low-income category, 322 (37.2%) had completed high school, and 700 (80.8%) were Orthodox Christians. Education, income, and religion ($p<0.001$) were all associated with infant malnutrition and ARI. Large proportions of study participants were primarily engaged in home duties (617, 71.3%), were partnered (832, 96.1%), and reported not having difficulties in accessing food (832, 96.1%).

Table 6.6: Socio-demographic characteristics of study participants for those with and without diarrhea, ARI, and malnutrition in Gondar town, Northwest Ethiopia, 2018 (N=866)

Variable/category	Diarrhea (n=147)		*p-value*	ARI (n=187)		*p-value*	Malnutrition (n=125)		*p-value*
	Yes, n (%)	No, n (%)		Yes, n, (%)	No, n (%)		Yes, n (%)	No, n (%)	
Age at enrolment			*0.571*			*0.057*			*0.947*
18–24 years	45 (30.6)	236(32.8)		51 (27.3)	230(33.9)		39 (31.2)	242(32.7)	
25–34 years	89 (60.5)	436(60.6)		117 (62.6)	408(60.1)		77 (61.6)	448(60.5)	
>=35 years	13 (8.8)	47(6.5)		19 (10.1)	41(6.0)		9 (7.2)	51(6.8)	
Infant age in months, mean(±SD)	4.98 (1.04)	4.73(1.29)	*0.024*	4.82 (1.21)	4.76(1.27)	*0.543*	4.09 (1.41)	4.9(1.19)	*<0.001*
Household monthly income			*0.942*			*0.793*			*0.022*
Low	70 (47.6)	352(49.0)		87 (46.5)	335(49.3)		71 (56.8)	351(47.4)	
Medium	61 (41.5)	294(40.9)		80 (42.8)	275(40.5)		49 (39.2)	306(41.3)	
High	16 (10.9)	73(10.1)		20 (10.7)	69(10.2)		5 (4.0)	84(11.3)	
Education			*0.201*			*0.091*			*0.028*
None	25 (17.0)	86(12.0)		33 (17.6)	78(11.5)		19 (15.2)	92(12.4)	
Primary	32 (21.8)	191(26.6)		43 (23.0)	180(26.5)		42 (33.6)	181(24.4)	
High school	50 (34.0)	272(37.8)		62 (33.2)	260(38.3)		45 (36.0)	277(37.4)	
Tertiary	40 (27.2)	170(23.6)		49 (26.2)	161(23.7)		19 (15.2)	191(25.8)	
Occupation			*0.079*			*0.661*			*0.101*
Domestic duties	107 (72.8)	510(70.9)		133 (71.1)	484(71.3)		98 (78.4)	519(70.0)	
Student	4 (2.7)	9(1.2)		1 (0.5)	12(1.8)		2 (1.6)	11(1.5)	
Government employee	25 (17.0)	99(13.8)		28 (15.0)	96(14.1)		9 (7.2)	115(15.5)	
Self employed	11 (7.5)	101(14.1)		25 (13.4)	87(12.8)		16 (12.8)	96(13.0)	

Religion			*0.155*			*0.000*			*0.467*
Orthodox	125 (85.0)	575(80.0)		176 (94.1)	524(77.2)		104 (83.2)	596(80.4)	
Muslim	22 (15.0)	144(20.0)		11 (5.9)	155(22.8)		21 (16.8)	145(19.6)	
Marital status			*0.196*			*0.568*			*0.124*
Single	3 (2.0)	31(4.3)		6 (3.2)	28(4.1)		8 (6.4)	26(3.5)	
Partnered	144 (98.0)	688(95.7)		181 (96.8)	651(95.9)		117 (93.6)	715(96.5)	
Difficulty accessing food in the last three months			*0.299*			*0.258*			*0.124*
Yes	8 (5.4)	26(3.6)		10 (5.3)	24(3.5)		8 (6.4)	26(3.5)	
No	139 (94.6)	693(96.4)		177 (94.7)	655(96.5)		117 (93.6)	715(96.5)	

***Note**: p-value was based on chi-squared test statistics*

6.3.2.2. Maternal and infant characteristics

Maternal and infant characteristics of the study participants are described in Table 6.7. Most (738, 85.2%) pregnancies were planned, and 333 (38.4%) were first pregnancies. Almost all (95.7%) of the study participants had engaged with ANC, and most had attended PNC services (76.7%). There were 26 (3.0%) LBW and 128 (14.9%) preterm births. There were 71 (8.2%) mothers who were underweight, 529 (61.4%) had initiated early breastfeeding, and 577 (66.6%) strongly agreed that their infants were satisfied with breastfeeding. An association was found between LBW ($p=0.016$), infant care ($p=0.004$) and risk of diarrhea. An association was also found between ANC ($p=0.014$), PNC ($p=0.016$), LBW ($p<0.001$), early initiation of breastfeeding ($p<000$) and risk of ARI. Early initiation of breast feeding ($p<0.001$), PNC ($p<0.001$), and breastfeeding satisfaction ($p<0.001$) appeared to associate with risk of malnutrition.

Table 6.7: Characteristics of maternal and infant participants for those with and without diarrhea, ARI, and malnutrition in Gondar town, Northwest Ethiopia, 2018 (N=866)

Variable/category	Diarrhea (Yes, n=147)		*p-value*	(ARI) (Yes, n=187)		*p-value*	Malnutrition (Yes, n=125)		*p-value*
	Yes, n (%)	No, n (%)		Yes, n (%)	No, n (%)		Yes, n (%)	No, n (%)	
Pregnancy intention			*0.562*			*0.397*			*0.688*
Planned	123 (83.7)	615(85.5)		163 (87.2)	575(84.7)		108 (86.4)	630(85.0)	
Unplanned	24 (16.3)	104(14.5)		24 (12.8)	104(15.3)		17 (13.6)	111(15.0)	
Parity of the mother			*0.793*			*0.675*			*0.432*
1	53 (36.0)	280(38.9)		77 (41.2)			43 (34.4)	290(39.1)	
2	47 (32.0)	224(31.2)		55 (29.4)			45 (36.0)	226(30.5)	
3–8	47 (32.0)	215(29.9)		55 (29.4)			37 (29.6)	225(30.4)	
Antenatal care service uptake (at least one visit)			*0.142*			*0.014*			*0.871*
Yes	144 (98.0)	685(95.3)		185 (98.9)	644(94.8)		120 (96.0)	709(95.7)	
No	3 (2.0)	34(4.7)		2 (1.1)	35(5.2)		5 (4.0)	32(4.3)	
Postnatal care service			*0.562*			*0.016*			*0.000*
Yes	110 (74.8)	554(77.0)		131 (70.1)	533(78.5)		76 (60.8)	588(79.3)	
No	37 (25.2)	165(23.0)		56 (29.9)	146(21.5)		49 (39.2)	153(20.6)	
Low birth weight			*0.016*			*0.000*			*0.452*
Yes	9 (6.1)	20(2.4)		14 (7.0)	15(1.9)		5 (4.1)	22(2.8)	
No	138 (93.9)	699(97.6)		173 (93.0)	664(98.1)		120 (95.9)	719(97.2)	
Preterm birth			*0.770*			*0.311*			*0.432*
Yes	23 (15.7)	108(14.7)		33 (17.2)	97(14.2)		21 (17.2)	107(14.5)	
No	124 (84.3)	611(85.3)		154 (82.8)	582(85.8)		104 (82.8)	634(85.5)	

Exposure to coffee in pregnancy			*0.429*			*0.065*			*0.075*
Daily	64 (43.5)	293(40.7)		89 (47.6)	268(39.5)		58 (46.4)	299(40.4)	
Sometimes	44 (30.0)	255(35.5)		52 (27.8)	247(36.4)		32 (25.6)	267(36.0)	
Never	39 (26.5)	171(23.8)		46 (24.6)	164(24.1)		35 (28.0)	175(23.6)	
Exposure to cigarette in pregnancy			*0.906*			*0.331*			*0.528*
Yes	12(8.2)	78(10.8)		19(10.2)	71(10.5)		11(8.8)	79(10.7)	
No	135(91.8)	641(89.2)		168(89.8)	608(89.5)		114(91.2)	662(89.3)	
Nutritional status of the mother			*0.193*			*0.109*			*0.186*
Normal	131 (89.1)	664(92.3)		177 (94.6)	618(91.0)		111 (88.8)	684(92.3)	
Underweight	16 (10.9)	55(7.6)		10 (5.4)	61(9.0)		14 (11.2)	57(7.7)	
Early initiation of breast feeding			*0.214*			*0.000*			*0.000*
Yes	97 (66.0)	435(60.5)		152 (81.7)	380(55.8)		112 (89.3)	422(56.8)	
No	50 (34.0)	284(39.5)		35 (18.3)	299(44.2)		13 (10.7)	319(43.2)	
Care given for infant by			*0.004*			*0.986*			*0.023*
Mother	136 (92.5)	701(97.5)		182 (97.3)	655(96.5)		125 (100.0)	712(96.1)	
Housekeeper	11 (7.5)	18(2.5)		5 (2.7)	24(3.5)		0 (0.0)	29(3.9)	
Maternal perception of infant satisfaction with breast feeding *0.110*						*0.279*			*0.000*
Strongly agree	87 (59.2)	490(68.1)		132 (70.6)	445(65.5)		74 (59.2)	503(67.9)	
Agree	56 (38.1)	214(29.8)		53 (28.3)	217(32.0)		42 (33.6)	228(30.8)	
Disagree	4 (2.7)	15(2.1)		2 (1.1)	17(2.5)		9 (7.2)	10(1.3)	

Note: p-value was based on chi-squared test statistics

6.3.2.3. Psychosocial characteristics

The psychosocial characteristics of the study participants are described in Table 6.8. Fifty-six (6.5%) participants had had antenatal depression and 74 (8.5%) had had postnatal depression. Antenatal and postnatal depression were not associated with diarrhea ($p>0.1$), ARI ($p>0.5$) or malnutrition ($p>0.1$). More than half of participants (564, 66.6%) reported having good relationship with their partners and 691 (79.8%) reported good social support. There were 403 (46.5%) participants reporting frequent support from their partners while 547 (63.2%) had poor stress coping ability. Diarrhea ($p=0.042$) and ARI ($p<0.001$) were associated with stress coping ability.

Table 6.8: Psychosocial characteristics of participants for those with and without diarrhea, ARI, and malnutrition in Gondar town, Northwest Ethiopia, 2018 (N=866)

Variable/category	Diarrhea (Yes, n=147)		*P-value*	ARI (Yes, n=187)		*P-value*	Malnutrition (Yes, n=125)		*P value*
	Yes, (n, (%)	No, (n, (%)		Yes, (n, (%)	No, (n, (%)		Yes, (n, (%)	No, (n, (%)	
Marital relationship			*0.776*			*0.052*			*0.946*
Very good	35 (26.4)	167(24.3)		48 (25.5)	158(24.4)		29 (25.6)	176(24.5)	
Good	93 (66.0)	466(66.6)		122 (70.1)	432(65.5)		77 (66.1)	477(66.6)	
Poor	10 (7.6)	61(9.1)		8 (4.4)	64(10.1)		9 (8.3)	64(8.9)	
Social support			*0.05*			*0.436*			*0.205*
Good	126 (85.7)	565(78.6)		153 (81.8)	538(79.2)		105 (84.0)	586(79.1)	
Poor	21 (14.3)	154(21.4)		34 (18.2)	141(20.8)		20 (16.0)	155(20.9)	
Partner support			*0.251*			*0.266*			*0.078*
Always	74 (52.4)	318(45.3)		93 (49.7)	302(45.6)		60 (50.4)	332(45.9)	
Most of the time	37 (27.2)	201(29.1)		51 (27.3)	190(29.2)		34 (29.6)	204(28.6)	
Some of the time	18 (13.6)	136(19.7)		37 (19.8)	120(18.4)		12 (11.2)	140(20.0)	
Rarely	8 (6.8)	40(5.8)		6(3.2)	41(6.8)		11(8.8)	39(5.5)	
Stress coping ability			*0.042*			*0.000*			*0.554*
Good	65 (44.2)	254(35.3)		91 (48.7)	228(33.6)		49 (39.2)	270(36.4)	
Poor	82 (55.8)	465(64.7)		96 (51.3)	451(66.4)		76 (60.8)	471(63.6)	
Antenatal depression			*0.197*			*0.714*			*0.225*
Yes	6(4.1)	50(6.9)		11(5.9)	45(6.6)		5(4.0)	51(6.9)	
No	141(95.9)	669(93.1)		176(94.1)	634(93.4)		120(96.0)	690(93.1)	

Postnatal depression			*0.140*			*0.559*			*0.135*
Yes	8(5.4)	66(9.2)		14(7.5)	60(8.8)		15(12.0)	59(8.0)	
No	139(94.6)	653(90.8)		173(92.5)	619(91.2)		110(88.0)	682(92.0)	

Note: p-value was based on chi-squared test statistics

6.3.2.4. Causal association between depression and infant diarrhea, ARI, and malnutrition

The incidence proportions of diarrhea, ARI, and malnutrition were 17.0% (147; 95%CI: 14.5, 19.6), 21.6% (187; 95%CI: 18.89, 24.49), and 14.4% (125; 95%CI: 12.2, 16.9), respectively. During the follow-up period, there were 1 to 5 episodes of ARI and 1 to 4 episodes of diarrhea. Incidence rate ratios and adjusted risk difference estimates of the association of antenatal and postnatal depression with the risk of diarrhea, ARI, and malnutrition are presented in Table 6.9. In the multivariable GEE model: (i) there were no significant associations between AND symptoms and risk of diarrhea (Adjusted IRR=0.57; 95%CI: 0.24, 1.31), ARI (Adjusted IRR=0.92; 95%CI: 0.47, 1.78), or malnutrition (Adjusted IRR=0.61; 95%CI: 0.19,1.97); (ii) there were also no significant associations between PND and risk of diarrhea (Adjusted IRR=0.92; 95%CI: 0.45, 1.78), ARI (Adjusted IRR=1.00; 95%CI: 0.58, 1.72), or malnutrition (Adjusted IRR=0.61; 95%CI: 0.19, 1.97).

In the fully adjusted TMLE models, there were no causal associations between antenatal depression and the risk of diarrhea, ARI or malnutrition. Compared with those without AND, the risk difference for AND was 0.8% (95%CI: –9.2, 10.9) for diarrhea, –1.3% (95%CI: –21.0, 18.5) for ARI, and –7.3% (95%CI: –22.0, 21.8) for malnutrition. Similarly, PND was not associated with diarrhea (risk difference=–2.4%; 95%CI: –9.6, 4.9), ARI (risk difference=–3.2%; 95%CI: –12.4, 5.9) or malnutrition (risk difference=0.9%; 95%CI: –7.6, 9.5) (Table 6.9).

A mediation analysis from GSEM showed that: (i) there was no indirect effect of AND on risk of diarrhea (p-value=0.213), ARI (p-value=0.660) or malnutrition (p-value=0.182) through PND; and (ii) there was no indirect effect of AND on risk of malnutrition through LBW (p=0.551) and early initiation of breastfeeding (p=0.705). No interaction effect was found between antenatal and postnatal depression with social support, partner support, and stress coping ability on the risk of diarrhea, ARI, and malnutrition (p>0.2 in each of the interaction terms). Perinatal depression had a VIF of 10.2 and was not adjusted in the multivariable model of GEE. A sensitivity analysis was conducted in the TMLE model by adjusting for covariates which were statistically non-significant but theoretically fulfilled a criterion for mediators. However, this did not appear to change the final estimates.

Table 6.9: Estimates from TMLE showing the association of antenatal and postnatal depression with risk of diarrhea, ARI, and malnutrition in Gondar town, Northwest Ethiopia, 2018 (N=866)

	GEE model			TMLE
	Unadjusted IRR (95%CI)	Adjusted IRR (95% CI)	Adjusted p-value	Adjusted Risk Difference (95% CI)
Diarrhea				
Antenatal depression				
No	1.00	1.00		
Yes	0.65 (0.29,1.45)	0.57 (0.24,1.31)	0.185	0.8% (–9.2, 10.9)
Postnatal depression				
No	1.00	1.00		
Yes	0.85 (0.46,1.60)	0.92 (0.45,1.78)	0.811	–2.4% (–9.6, 4.9)
Adjusted for history of CMDs, LBW, husband support, social support, stress coping ability, pregnancy condition, food access of the family, and maternal health care services.				
Acute Respiratory Infection (ARI)				
Antenatal depression				
No	1.00	1.00		
Yes	0.85 (0.45,1.60)	0.92 (0.47,1.78)	0.798	–1.3% (–21.0, 18.5)
Postnatal depression				
No	1.00	1.00		
Yes	1.10 (0.66,1.81)	1.00 (0.58,1.72)	0.994	–3.2% (–12.4, 5.9)
Adjusted for age of the mother, age of the infant, maternal service uptake, fear to give birth, marital situation, husband support, social support, pregnancy need, food access, and occupation.				
Malnutrition				
Antenatal depression				
No	1.00	1.00		
Yes	0.47 (0.16,1.40)	0.61 (0.19,1.97)	0.407	–7.3% (–22.0, 21.8)
Postnatal depression				
No	1.00	1.00		
Yes	1.48 (0.83,2.64)	1.43 (0.71,2.89)	0.314	0.9% (–7.6, 9.5)
Adjusted for maternal services, parity, income, food access, occupation, educational status, marital situation, marital status, partner support, social support, history of CMDs, pregnancy condition, and nutritional status of the mother.				

6.3.3. Discussion

This study evaluated potential causal associations between perinatal depression and risk of diarrhea, ARI, and malnutrition among infants aged up to six months. The incidence proportions of diarrhea, ARI, and malnutrition were 17.0%, 21.6%, and 14.4%, respectively. Neither antenatal nor postnatal depression appeared to be causally associated with risk of diarrhea, ARI, or malnutrition.

The incidences of diarrhea and ARI were found to be lower than those estimated in a prospective study conducted in predominantly rural areas in Ethiopia, which reported incidence of diarrhea and ARI of 26.0% and 25%, respectively (106). These differences may be due to the method of measurement, the age of the included infants and the study setting. Lower incidence for diarrhea (13%) and higher incidence for ARI (33.6%) were reported in a prospective birth cohort study conducted among infants aged 3 to 12 months elsewhere (328). Compared with the present study, higher prevalence of diarrhea (22.1%) was found in the rural setting of Northern Gondar (639) while lower prevalence (14.5%) was reported in a cross-sectional survey conducted in children aged under five years in Bahirdar city (640). These variations may be due to differences in the age of infants included in the study or the study setting, because diarrhea prevalence is reported to be higher in rural than urban areas and it increases as the age of infants increases (639). Despite a substantial reduction in diarrheal and ARI infections in Ethiopia in the last 15 years (641), the estimates from the current and previous studies indicated high prevalence of disease, showing that infant diarrhea continues to be a significant public health problem in Ethiopia.

In this study, the incidence proportion of malnutrition (14.4%) was lower than estimates from a similar population-based cohort study conducted in predominantly rural areas (21.5%) in infants aged 6 months (105). However, the current finding was consistent with a recent analysis of Ethiopian Demographic and Health Survey data in which a prevalence of 15.5% was reported (569). The observed variation in incidence could possibly be due to differences in the type of measurement used to screen malnutrition. In the current study, a MUAC of less than 110mm was used as a cut-off value (379, 642), which was assumed to indicate a sufficiently severe stage of

malnutrition to be predictive of infants at higher risk of dying. However, this cut-off value had not been validated nor routinely used for screening for malnutrition in infants below six months of age in Ethiopia. Irrespective of the type of measurement used, the burden of malnutrition in this age group remains a significant public health concern, given it is reported to be the leading underlying cause of infant mortality and morbidity (643, 644).

In this study, AND was not found to be causally associated with the risk of diarrhea, ARI, or malnutrition. Because no Ethiopian studies using similar methods have been identified, other related studies were used for comparison. Our findings were dissimilar to those of community based cross-sectional (104) and cohort (106) studies conducted in Ethiopia, which variously reported a significant association between maternal CMDs and risk of diarrhea and upper respiratory infection (20) but not with ARI (21). In a population based cohort study in the UK, children under the age of four years had a 27% higher risk of episodes of lower respiratory tract infection when their mothers had experienced perinatal depression compared with children of mothers without perinatal depression (645). Moreover, AND predicted a higher risk of respiratory tract infections in offspring aged up to 10 months (646) in Finland. On the other hand, consistent with the current study, meta-analysis of two prospective cohort studies demonstrated no significant association between antenatal depression and the risk of diarrhea (647). Wasting, underweight, and stunting were also found not to be associated with CMDs in community-based cross-sectional and cohort studies in Ethiopia (104, 105).

However, there were significant variations observed across studies, including instruments used to measure depression, the time when depression was measured, and infant age after delivery when these outcomes were measured. Differences in nutrition measurement and other methodological approaches might also inhibit direct comparisons between the studies. In the current study, not considering a potential confounding effect of sanitation, immunisation, and safe water may have affected the effect estimates in either direction (641, 648). More importantly, specific to the present study, women with a high probability of depression were excluded for ethical reasons which could have affected the number and comparability of exposure between the outcome category, introducing bias that possibly led to underestimation (649). Despite the equivocal evidence, various potential mechanisms have been suggested to

explain the potential link between CMDs during pregnancy and the risk of infant illnesses. For instance, CMD during pregnancy is thought to affect hypothalamic–pituitary–adrenocortical function, thereby influencing the development of the immune system in the offspring and subsequently increasing their susceptibility to infections (650-652). CMDs might also negatively or positively affect health-seeking behaviour and lifestyle of the parents (653, 654).

In the current study, no association was found between PND and risk of infant malnutrition measured using MUAC. Consistent with this, no association was found between CMDs during the postnatal period and underweight and stunting elsewhere (515) or in two other community-based studies in Ethiopia (104, 105). However, a recent study reported PND as a risk factor for stunting in infants aged five to ten months (237). While most studies from Ethiopia reported no association between CMDs and risk of infant malnutrition, a few studies from other African countries have shown a significant association (92, 324, 326, 516). Other infant illnesses that were not related to PND in this study were diarrhea and ARI. Similar findings were reported in community based cross-sectional (104) and cohort (106) studies in which PND was assessed using SRQ-20, in children aged from 0 to 5 years, and in infants aged under two months, respectively. Similarly, a cross-sectional study conducted in Zambia among mothers of infants aged 2 to 12 months reported lack of association between PND measured with SRQ-20 and infant illnesses (324). In contrast, PND was reported as a risk factor for illnesses in infants aged four to twelve weeks and children under five years in prospective cohort studies conducted in Ghana (329) and Bangladesh (327), respectively. Furthermore, a systematic review and meta-analysis reported PND as a risk factor for diarrhea (647). Thus, while the current and other studies in Ethiopia have discounted PND as a risk factor for diarrhea and ARI, studies in other African countries have reported PND to be a risk factor for these childhood illnesses. It is likely that differences in the type and time of measurements for screening depression and age of infants included in the studies may explain some of the differences in findings.

This is the first prospective cohort study conducted in an urban setting of Ethiopia investigating the effects of antenatal and postnatal depression on the risk of diarrhea, ARI and malnutrition among infants aged under six months. This study was also the first to apply a causal model using the TMLE. However, the results of this study should be considered under the assumptions of valid

causal inference. Positivity assumption, which states that all individuals have a positive probability of exposure, may not have been met in this study because women with high likelihood of having severe depression were excluded. The exclusion of high-risk women for the primary exposure would differentially affect the sample size and the quality of exposure category. This could have introduced potential bias and affected the magnitude and direction of the effect size.

The no unmeasured confounding assumption, which states all manifestation of the exposure must be adjusted for a baseline confounder, was not possible to meet in this study. This is because potential confounders such as personal hygiene, water access, latrine availability and cleanliness, different forms of violence, and immunisation status were not investigated. Although the TMLE model is thought to be robust for such model misspecifications, these issues should be kept in mind when interpreting the evidence. We used the MUAC to measure malnutrition in infants of aged under six months, an instrument which has not been validated for use in the Ethiopian context. However, the effect size for the association and degree of significance has been investigated at different cut-off values for MUAC as a sensitivity analysis, and no significant change was observed. The study also used proxy indicators or symptoms in the Integrated Management of Newborn and Childhood Illnesses (IMNCI) guideline to identify infants with diarrhea and ARI, which may have resulted in over- or under-diagnosis of the cases. Nonetheless, the guideline is recommended by the WHO to be used in primary health facilities and has demonstrated high sensitivity and specificity.

6.3.4. Conclusions and recommendations

This study provides somewhat comforting evidence for the lack of any causal association between perinatal depression and the risk of adverse infant health outcomes (diarrhea, ARI and malnutrition) in Ethiopia. Previous studies may have overestimated the risk of poor health outcomes in infants amongst women with perinatal depression. Further studies using similar causal inference methodology are required to confirm these findings.

Chapter Seven: Implementation of perinatal depression health services: barriers and enablers

7.1. Introduction

As stated in chapter one of the thesis, in low- and middle-income countries, mental health services are highly compromised and maternal mental health services even more so (118). Similar to other low-income countries, little attention is given to maternal mental health in Ethiopia (112). This chapter describes a qualitative study conducted to explore barriers to, and enablers of, perinatal depression health service implementation in Ethiopia. The chapter presents a summary of the methods used followed by the results, discussion, and conclusion sections.

7.2. Method summary

A total of 13 in-depth interviews were conducted with mental health and maternal healthcare administrators working at different levels of the Ethiopian healthcare system. The interviews were conducted in Amharic (a local language), translated and transcribed into English, and imported into NVivo. The transcribed interviews were analysed inductively using a thematic framework analysis. Smith's et al. (336) multilevel conceptual framework was used to guide the analysis and interpretation of the study findings. The model posits that mental health service delivery is affected by individual, socio-cultural, organisational, and structural level barriers.

7.3. Results

7.3.1. Characteristics of the study participants

Socio-demographic characteristic of the participants are described in table 7.1. A total of 13 participants was involved in this study, nine of whom were male (69%). Median age of participants was 34 years (range 26–55 years) and the median work experience was 11 years (range 4–35 years). Participants' professional backgrounds were varied, with midwifery (6) and public health (4) being the two largest groups. Most participants were married (77%) and of Orthodox Christian religion (85%).

Table 7.1 Socio-demographic characteristics of participants involved in qualitative study in Ethiopia, 2018 (N=13).

Participant characteristics	Participants (N=13)
Median age (range)	34 (26–55)
Sex	
Male	9
Female	4
Median work experience in the health system (range)	11 (4–35)
Professional background	
Midwifery	6
Psychiatrist	2
Psychologist	1
Master of Public Health	4
Place of work	
Health offices	6
Hospitals	4
Health centres	3
Marital status	
Married	10
Single	3
Religion	
Orthodox	11
Protestant	1
Muslim	1

Three main themes, with 13 sub-themes, emerged as barriers to, enablers of, or opportunities for perinatal depression health services implementations in Ethiopia: (i) health administrators' and community knowledge about perinatal depression, (ii) fragmentation of health system, and (iii) enablers and opportunities. These are described in detail in table 7.2.

Table 7.2 Summary of barriers to perinatal depression health services implementations in Ethiopia, 2018 (N=13)

Themes	Sub-themes
Health administrators' and community knowledge or awareness about perinatal depression	1. Conceptualising perinatal depression 2. Risk factors 3. Signs and symptoms 4. Onset of symptoms and screening 5. Consequences 6. Interventions 7. Community awareness and culture
Fragmented health system	8. Government capacity, readiness, and prioritisation of perinatal depression 9. Perinatal mental health policy and strategy 10. Lack of perinatal mental healthcare system
Enablers and opportunities	11. Introduction of the new mhGap action program 12. Health professionals' commitment 13. Simplicity of screening program

7.3.2 Health administrators' and community (public) awareness about perinatal depression

Seven key sub-themes emerged from the first theme, explaining the roles that health administrators and community mental health awareness and cultural issues played as barriers to implementing perinatal depression health services in Ethiopia.

7.3.2.1. Conceptualising perinatal depression

Proper conceptualisation of perinatal mental health or depression by health administrators is a crucial step in developing appropriate strategies to address the disorder. Some administrators related the concept of perinatal depression to the WHO definition, which proposes health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (655). Thus, the concept of health should account for mental health, which is important in keeping the psychological, spiritual, and emotional component of human health. One health administrator interviewed said:

> *A mother is said to be healthy as defined by the WHO: if she can use her mind properly, if she can resist for any source of stressors, if she is fruitful in any work or activity, and if she can manage or administer her family properly. In line to the WHO definition, health is not merely the absence of disease but should also include mental wellbeing. (Male, aged 32 years)*

Other participants used a range of indicators to define maternal mental health. According to their perceptions, if the mother is free from depression, she would: (i) adhere to perinatal follow-up and usual activities; (ii) overcome challenges (e.g. adjust or withstand life stressors or events related to parenthood); (iii) be confident about herself and her pregnancy (e.g. she has positive thoughts, she is happy and feels healthy during pregnancy or after birth); (iv) have good social and personal interactions. These assertions are seen in the following quote.

> *So, if the mother is mentally healthy, she should be socially, physically, and mentally healthy. In the other way, if she can perform her usual activity, comes for follow-up services, and if she can comprehend what clinicians have said about her health, we can say she is mentally healthy. (Female, aged 50 years)*

Nearly half of participants stated that they did not know about perinatal depression, or they were not sure about it. Other respondents argued that there was no literature or documents written about perinatal depression and the available working guidelines by the government did not

mention perinatal depression. Some respondents tried to use perinatal depression and PND interchangeably. One of the interviewees mentioned:

> *I do not have any idea about perinatal depression though I am a non-communicable disease officer. We are using the new non-communicable disease guideline developed by the Federal Ministry of Health and perinatal depression is not included in the guideline. (Male, aged 41 years)*

7.3.2.2. Health administrators' knowledge about risk factors for perinatal depression

Health administrators' knowledge of risk factors for or causes of perinatal depression is important to enhance their active involvement in designing interventions that would help in prevention and management of perinatal depression. Four main categories of participants and their ideas about how they viewed risk factors for perinatal depression emerged from the analysis of data: (i) participants who lacked awareness about perinatal depression and focused on mentioning risk factors for general depression; (ii) participants who mentioned that the perinatal period by itself could lead to depression; (iii) participants who argued that the perinatal period could not be a risk factor for depression unless other personal issues were considered; and (iv) participants who argued that risk factors for perinatal depression are unknown and remain a matter for debate. These categories are described further below.

i. Participants who lacked awareness about perinatal depression risk factors

A number of respondents mentioned that individual characteristics such as female sex, younger age or older age, and personal misbehaviours such as substance use, alcoholism, drug and smoking are risk factors for depression. It was noted from the interviews that these participants did not have adequate awareness or knowledge about perinatal depression because they were focused on mentioning risk factors similar to those for depression in the general population. One of the participants mentioned,

Those who are addicted to alcohol, chat, cigarettes are more depressed. After they already immersed into it, and when they could not get these substances, they would develop depression symptoms. (Male, aged 52 years).

The reason for this (depression) might not be clear but the epidemiology showed that depression is higher in females than males. This might be because women are not emotionally strong than males. (Male, aged 29 years)

ii. Participants who agreed on perinatal period as a risk factor for depression

Less than a quarter of participants agreed that the perinatal period by itself could be a risk factor for depression. They mentioned that stress associated with the physiological and hormonal changes happening during pregnancy and the postnatal period would lead to depression. Furthermore, women might start to develop stress in the early stage of pregnancy, when they feel that their body size changes as a result of pregnancy or think about their responsibilities for childcare and other family burdens. To demonstrate this, participants said:

Depression could occur during pregnancy or after birth because of some hormonal imbalances and the women would benefit from psychosocial support given by partner or any family members. (Male, aged 26 years).

...especially pregnant women, if in their early stage of pregnancy, when they feel different or start thinking about their pregnancy and the new environment after birth, they might be exposed to depression. (Male, aged 29 years)

iii. Participants who disagreed that the perinatal period was a risk factor for depression

Most participants, however, argued that the perinatal period by itself was not a risk factor for depression except for women facing additional risk factors. The proposed factors included: early age or first-time pregnancy, cultural beliefs, low economic condition, personal misbehaviour such as having substance abuse, poor health condition during the perinatal period, sleep problems, psychosocial problems such as marital problems, lack of partner and social support, unwanted or unplanned pregnancy. Health administrators' thoughts are shown in the following quotes:

Sometimes it (depression) might happen to women when they are in low economic condition or financial struggle. Mostly, pregnant mothers who were pregnant for unwanted or unintended pregnancy are also stressed. If there are young to their age and very difficult for them to handle the pregnancy or they have other duties, they might start to feel depressed. However, I do not believe that pregnancy by itself is a risk factor for depression. (Female, aged 55 years).

… as a culture, when everybody comes to visit the mother, coffee should be served, and such gathering having repeated coffee ceremony might affect their (women) sleep frequency and quality as it is known that caffeine interferes with sleep. Taking care of their kids for long time in the night and their responsibility of leading family put these women not to have adequate sleep leading them to stress and depression. (Male, aged 29 years)

Further cultural risk factors identified for depression included the lack of a person accompanying the mother during delivery. It was suggested that unaccompanied women immediately after delivery might be fearful or even begin to develop psychotic thoughts. The lack of partner or family support may lead her to feel lonely, worthless, or ignored. To express how maternal feelings of loneliness after delivery may lead to depression, one participant said:

…, for example, there is a saying after delivery called, "they leave me alone" or "she/he left me alone". Psychosis or post psychosis might occur like this. Isn't it? They might be tensioned for unknown reasons; can't we say this a peripheral psychosis? (Female, aged 55 years).

iv. Participants who argued that risk factors for perinatal depression are unknown

Apart from psychosocial, genetical, and biological changes related to pregnancy and childbirth, a few participants also mentioned that the cause of perinatal depression is not well known. They mentioned that the disorder is mostly suspected when the mother starts accidentally hating her baby. The participants believed that specific causes of perinatal depression are still subject to debate in scientific literature.

The cause of depression could be related to delivery, pregnancy, genetics or natural, but this is one of the controversial issues for debate. (Male, aged 32 years).

7.3.2.3. Health administrators' awareness about signs and symptoms of perinatal depression

Knowledge about signs and symptoms of perinatal depression is important for early identification and intervention. This sub-theme reflects health administrators' understanding of the signs and symptoms of perinatal depression. Most participants described signs and symptoms of perinatal depression that fell into either physical or psychosocial categories. Physical symptoms included feeling tired, being sleepy, loss of appetite, weight gain, headache, disorganised speech, not responding, inability to speak, unable to accomplish daily activities, over-sleeping, or mood changes. Psychosocial symptoms proposed by participants included feelings of worthlessness, sadness or sorrow, hopelessness, stress or anxiety, loneliness or self-isolation, dissatisfaction with health services, agoraphobia, inappropriate clothing, suicidal ideation or even suicide attempts, shivering, and unconsciousness. Many of the proposed symptoms reflected the more severe forms of depression, rather than milder depression which is most common during pregnancy or the postnatal period, with the rare exception of psychosis which can be severe but is easily diagnosed.

Mother with depression might shows signs and symptoms such as not want to speak, not give right answers for what she has asked, not hearing what she has told, having disorganised speech. For example, I have encountered a mother on her postnatal follow-up and not considered the child as her own, and after repeated discussion, she did not hear us. (Male, aged 27 years)

Mother with depression could show signs such as lethargic, not speaking correctly, unable to give their address, I know these. For example, they might not care for themselves or their foetus or infant. if they have HIV, they might not use condoms correctly. They might not be satisfied with their routine life, they might hate to do their usual activity, or they hate to speak to you. They might show feeling of worthlessness, suicide, sad, sorrow, tiredness, and they would not dress their clothes properly. (Female, aged 55 years)

One participant indicated that they were not sure whether depression symptoms were different for perinatal women than the general population because he was from a different educational background. He was able to mention general signs and symptoms that everybody with depression shows.

> *It is not specifically to mothers, that I do not know, but I can tell you the general signs and symptoms of depression that anybody with depression could show. (Male, aged 32 years)*

7.3.2.4. Health administrators' knowledge about the onset of symptoms and screening of perinatal depression

Health administrators' knowledge about the specific time of onset of perinatal depression symptoms would help the development of protocols to initiate and implement screening programs at its most detectable time, but participants' knowledge or awareness about perinatal depression signs and symptoms was not specific. Their descriptions better reflected signs and symptoms of general depression. Participants commonly compared the extent of depression occurring during pregnancy and after birth. Some suggested that depression occurred more commonly during pregnancy than after birth. Another argued that depression rarely occurred during pregnancy but was more common after birth.

> *In some of the mothers, it might occur early like during their first trimester, but most of the time, it occurs at the end of the pregnancy. After birth, it is not common, but depression might occur in a few of the mothers. (Female, aged 32 years)*

> *Sometimes depression might occur at the time of delivery though it was not reported in our institution. However, most of the time it occurred after delivery or during the postnatal period. (Male, aged 27 years)*.

Health care administrators need good awareness about the timing of specific signs and symptoms of perinatal depression to detect it early and provide appropriate care for perinatal women. However, concerningly, there were participants who were not able to identify the period by which signs and symptoms of perinatal depression might manifest.

Honestly speaking I do not really know the time by which these mothers start to show signs of depression or develop signs of depression. (Male, aged 32 years).

Participants' attitudes towards a specific time of screening for perinatal depression correlated with those about the time of occurrence of depression. Those who believed that depression is a problem of pregnancy perceived that screening should be conducted during any contact made with pregnant women during pregnancy, and they proposed the ANC visit as an appropriate time. Those who believed that depression was a problem of the postnatal period stated that depression screening should take place during the postnatal visit. In general, the best time proposed by many participants was at the time of ANC and PNC visits. This is justifiable because, while perinatal women present to health facilities for pregnancy and postnatal check-ups, in Ethiopia few postnatal women attend PNC visits.

The screening should take place starting from the time of pregnancy until the postnatal period as we do not exactly know when the depression signs start to manifest. However, we give focus to postnatal depression as its prevalence is high. When we say postnatal, it includes from four to six weeks. (Male, aged 28 years).

Mainly if it (depression) should be screened, screening should be conducted during pregnancy when she comes for ANC follow up, when she comes for delivery, and thirdly after delivery when she comes for PNC follow up. (Male, aged 27 years).

Some participants indicated that screening for depression should be conducted at outpatient departments in health facilities. In the Ethiopian context, outpatient departments are areas in health facilities where patients receive immediate assessment and treatment. Most often, however, perinatal women attend maternal health clinics for issues associated with their physical health rather than visiting outpatient departments. This might suggest that participants were not adequately aware of perinatal depression.

I would be happy if screening could be done all the times. For example, in the outpatient department. Yet, we do not have psychiatry nurses in our health centre, and if we have one that can screen depression, this will help in reducing its burden. (Female, aged 55

years).

Other participants suggested that perinatal depression screening could be conducted during house to house visits. This idea was in reference to the use of health extension workers. These workers implement the Health Extension Program, which is a vertical program designed in Ethiopia in 2003 to improve access and affordability of primary health care services. The program has been designed in two implementation modalities. The first is the Rural Health Extension Program implemented in rural areas, while the Urban Health Extension Program was implemented in urban areas in 2007 using urban health extension workers. These are nurses who have completed specialist training about the program for three months. Urban health extension workers make house to house visits to provide maternal and child health services. One component of this work is mental health assessment and referral. Participants' suggestions that perinatal depression screening should be conducted through house to house visits was made in reference to urban health extension workers.

> *The screening of depression for mothers should be started at their home by health extension workers as the urban health extension workers' package addresses mental health issues. (Male, aged 41 years).*

Disagreeing with the above, another participant working at a higher level in the healthcare system claimed that there was no evidence clearly showing that depression during pregnancy is common or that screening should be implemented. Furthermore, the participant stressed that the specific time at which this depression should be assessed and how to assess it is unknown.

> *There is nothing that says pregnant mothers are at risk of depression, and they should be assessed at this point. For example, I know that a pregnant mother who has suspected to have sexually transmitted diseases should be checked and treated after three months. But there is no study that recommended time by which depression during pregnancy should be assessed and treated. There is no screening procedure for depression in pregnancy. (Male, aged 52 years).*

7.3.2.5. Health administrators' knowledge about the consequences of untreated perinatal depression

Health administrators' knowledge or awareness about consequences of untreated perinatal depression is crucial in order to give the matter attention or priority in government planning. Four categories of responses emerged concerning consequences of perinatal depression: (i) depression exacerbates to a severe form or leads to suicide; (ii) depression affects foetal development and birth outcomes; (iii) depression affects newborn health and development; and (iv) depression could results in family or social disruption.

i. Depression exacerbates to a severe form or leads to suicide

Almost all participants raised concerns that untreated depression would develop into a severe mental health disorder and potentially lead to suicide. However, the type of depression referred to would appear to be a severe form. Depression that occurs during the perinatal period is more commonly mild or moderate, which can be difficult to identify and diagnose. The severe form of depression that most participants discussed was severe psychotic disorders. It is possible they felt that perinatal depression, which is usually categorised as a non-psychotic disorder, could further develop into a psychotic disorder, as they stated:

> *If they stop taking their drugs, this might lead them to leave and sleep on roadsides or outside their house. (Female, aged 55 years)*
>
> *Unless we diagnose and treat depression at an early stage, it might develop into an irreversible psychiatric problem such as dementia, which is unwanted. (Male, aged 29 years).*

Most participants also suggested that untreated depression could lead to maternal suicide and death. This could be through worsening to a severe form of health disorder that affects health seeking behaviour or makes women feel lonely and hopeless, leading to deteriorating health conditions including suicide or death. Other participants suggested that depression directly leads to death because it is reported to be a major cause of death worldwide. Interviewed hospital workers stated:

Finally, if they are not treated from depression, they start to feel hopeless and, at last, go to suicide. When they had severe thought of hopelessness, they start asking about what is living for them. As they lose the meaning of life, living in this world would be nothing for them. So, they start with the idea of suicide, then they attempt and commit suicide at the end. (Male, aged 34 years).

The end consequence is death as depression by itself is a disease that cause death. (Male, aged 27 years)

ii. Depression affects foetal development and birth outcomes

The effect of perinatal depression on foetal development and birth outcomes was discussed. Participants explained the link in several ways. (a) Not using antidepressant medication correctly could affect foetal development and birth outcome; (b) genetic transmission of depression via placenta could lead the newborn baby to foetal distress and death; (c) depression could cause high blood pressure that would complicate the pregnancy and lead to abortion; and (d) depression could affect the nutritional status of the pregnant woman and foetal development.

Her foetus might have retardation, and in our culture, it is having been believed that, if the mother has depression, it also passes to the kid genetically. Based on my information or what I have heard, your foetus is healthy if you are healthy or your foetus is active if you are active. (Female, aged 55 years)

During pregnancy, a mother in severe depression might not feed herself well; if she feels unmotivated or inactive, the foetus will not develop well, its growth would be restricted, or the pregnancy might end up in abortion. (Male, aged 26 years).

iii. Depression affects newborn health and development

The adverse effects of perinatal depression on infant health (morbidity) such as malnutrition, illnesses, and death were mentioned by the participants. Potential links between perinatal depression and infant morbidity that were proposed included reduced infant care, difficulty breastfeeding, and poor health-seeking behaviour. Perinatal depression as a cause of infant

death was explained by the participants in two ways. The first is because of psychosis, which may present with sudden onset because of major hormonal imbalances after birth and that leads the mother to kill her newborn (infanticide). This is possibly an indication of a lack of clarity among study participants, because depression and psychosis are different conditions. The second is through maternal death caused by depression, leaving the newborn orphaned and vulnerable to diminished care and development. Perinatal depression as a potential cause of mortality is also unlikely, which may indicate low awareness among participants.

> *If the mother is depressed, she might not breastfeed her infant properly; she might not take to immunization; nutritional status of the newborn might be affected. If not properly fed, the infant might be stunted or died. (Female, aged 55 years).*
>
> *The mother starts to hate her infant and if she has no social support or if there is nobody around her, she might kill her infant by choking or by any other means. (Male, aged 34 years).*
>
> *The mother might die from depression or other related conditions leaving the newborn orphaned, which affects cares to be given for the newborn that leads to poor growth or death. (Male, aged 27 years).*

iv. Depression as a cause of family or social disruption

Nearly half of the participants identified the consequences of perinatal depression on social or family disruption through reduced income, disrupted relationships, and inability to work. Mood swings and inability to communicate effectively because of depression symptoms would affect social and family interpersonal relationships. Similarly, because of decreased desire to work and perform routine activities in the home or outside, the woman's acceptance, family income and relationships would be compromised. This could directly or indirectly lead to family or social disruption. Their behaviour change would also affect women's interaction with their social circle or family.

She might not correctly work what she has been working because of the depression. So, she might affect her family income as depression affects her work interest and productivity. (Male, aged 52 years).

Depression affects health of the mother and this indirectly affects the family. For instance, the mother might be unable to handle her family or not well functioning in performing routine activities in the family. (Male, aged 41 years).

7.3.2.6. Participants' views about perinatal depression interventions

This sub-theme highlighted health care administrators' views on how to care for perinatal women with depression. Two main views emerged from the analysis: (i) mothers with depression symptoms should be referred to hospitals because these are the only places where antipsychotic drugs are available, (ii) psychosocial support should be provided by health professionals, partners or families of mothers. Almost all participants recommended psychosocial support in the first place, with treatment for psychosis if the condition was severe. The following quotes show this:

For those who had depression, we provide social support by identifying possible sources of depression through psychological treatment or psychotherapy. If it (the depression) is severe enough, we provide them with psychotic drugs. And for mothers who have minor depression, their family should be informed or advised on how to provide them (the mothers) with support. (Male, aged 34 years)

If they are in a severe state, they might commit suicide or attempt committing suicide. Care should start by discussing with the mother to share the cause of the stress with their partner and families. During the discussion, they might get relief from their stress. But if it (depression) turns to a severe stage, they should visit health facilities for better care and treatment. (Male, aged 32 years)

7.3.2.7. Cultural perspectives and lack of community (public) awareness about perinatal depression

Low community health literacy or awareness, low health-seeking behaviours for mental health, and cultural norms about perinatal depression indirectly affected implementation of perinatal

depression health services. Community awareness about perinatal depression and good health-seeking behaviour are very important to prevent and control the problem. Participants were concerned that women might seek out cultural and religious approaches to manage their depression rather than conventional health services by thinking of the disorder as evil and giving it other cultural meanings. Participants mentioned that public (community) awareness about mental health disorders, including depression, is low and people were not aware that such mental disorders are treatable. Participants raised the issue of community health literacy and poor health-seeking behaviour related to public cultural practices:

> *In fact, in addition to the lack of data, in our area where we are living, culturally, mothers would not prefer to go to health facilities when such disorder is happening to them. As depression is considered evil and demonic, most of the time, perinatal women prefer to go other places for service such as spiritual places to use holy water. (Female, aged 36 years)*

> *The other barrier is community awareness on mental health condition or depression, they do not know that this condition is treatable. (Male, aged 52 years).*

7.3.3. Fragmented healthcare system

Three sub-themes emerged from interviews under the main theme of the fragmented healthcare system: (i) perinatal mental health policy and strategy; (ii) perinatal mental healthcare system; and (iii) government capacity, readiness, and prioritisation of perinatal depression

7.3.3.1. Perinatal mental health policy and strategy

The Ethiopian National Health Policy is an overarching document that provides guidance on how the country should address long-standing and emerging health priorities. This sub-theme assessed health administrators' views about how Ethiopian health policy addressed the issue of maternal mental health. Most participants expressed concerns that mental health services in general were compromised. Participants tried to underline the lack of attention to mental health services in Ethiopia by highlighting the lack of mental health policies and programs that should guide government activities. The following quotes reflect these concerns:

So, I can say mental health issue and concerns are not receiving much attention from the top government. For example, if you try to contact the health bureau for issues concerning mental health, nobody gives you attention and services. Even when it is related to our ward (psychiatry ward). Generally, there is a lack of attention, starting from the policy framework, curriculum, and training. (Male, aged 34 years).

I personally would like to say interventions for mental health morbidities at the country level are at a very infant stage. (Male, aged 34 years)

The lack of clear policy frameworks and programs might also affect appropriate training and allocation of human resources for mental health. The lack of properly organised mental health structures at different levels of the Ethiopian healthcare system may also stem from the lack of a national mental health policy and related programs. Despite being the second most populous region in the country, it does not have organised teams of mental health experts or mental health specialists able to plan and establish mental health services at the regional level. One participant said:

There is no mental health focal person at the regional level. If there is no focal person, nothing would be done. But if there is a focal person, he/she can plan, deal, arrange … (Male, aged 34 years)

The general national mental health strategy developed in 2012 did not specifically address mental health need of vulnerable groups such as perinatal women, peoples with disabilities, and incarcerated people. Nearly all participants confirmed that the available national mental health strategy did not specifically focus on the diagnosis and treatment of perinatal depression. The following quote demonstrates this:

We do have a general country-level mental health strategy, but it is not specified for age, sex, or specifically designed for pregnant mothers, and it is a general approach. (Male, aged 34 years)

7.3.3.2. Perinatal mental healthcare system

A healthcare system is the organisation of institutions, departments, health professionals and resources that are essential to deliver all healthcare services required to meet the needs of a given population. To undertake screening and manage perinatal depression, therefore, there should be an established and clear healthcare system at all levels that can address the 'who, how, where, when and what should be done' questions. The main barrier, agreed by almost interviewees, was the lack of an established system to prevent, screen, and treat perinatal depression. As one participant described:

> *The system might be challenging; for example, it would be difficult to say that clinicians in the area of ANC can know and screen depression. If you go to other health facilities or such clinics and ask how they are screening pregnant women with depression, they would tell, we use nothing. This itself can be part of the system. So, if the mother has depression during pregnancy or after delivery, she might be missed or misdiagnosed because of the lack of provision to identify the problem. And as a psychiatry clinic leader, if I want to create a system like if I want to assign a psychiatrist in ANC or PNC department to screen depression, nobody allows me, and this is part of a system too. (male, aged 28 years)*

7.3.3.3. Government capacity, readiness, and prioritisation of perinatal depression

This sub-theme includes healthcare administrators' perspectives of government capacity, readiness, and priority for screening and managing perinatal depression at health service delivery points. The actual activities implemented at service delivery level to address perinatal depression were explored. All those interviewed agreed that there was no effective or adequate guidance for managing perinatal depression in health facilities at different levels of healthcare delivery. One health administrator from a health centre said:

> *Yes, I can say the Federal Ministry of Health (FMOH) has no initiative, plan, and readiness to screen, treat, prevent, and control perinatal depression in the healthcare system. So, if FMOH has no such initiatives, it isn't very easy, or it is obvious that health structure*

beneath the FMOH would have no such initiative as every activity we are doing is based on the FMOH direction. (Female, aged 36 years)

Participants identified reasons for such little attention as: (i) there was lack of priority; (ii) there was lack of knowledge on the burden and consequences of perinatal depression; (iii) health professionals were not trained to screen depression; and (iv) high patient load

i. Lack of priority

Because Ethiopia is a low-income country, resources are limited, and it is not possible to tackle every health problem. As such, a focus on priority health conditions is considered mandatory. Priority has been given to conditions that are the leading causes of mortality and morbidity. It has been believed that perinatal depression is not a leading cause of mortality and morbidity in Ethiopia, compared with other communicable and non-communicable diseases of pregnancy and childbirth. One participant mentioned the following to show that perinatal depression is not a priority issue for the government:

Because of many other communicable and non-communicable diseases that need fast attention, perinatal depression is not given a high priority. To reduce maternal and child mortality, hypertension, obstructed labour and infections causes higher numbers of deaths than depression. As such, if we strictly work on these issues, we might bring more changes in maternal health. We are also one of the low-income countries with limited resources, and the Ministry of Health might believe that more attention should be given for such conditions than depression. As you see, due to there being many health issues in the country, the government prioritises and focuses on interventions that benefit most of the women. (Male, aged 29 years).

ii. Lack of knowledge on the burden and consequences

The second reason for the low priority given to perinatal depression might be related to health administrators' limited knowledge about its burden and consequences. As was concluded in the previous section (section 7.3.1), health administrators' knowledge about the burden and

consequences of untreated perinatal depression was low. More importantly, health administrators working at higher levels of the healthcare system, where policy and strategy is crafted, were found to have less knowledge than those working at lower levels of the healthcare system. This would significantly affect health administrators' motivation towards prioritising, planning, and initiating perinatal depression health services. There also appeared to be insufficient information on the consequences of perinatal depression to make perinatal depression a priority focus of the government, as one participant working at a higher level of the health care system said:

> *As I told you about this, there are no separate and specific activities. The primary thing about perinatal depression is that we do not consider it as a public health problem of significance, and we do not have data about it. It has not been the forefront of public health priority threats in this region. (Female, aged 50 years)*

iii. Health professionals were not trained to screen for depression

The lack of trained health professionals or psychiatrists was mentioned as an important barrier to screening for and treatment of perinatal depression. The question about who should be responsible for screening needs to be clearly addressed in the healthcare system and enough personnel should be trained and made available in all health facilities that are expected to intervene in perinatal depression. This comes back to perinatal depression not being included as a priority health item in the country. Human resource development is a main issue for any perinatal mental health strategy and plan, but without such plans, attention given to human workforce development would be compromised. One participant working as a coordinator at a higher level of the health care system said:

> *Starting screening service is not easy. We do not have health professionals who trained in mental health. It needs a psychiatrist to screen and manage perinatal depression, and these professionals are minimal, including those who are in schools. So, we do not have trained professionals now, and it is challenging. (Male, aged 52 years)*

iv. High patient load

Another barrier described by participants as a reason for government giving low priority to perinatal depression was high patient loads in health facilities because of other morbidities. As explained in a previous section, Ethiopian health facilities always have to treat large numbers of patients with different acute and chronic health problems. At the same time, the country is placing increased demands on health professionals in health facilities. This might affect perinatal depression screening and management because of the time required for even relatively brief consultations with perinatal women. One interviewee said:

> *As this is a tertiary hospital, every client comes for better service. As such, due to time limitation, it is not easy to rule out additional problems like depression. (Male, aged 29 years)*

7.3.4. Enablers for or opportunities to start perinatal depression screening services

This theme presents health system administrators' views about the current situation of mental health services and the enablers for or opportunities to start perinatal depression screening services in Ethiopia. Participants mentioned that mental health services are very compromised and were only focused on treating those who were presenting to health facilities and had severe problems. They further added that there was no system for early detection and prevention of mental health disorders in the community. However, participants identified three potential opportunities or enablers that could help the Ethiopian healthcare system to start screening for depression in women during perinatal period and put in place effective management of it. These were: (i) the introduction of the WHO Mental Health Gap (mhGap) (119) action program, (ii) health professionals' commitment, and (iii) simplicity of the screening program.

7.3.4.1. The introduction of the WHO Mental Health Gap (mhGap) action program

The mhGap action program is a national and international initiative developed by the WHO to fill a mental health service gap between what is available and what is urgently needed to reduce the burden of mental disorders. Participants mentioned that the introduction of the mhGap initiative could potentially provide an opportunity to start and expand maternal mental health

interventions in Ethiopia.

> *Until now, the available policy does not allow non-psychiatry health professionals to provide psychiatric services. Mental health services have been limited at the hospital level. But nowadays, because of the findings by WHO that the burden is becoming high, mental health is getting attention. One psychiatrist used to serve a population of 100,000. These days, health professionals are being trained, protocols are being under preparation, and activities have been started under MhGap initiatives to bring mental health services to health centre level. (Male, aged 52 years)*

7.3.4.2. Health professionals' commitment

Health professionals' commitment would also be needed to enable screening for perinatal depression in health facilities. Participants hoped that screening perinatal women for depression would not be more challenging than what they currently do for everyone visiting a health facility. Health administrators mentioned that health professionals and themselves were highly motivated to make screening available and to manage perinatal depression if the health system could be made ready for this. One participant mentioned that it is possible to make screening for perinatal depression available if the environment is ready:

> *There is no guideline and system for screening and management of perinatal depression. If there was a system, we could identify perinatal depression. I don't think there would be a problem for us to implement if the screening program was made available. I believe there should be such a service for our women (screening, referral, treatment), I understood now. (Female, aged 37 years).*

7.3.4.3. Simplicity of the screening program

Simplicity of the screening activity was another identified enabler for instituting screening in health facilities. Participants mentioned that screening would not be difficult when compared with assessment of physical and internal conditions of patients using laboratory samples, which requires laboratory facilities, reagents, and additional skilled professionals. Using a brief

screening tool, screening for depression would require a maximum of 15 minutes to implement. Similarly, additional physical space would not be required for screening because assessments could be undertaken in the same rooms where ANC and PNC services are delivered. One participant stated that health professionals are motivated and committed to undertake screening, and the only problem is lack of skill and a supportive system.

> *Yes, maybe we would screen and refer, this would be simple. I can see it is possible to screen pregnant and postnatal women with depression. I saw a Master's student who did the screening in our health centre, so it is also possible as you are also doing the screening as well. (Female, aged 50 years)*

7.4. Discussion

Mental health literacy of policy makers and healthcare system leaders and the organisational context of the Ethiopian healthcare system are bottlenecks for effective mhGap action program implementation (114). In support of this, the following barriers were identified in the current qualitative study: (i) At the individual level, health administrators have little knowledge about perinatal depression risk factors, symptoms, optimal time for screening, treatment options, and consequences. (ii) At the socio-cultural level, there is low awareness about perinatal depression in the community, and health-seeking behaviours and cultural norms are barriers. (iii) Organisational level barriers include lack of government capacity, readiness, and priority to screen and manage perinatal depression. (iv) Structural level barriers include lack of perinatal mental health policies and strategies, and transparency in the healthcare system. In addition, the study found that the introduction of the new mhGap action program, health professionals' commitment, and simplicity of screening program could represent opportunities for or enablers of implementation of perinatal mental health services.

Health administrators' low knowledge about perinatal depression risk factors, signs and symptoms, time of screening, health consequences and interventions are identified as individual level barriers for perinatal depression service implementation. Health administrators' low level of knowledge in defining and conceptualising perinatal depression also emerged as a barrier for diagnosis and treatment of perinatal depression in other studies (656, 657). Similarly, health

professionals' low level of knowledge about signs and symptoms of perinatal depression and difficulties in identifying women with perinatal depression have also been previously reported as barriers (658, 659). This low level of knowledge about perinatal depression among health administrators and health professionals knowledge could constitute a major barrier for effective integration of maternal mental health and routine health services at the primary health care level (660). Good mental health literacy is important for improving health, healthcare systems, and health policy (661, 662) and this should be a priority issue for health professionals working at administrative level. As such, previously conducted reviews in low- and middle-income countries have highlighted the need to build capacity of policy makers and planners to help strengthen mental healthcare systems (663, 664).

Study participants identified that low community awareness about perinatal depression, health-seeking behaviours, and cultural norms were socio-cultural level barriers to implementation of perinatal depression healthcare services. As described by participants, cultural norms often consider depression as 'evil' or 'demonic' rather than as a health problem that could be treatable, which could be also related to fear of stigma to seek health intervention. This is similar to cultural and community level barriers to access for mental health services identified in a systematic review and meta-synthesis of qualitative studies in the UK (336) and elsewhere (665-667). Similarly, low community mental health literacy and lack of models for multisectoral collaboration with traditional and religious healers were also reported as key challenges for implementing integrated mental health care in low- and middle-income countries (668). As such, health information on common perinatal mental health disorders should be provided for perinatal mothers in the community through health extension workers using a culturally sensitive approach. Furthermore, creation of awareness about the differences between normal pregnancy feelings and perinatal depression symptoms might be required to increase health seeking behaviour of women. Nonetheless, simply increasing community awareness in a healthcare system where perinatal mental health services are not well organised or functioning, is likely to have only limited success.

Lack of government capacity, readiness, and priority for screening and managing perinatal

depression were organisational level barriers to perinatal mental health interventions discussed by study participants. Patient loads, lack of trained workforce and resources such as screening tools, guidelines, working manuals, and treatment protocols were potentially linked to lack of government capacity, readiness, and priority. These barriers should be addressed to establish an efficient depression screening and management program in the country. This finding was consistent with organisational level factors reported by Smith (336) in a multi-level model of barriers to perinatal mental health interventions. Staff workloads and lack of time with health professionals for health service linkage were reported to be barriers to screening and referral for perinatal depression in high-income countries (120, 669, 670). Furthermore, lack of training in mental health care, resources, and locally validated screening tools, together with health professionals' lack of positive attitudes towards screening were reported as barriers in systematic reviews of qualitative studies (118, 671-673). Insufficient or lack of training, unexplained long waiting times, inconsistent screening practices, and not knowing the scope of practice were mentioned as common barriers for identification and treatment of perinatal mental disorders in other systematic reviews (674, 675). Low levels of funding have also been reported as a key challenge for sustainable mental health services because of widespread poverty and inequalities of access in low-income countries (676). As such, it has been suggested that both perceived and established barriers associated with client or service providers should be addressed to create a suitable environment for implementing and maintaining mental health continuity of care in health facilities (144, 677).

Lack of perinatal mental health policies and strategies were proposed as structural level barriers to implementation of perinatal depression health services in Ethiopia. Lack of clarity in policies about how to screen for perinatal depression, and lack of clear pathways of care for those who had symptoms, were reported as structural level barriers to perinatal mental health interventions in a systematic review of qualitative studies (336). The health policy of the government of Ethiopia has a central focus on preventing and treating diseases (678), but it does not address the issue of perinatal depression. Moreover, in the National Mental Health Strategy developed in 2012, only two paragraphs were devoted to reproductive mental health. There is lack of clarity on what should be done and how, and, generally, issues with its implementation have not been

well addressed (402). A situational analysis in five low- and middle-income countries including Ethiopia revealed a lack of evidence for feasible detection and treatment strategies for mental health disorders (118). The probable reason was a lack of priority that possibly emanated from lack of information or data on the burden and consequences of perinatal depression.

The absence of clear pathways in the healthcare system was the other most discussed structural level barrier to implementation of perinatal depression services. This is consistent with structural barriers reported in a multi-level model of barriers of perinatal mental health interventions in high-income countries (336). Perinatal women with depression symptoms in Malawi proposed that strengthening the healthcare delivery system was the most important issue to address their needs (679). Lack of clear work structures or systems for identifying perinatal women with depression and broken referral pathways were identified as important structural barriers to perinatal mental health intervention in a systematic review (665). In another study, structural or system level barriers to perinatal mental health implementation included complex and unclear pathways such as unlinked services, lack of continuity of care, scarcity of referral resources, and complex bureaucratic procedures (674).

Several studies have indicated that perinatal depression is both a complication (680) and/or a consequence of complications in pregnancy (681-683). Perinatal depression could be a cause of complications that significantly affect pregnancy outcomes (677, 684, 685), child development, and leave mothers at higher risk of psychological morbidities (118, 647, 686-688). Screening and providing psychotherapy to perinatal women at higher risk of depression would not significantly increase the overall cost of health expenditure in the health care system, and its benefit would outweigh the cost (689-691). Antenatal and postnatal depression prevalences as high as 32% (255) and 34% (81), respectively have been reported in Ethiopia, and perinatal depression is documented as having multifaceted consequences for children (692, 693) and mothers (694). In this context, the American Psychiatric Association (695), College of Obstetrics and Gynaecology (696), US Preventive Service Task Force (697), and the World Health Organization (698) have recommended screening and treatment. The effectiveness of screening and preliminary counselling interventions in preventing perinatal depression has also been documented in recent literature (689-691). Given this evidence, it is important for the government of Ethiopia to

consider the integration of perinatal depression into routine maternal health services by overcoming the current complexities (699). The following opportunities and enablers that were discussed by study participants might help to simplify this integration.

Health administrators in this study discussed the introduction of the new mhGap action program, health professionals' commitment, and simplicity of screening programs as enablers or facilitators for perinatal mental health service implementation. This is in line with a qualitative study that explored health professionals' positive attitude towards the integration of mental health services as a facilitator for the acceptability of mental health services to perinatal women in Ethiopia (700). The mhGap action program has a priority for integrating mental health services into primary care services, and maternal mental health has been considered as an essential component of this integration (119). The mhGap initiative aims to train and use generalist nurses to diagnose and treat mental health disorders at the health centre level, which could potentially help to overcome shortage of human resources. It also aims to increase mental health awareness in the community to improve early detection and treatment. Perinatal women are more likely to be screened when health professionals are sensitive and interested, when there is continuity of care, and women are reassured that depression screening is part of a routine antenatal care (666, 701-703). Similarly, both qualitative and quantitative studies have shown a high level of acceptance of perinatal depression screening by health providers and perinatal patients (667, 669, 704, 705). The simplicity of screening programs adds support because any health professional can undertake screening, or the screening tool could be self-administered by mothers (706), assuming the screening tool is validated and culturally acceptable (373, 707).

There are limitations that should be born in mind during the interpretation and use of these findings for decision making. Some younger participants had limited experience, and this could affect an in-depth understanding of health policies, programs, and strategies of the country in general and perinatal depression in particular. The other limitation was the potential introduction of social desirability bias, for instance through concerns that their responses might be communicated to higher officials. Despite these limitations, this is the first attempt to explore barriers to and enablers of perinatal depression service implementation in Ethiopia. As such, the

findings will therefore be useful to health planners, researchers, partners and, ultimately, perinatal women and their infants.

7.5. Conclusions and recommendations

The study identified health administrators' low literacy about perinatal depression as an individual level barrier; community low awareness, health-seeking behaviours and cultural norms about perinatal depression as socio-cultural level barriers; lack of government capacity, readiness, and priority for screening and managing perinatal depression as organisational level barriers; and lack of perinatal mental health policies, strategies, and healthcare systems as structural level barriers for perinatal mental health service implementations in Ethiopia. On the other hand, introduction of the new mhGap action program, health professionals' commitment, and simplicity of screening programs were identified as enablers or facilitators for perinatal mental health service implementation. Building the capacity of policy makers and planners should be a first step in mental healthcare system building related to perinatal depression in Ethiopia. Strengthening the mental healthcare system and governance to produce clear mental health policies, programs, strategies, structures, and legislative framework is mandatory for effective integration of maternal mental health care with routine maternal health services in Ethiopia.

Chapter Eight: General discussion

8.1. Introduction

Depression is a leading mental health problem compared with other CMDs (3). Females of childbearing age are highly vulnerable to depression (708, 709) because of the large fluctuations in peptide and steroid hormone levels associated with pregnancy and childbirth (710). Depression during the perinatal period has been under-investigated and poorly treated in low-income countries (708, 709). In Ethiopia, comprehensive studies on perinatal depression and its association with the risk of adverse birth and infant health outcomes are lacking. This PhD thesis therefore attempted to fill this gap by: (i) prospectively and sequentially addressing four quantitative research questions that have been presented in detail in chapters five and six; and (ii) qualitatively exploring the barriers to and enablers for implementation of a perinatal depression service in the Ethiopian healthcare system, presented in chapter seven. The current chapter synthesises the findings from previous chapters to inform general discussion. The content of this chapter is presented in three sections. The first section presents the prevalence of antenatal and postnatal depression and their potential causal mechanisms. The second section describes the association of antenatal and postnatal depression with the risk of adverse birth and infant health outcomes. The qualitative study has been integrated and presented within the quantitative findings. The last section addresses the strengths and limitations of the thesis.

8.2. Perinatal depression and its causal mechanisms

Perinatal depression is a major contributor to disease burden in both developed and developing countries (417, 711, 712). It poses a high economic burden for the health system and represents the largest contributor to maternal psychological disturbances (713, 714). Perinatal depression also affects maternal quality of life and adherence to medical and psychological interventions (710, 715). According to the systematic reviews described in chapter five, on average about one in four pregnant and postnatal women has experienced depression symptoms in LMICs. This is far higher than the magnitude of estimates in high-income countries (21-23, 73, 75, 524). The burdens of antenatal and postnatal depression are found to be heterogeneous in Africa (228). In

Ethiopia, depression is reported to be a common health disorder of pregnancy and childbirth (39), but compared with AND, PND is rarely studied.

Prevalence of antenatal (6.9%) and postnatal depression (9.3%) estimated in the current study was lower than estimates in previous studies in Ethiopia and other low-income countries (78-82). The prevalence of perinatal depression (11.7%) and incidence of PND (7.8%) estimated in the current study were also lower than in a study conducted in the rural part of Ethiopia (79). The low prevalence of perinatal depression observed in the current study was probably because of the exclusion of women in higher-risk groups and those in their first trimester of pregnancy or first 15 days of the postnatal period. There is equivocal evidence regarding when depression symptoms tend to be high and the ideal time for screening (20, 166, 716). However, recent evidence on trajectories of depression during the perinatal period suggest that depression should be considered as a continuous risk for the mother and newborn regardless of its onset (717). As in previous prevalence studies using screening tools in Ethiopia, this thesis found that the prevalence of antenatal and postnatal depression is a major public health problem.

The evidence that depression is common during the perinatal period can be well explained by a combination of hormonal changes and other environmental factors (423-426). Perinatal depression is a multi-level phenomenon (718). Biological (genetic or biochemical), psychological (personal history or familial environment), and socio-cultural (socio-economic, social isolation, cultural diversity, socio-political situation and inequalities) characteristics are important sets of causes theoretically emphasised in the literature (718). Despite the challenge of understanding the complex interaction among biological, psychological, and socio-cultural level factors that can be difficult to quantify, treatment approaches in clinical practice should take each person's total life situation into account. Further investigation into the biological and cultural risk factors for perinatal depression is required.

This thesis focused on identifying individual-level factors associated with perinatal depression with its conceptualisation guided by a stress process model (131). The use of the model advanced the existing body of literature on factors associated with antenatal and postnatal depression by proposing their potential causal mechanisms. The conceptualisation of a stress process model

was described in the first section of the methodology chapter. Based on the proposed potential causal models: (i) a history of CMDs, fear of giving birth, unplanned pregnancy, and food inaccessibility directly and significantly increased the risk of AND; (ii) the risk of AND was significantly reduced through the buffering effect of social and partner support and satisfactory marital relationships; and (iii) AND, LBW and self-reported labour complications increased the risk of PND, and were also directly or indirectly linked to the risk factors associated with AND.

Substantial global evidence exists about the direct effect of a history of CMDs before pregnancy on the risk of subsequent depression symptoms during the perinatal period (75, 76, 84, 125, 127, 165, 182, 183, 411). For example, more than one-third of those who had depression during pregnancy went on to have PND, and nearly half of those with PND had a history of depression during pregnancy (608). Similarly, in the current study, 7% of women free from AND developed PND and more than 2% had depression at both times. Study participants from the qualitative study also discussed how a history of depressed mood before pregnancy could continue to manifest during pregnancy and the postnatal period. Because the participants in the qualitative study were clinicians or health professionals leading the healthcare system, it is reasonable to assume they would have had practical experience in managing depression during the perinatal period. Furthermore, depression tends to recur and natural (untreated) remission would be difficult when most psychological, socio-economic, and cultural characteristics remain unchanged (718).

Economic adversity and various forms of interpersonal violence were among the most commonly reported risk factors for perinatal depression in the scoping and systematic reviews presented in chapter four (166, 716). It is likely that these risk factors are highly interrelated and co-occur in societies sharing similar geography and culture (719, 720). Epidemiological studies showed that perinatal women with depression were likely to have been exposed to violence in their lifetime (166, 541). The causal link between lifetime violence and depression has been also established in biological studies (434-439). Domestic violence is most likely to have been perpetrated by partners in patriarchal societies such as Ethiopia, because of male dominance particularly in regard to financial capacity and decision-making processes (721). Entrenched gender roles in patriarchal societies significantly affect the financial resilience of many women, increasing their

overall stress (125, 337, 722). This was also demonstrated in the quantitative and qualitative findings of this thesis. This stress could be worse for women with unplanned pregnancy because this could potentially affect partner relationships and support (127, 165, 182, 187, 255). Furthermore, living in economic hardship triggered by unplanned pregnancy may affect maternal self-esteem, personal coping ability, and psychological preparedness for the delivery (520).

Social and partner support are important sources of psychosocial therapy for depression and have been shown to reduce maternal stress through increasing stress coping and resilience (166, 409, 541, 723). The causal model hypothesised in this thesis for AND also revealed a potential buffering role of partner and social support through the reduction of the potential effect of other stressors. Health administrators participating in the qualitative study also repeatedly mentioned social and partner support as the main approach for treating perinatal depression. Natural remission from depression does not often occur in women with poor support, and women with AND tended to continue to have depression during the postnatal period and beyond (724, 725). Women at risk for depression are more likely to report low support, economic adversity, and history of various forms of violence, which could be used as biomarkers for identifying women at higher risk of perinatal depression (93, 726). This could have important clinical implications in terms of screening, referral, and treatment of depression in low-resource settings such as Ethiopia.

It was difficult to measure women's birth experience to gain full understanding of its relationship with PND. However, available data on proxy indicators, such as self-reported labour complications and LBW, showed a positive relationship with the risk of PND in this thesis, as was also reported in other studies (78, 107, 219, 222, 266, 273, 338, 619, 727). LBW was an objective measurement which is easy to compare across different studies. However, the measurement of negative birth experience using a single question (labour complications) might be difficult because birth experience could be seen in two general dimensions: the physical and the psychosocial experience. The physical birth experience commonly represents women's perceptions of labour pain and duration, caesarean delivery, adverse birth outcomes, and the fulfilment of their antenatal expectations. A negative physical birth experience for mothers commonly leads to post-traumatic stress, which is the most frequently reported comorbid

psychopathology of PND (728-730), but this was not investigated in this thesis. The psychosocial birth experience commonly measures a mother's satisfaction with the health care system, such as feeling supported, not patronised, involved with decision making, and safe (107). A negative psychosocial birth experience is the most agreed upon risk factor for PND and it is also suggested to be a strong moderator of the link between negative physical birth experience and PND (475). The issue of poor psychosocial birth experiences in low-income countries has been a major concern and it is reported to be a major barrier to women when seeking maternity services (731-733). This needs to be addressed through changes in policies and programs. While difficult to address fully, negative physical birth experiences could be reduced by promoting positive caregiver interaction. Further study is required to fully understand the effect of negative physical and psychosocial birth experiences on PND in Ethiopia, to design appropriate interventions.

Maternal mental health is key for progress towards achieving the Sustainable Development Goals (SDGs) related to maternal morbidity and mortality (488, 734). For example, a one-third reduction in premature mortality from non-communicable disease by 2030 is stated in target 3.4 of the SDGs. Prevention and control of CMDs such as depression is part of reducing the impact of non-communicable disease. As such, empirical evidence should support this initiative by identifying modifiable risk factors, and this thesis has helped by identifying potentially amenable risk factors and their pathways. Interventions aiming at tackling such a societally entrenched disorder could potentially consider these modifiable pathways. Interventions with most potential impact include increasing the economic capacity of women, empowering women by improving autonomy, striving for gender equality, and reduction of child and intimate partner violence at the grassroots. However, these interventions might not be easily or quickly addressed because depression hypothetically involves both social causation and social drift in low-income countries (75, 409, 491, 735). However, small steps could be taken in the form of policy revision because promotion of mental health and wellbeing has been made part of the SDGs (736). Improving family planning services, greater partner involvement in the pregnancy continuum of care, initiating screening for AND, and delivering institution-based psychotherapy might be considered useful short-term interventions.

The WHO special initiative for mental health (2019–2023) (734) pledged that mental health should be an integral part of universal health coverage. The mhGAP action program is designed to change this intention into action (737). As part of the mhGAP action program, mental health services should be integrated into routine health services, which means pregnant women should be routinely screened for depression and treatment should be sought when required. Effective integration of mental and maternal health services requires a clear national mental health policy, legislative framework, and a strong mental health system and governance. However, as indicated in the qualitative study, the Ethiopian health system is not currently well suited for this and integration has lagged. As a result, a substantial number of pregnant women with depression remain unidentified and/or untreated, and likely to suffer from the short- and long-term consequences of this condition.

8.3. Association of perinatal depression with the risk of adverse birth and infant health outcomes

The short-term risks hardly associated with depression during pregnancy in this study are adverse birth outcomes such as LBW and preterm birth (42, 166, 248, 296-304, 541). This link has also been suggested by biological or genetic (738-745) and environmental (746-752) evidence. In Ethiopia, the link between depression during pregnancy and the risk of adverse birth outcomes had not previously been investigated, with the exception of one study that found a positive risk of AND on LBW, mediated by social support (55). This thesis built on this information and investigated the association between antenatal depression and risk of LBW, preterm birth, and stillbirth. In this thesis, depressed pregnant women with low partner support were more at risk of having a preterm birth and LBW and this is consistent with the previous Ethiopian study (55). The most important additional finding was in identifying the positive link between antenatal depression and stillbirth. This contrasts with findings from a limited number of studies conducted in developed countries (295, 296) but supports findings of genetic studies (738-741). The lack of direct association between AND, LBW, and preterm birth might be confounded by the exclusion of women at high risk of depression, the relatively small sample of depressed women, and the severity and chronicity of depression. As has been reported, women with severe chronic

depression symptoms are more likely to have adverse outcomes compared with women with severe but transient symptoms (753-755). This thesis further advances the evidence on this area by investigating the causal mechanisms of adverse birth outcomes and conclusively finding that partner support is an important factor in the causal paths.

Antenatal depression is the most prominent risk factor for PND in this thesis and in previous studies (75, 191, 604, 608). A multilevel causal phenomenon of depression during the perinatal period found that there was strong correlation between CMDs before pregnancy, depression during pregnancy, and the postnatal period. Perinatal depression is associated with a 30% risk of reduced maternal–infant responsiveness (94, 95) and PND is associated with impaired growth and poor cognitive development among infants (96-98). Children of antenatally depressed women in LMICs had an increased risk for early cessation of breastfeeding, stunting and underweight (75, 99-101), although these findings are equivocal (96, 97, 101, 102). Investigating the long-term effects of perinatal depression such as impaired growth, emotional, mental and cognitive development is beyond the scope of this thesis. However, this investigation was able to study the short-term effects of antenatal and postnatal depression on the risk of newborn illnesses and malnutrition. In Ethiopia, the associations between maternal CMDs and the risk of infant illnesses in observational studies are uncertain (104-106). This thesis builds on the previously reported non-associated findings by drawing evidence from an apparent causal model and found lack of causal association between antenatal or PND and the risk of infant diarrhea, ARI, and malnutrition. Previous studies on trajectories of perinatal depression have strongly argued that the severity and chronicity of depression play an important role in causing adverse infant health outcomes (754, 756). Given the relatively mild and one-time exposure of depression in this thesis, it is perhaps unsurprising that the association between depression and infant health outcome was not so apparent. This issue will require further investigation.

8.4. Methodological reflections on the thesis

8.4.1. Strength of the thesis

The strength of each study has been discussed earlier in the relevant chapters, and this section summarises the overall strength of the thesis. To the best of my knowledge, this is the first study

that comprehensively addressed the epidemiology and effects of perinatal depression on the risk of adverse birth and infant health outcomes using prospectively collected community-based data from a sample of considerable size. The gap in knowledge was identified by a thorough systematic review and synthesis of evidence from the global to the local setting, as presented in chapters two and four. The review further helped to provide clarity on the importance, feasibility, and best methods needed to fill the knowledge gap. The review also helped to identify potential theories, confounders, and mediators in the area of maternal depression that were entirely considered in the thesis. Further, the systematic reviews assisted in the identification of the best tool for measuring perinatal depression. Hence, the EPDS was found to be the most reputable tool because it has been used for more than 40 years and in over 70% of the studies identified. It has also been validated in urban Ethiopia, which enabled simple and valid comparison across studies. So, the EPDS was used in the current thesis. Application of the stress process theoretical model and structural equation modelling helped to establish potential causal mechanisms of antenatal and postnatal depression.

The thesis used a community-based prospective cohort study to address the perinatal depression continuum, and it therefore had the following methodological strengths (343, 757). Being community-based made the study findings more representative and generalisable. The prospective cohort study design helped to establish temporal relationships between exposures and outcomes. Except for the first study (chapter five, section 5.2), the temporal relationships between exposures and outcomes, the important criteria for causal interpretation, have been reasonable. The prospective approach allowed calculation of incidence and use of relative risk rather than probability to report outcomes. Furthermore, the application of robust statistical models helped to provide plausible evidence about the association between perinatal depression and the risk of adverse birth and infant health outcomes. As such, the establishment of temporal relationships in the context of having valid associations and potential mechanisms would make causal relationships more apparent. Regarding level of evidence, prospective cohort studies are the primary option for studying risk because experimental studies may be hard to conduct because of ethical concerns (343, 757). Antenatal and postnatal depression (primary exposures) to study the risk of adverse birth and infant health outcomes were found to be rare, and a

prospective cohort design has been suggested to study the effect of such rare exposures (343, 757). As primary data were collected, the quality of the data was enhanced, and potential confounders and mediators were well accounted for to improve the quality of evidence generated from the thesis. Further, the thesis included qualitative data, used to study the barriers to and enablers of perinatal depression healthcare interventions in Ethiopia. The rich contextual knowledge provided will inform effective services and local theories which define mental health including perinatal issues, and factors that affect access and delivery of services in Ethiopia.

Regarding dissemination, findings from three systematic reviews and three primary studies have been published in high quality, peer-reviewed journals where the scientific community and policymakers can access and use this information as appropriate (166, 541, 716, 758, 759). Similarly, media releases of two systematic reviews were made and broadcasted to a range of international media to enhance public health knowledge on perinatal depression and its consequences (345, 346, 760). Furthermore, abstracts of the findings have been submitted and presented at national and international conferences (761-764). Manuscripts on the findings from the remaining quantitative and qualitative studies have been drafted and/or submitted to public health journals. The main findings of the thesis will be translated into a local language and provided to the Gondar Town Health Office and the Amhara Region Health and Research Institute for local planning. The comments and feedback obtained from reviewers of journals and abstracts were also used to further enrich the content and quality of the thesis.

The cumulative research and community experience of the PhD student enhanced the strength of the thesis. Before being enrolled in the PhD program, the student had over nine years of community and research experience. While working in the community, he led government health offices for four years, where all health interventions were planned, executed, monitored, and evaluated under his leadership. Similarly, while working in an academic institute, he was a researcher and Head of the Department of Epidemiology and Biostatistics for three years. During this period, he investigated and published several research findings on maternal, child, and mental health problems as a principal investigator, senior author, and co-author. These research experiences helped the student to design the study, collect the required data, clean, analyse and

interpret the data effectively and efficiently. His administrative experience in the Ethiopian healthcare and higher education systems also helped him to make effective communication with government officials working at different levels.

However, this PhD training also provided the student with additional skills including the application of new study designs, analysis, online data collection, and research methods, which provided him with further opportunities to improve his quantitative and qualitative research capacity. For example, (i) designing and conducting a prospective cohort study was his first experience as an epidemiologist; (ii) designing and applying an online data collection method was also his first experience; (iii) the application of advanced statistical models to analyse data for this PhD study was his first experience as a biostatistician; and (iv) designing and conducting qualitative research was also his first experience. These practical experiences have enabled the PhD student to explore complex research topics and facilitate his ambition to be an independent researcher in his future career.

8.4.2. Limitations of the thesis

A detailed presentation of the limitations of each study objective was provided earlier in the relevant chapters. This section summarises the overall limitations of the thesis that should be borne in mind. This study was conducted in a small urban area, with a total population of less than 333,103 at the time of data collection, hence its generalisability to rural and national levels might be limited. Although the EPDS was found to be the most reputable tool to screen perinatal depression around the world, its reduced specificity and sensitivity compared with diagnostic tools could affect the validity of the results. This implies that the findings from the thesis might not rule out the known limitations of screening tools. For example, according to a validated study conducted in urban areas of Ethiopia, the current estimation of AND using EPDS has a false positive rate of 16% and a false negative rate of 23%. Similarly, the estimation of PND has a potential risk of having false positive and false negative rates of 21% and 24%, respectively. These would have also the effect of underestimating the true risk of antenatal and postnatal depression on adverse birth and infant health outcomes.

Another important limitation was the exclusion of study participants with high depression scores (≥ 17 on EPDS), which was a necessary ethical precaution. The exclusion of these potential participants could significantly reduce estimates of the burden of depression. Likewise, for objectives that estimated the effect of perinatal depression on risk of adverse birth and infant health outcomes, the exclusion of such participants could underestimate the true effect. As has been mentioned elsewhere, depression severity and chronicity may play a larger role in adverse birth and infant health outcomes relative to minor depression (753-755). The exclusion of moderate to severely depressed participants also reduced the power of the thesis because it significantly reduced the sample size estimated for answering all research questions. The requirement to reduce participant burden and distress resulted in the omission of important confounding and mediator variables such as violence, history of childhood abuse, pregnancy complications (pre-eclampsia, gestational diabetes), environmental hygiene and sanitation variables. This could have resulted in residual confounding and measurement error. Although the use of advanced models provided empirical support, a range of possible alternatives to the potential causal mechanisms of antenatal and postnatal depression and their effects on risk of adverse birth and infant health outcomes cannot be ruled out.

The other limitation is associated with the challenges of measuring preterm birth, because of the accuracy of the last menstrual cycle date and birth weight where births had taken place at home. Another limitation involves the use of MUAC to measure infant malnutrition, because this tool has not been validated for assessing malnutrition in infants aged under six months in Ethiopia. Finally, infant diarrhea and ARI were measured using the WHO Integrated Management of Newborn and Childhood Illnesses (IMNCI) guideline. Although the IMNCI is validated and recommended for use in primary level health facilities, this is a proxy indicator and its sensitivity and specificity are lower than standard procedures. However, the effects of the aforementioned limitations were minimised through making statistical corrections.

Regarding the qualitative study, the younger age and limited experience of some study participants would affect their in-depth understanding of health policies, programs, and strategies for perinatal depression in the country. The other limitation includes the likely introduction of social desirability bias due to masking or exaggerated representation of the real

problems on the ground. This might be because of fear of being seen to criticise their organisations or government, or the belief that problems would be solved.

Chapter Nine: Conclusions, recommendations, and implications

9.1. Introduction

This chapter summarises conclusions and their implications and presents concluding remarks and recommendations. The first section summarises the conclusions of the findings. The second section presents recommendations and discusses implications for policy, community, and further research.

9.2. Conclusions

Perinatal depression was believed to be a problem of high-income countries but more recently it has also been recognised as a problem in LMICs. This is based on recent evidence that depression could be explained by both social causation and social drift hypothesis, in which economic hardship can increase the risk of depression and depression can also inhibit the attainment of better economic status (75, 409, 491). The widespread detrimental effects that perinatal depression poses to individuals, communities and countries has been found to be more pronounced in low-income than high-income countries. The argument raised from ecological studies shows that perinatal mental health problems are generally linked to the socio-economic, cultural, and psychosocial context of a given country. This argument has been well explored in the three systematic reviews presented in chapter four. As such, local studies are important to explore the real context of the problem and to inform targeted interventions. The 'why' and the 'how' questions of perinatal depression, its short-term effects on the birth and health of the newborn, and the capacity of the Ethiopian health system to address this disorder were not well documented. In this PhD thesis, four sequentially interrelated quantitative studies aimed at investigating the magnitude of perinatal depression, its potential causal pathways and effect on birth and health of the newborn were conducted in Gondar town. Furthermore, the qualitative enquiry addressed barriers and enablers in addressing health service need of women with perinatal depression.

The first objective of this thesis was to determine the prevalence of antenatal depression and its potential causal mechanisms. The study found that the prevalence of AND in Gondar town was

lower than in previous studies. The potential causal model revealed that unplanned pregnancy, having a history of CMDs, inadequate family food access, and fear of giving birth in the current pregnancy were stressors that directly or indirectly increased the risk of AND. The study also identified the potential buffering effect of marital satisfaction, social and partner support in reducing the risk of AND. Chapter four of this thesis also reported that there were no direct effects of AND on the risk of LBW and preterm births. However, the moderation role of partner support revealed that the risk of having preterm birth and LBW was higher among depressed pregnant women with poor partner support. The direct effect of AND on stillbirth was non-conclusive, although the risk of stillbirth was found to be higher among antenatally depressed women. Based on the findings presented in chapter four, it was concluded that the psychosocial resources of women played a major role in the causal link between antenatal depression and risk of adverse birth outcomes.

The third objective, which was presented in chapter five, dealt with PND and its potential causal mechanisms. The incidence and prevalence of PND estimated in this thesis were found to be lower than previously reported estimates in Ethiopia. The incidence of PND was higher among participants who had no PNC service, had a history of CMDs, and depression during pregnancy. The potential causal pathways of PND showed that a history of CMDs before pregnancy and LBW directly increased PND scores through the mediation effect of antenatal depression and history of labour complications. The last quantitative study, also reported in Chapter 5, examined the causal association between antenatal and postnatal depression and the risk of diarrhea, ARI, and malnutrition. No evidence was found for causal associations between AND or PND and the risk of diarrhea, ARI, and malnutrition in infants of age under six months.

The qualitative study revealed a number of substantial barriers to the implementation of effective perinatal mental health services. These included low levels of health literacy in health administrators and the wider community, maternal health-seeking behaviours, and cultural norms about perinatal depression; lack of government capacity, readiness, and priority; the absence of a perinatal mental health policy and strategy; and lack of clear pathways in the healthcare system act as substantial barriers to the implementation of effective perinatal mental

health services. The study also found the introduction of the new mhGap action program, health professionals' commitment, and simplicity of a screening program as potential enablers or facilitators for perinatal mental health service implementation in Ethiopia.

9.3. Implications and recommendations

The findings from this thesis make an important contribution to the body of knowledge of perinatal epidemiology in urban areas in Ethiopia. They also further the evidence associated with antenatal and postnatal depression by investigating influences on the risk of adverse birth and infant health outcomes. Moreover, this thesis has explored the context and addressed the gaps of the healthcare system and government policy in managing perinatal depression. In total, this evidence has implications for mental health services for perinatal women in Ethiopia. The study also sheds light on prevention and control strategies that should be put in place to reduce the burden and consequences of perinatal depression. Recommendations and suggestions from the thesis findings have been made in the following sections by considering the Ethiopian healthcare system.

In this study, a history of CMDs before pregnancy was found to be a strong predictor of antenatal and postnatal depression. This showed that women with depression before pregnancy tended also to have the symptoms during pregnancy and in the postnatal period. This suggests that interventions taken to prepare women for pregnancy should account for their mental health. However, this could be difficult for low-income countries such as Ethiopia where health facility visits for pregnancy preparation are rare. Thus, it is important to start depression screening as early as possible in pregnancy and this screening should continue into the postnatal period. The best time would be during the antenatal care (ANC) and postnatal care (PNC) visits, as discussed by qualitative participants. More than 80% of pregnant women in urban areas of Ethiopia have at least two ANC visits, which would give the best opportunity for screening for depression.

The Ethiopian Urban Health Extension Program provides another opportunity to reach more than 80% of perinatal women in their homes. Urban health extension workers are nurses by profession, and they are trained to make house to house visits to provide a range of maternal

and child health services. Because antenatal and postnatal care services are provided by health extension workers to every household, this could provide opportunities to undertake depression screening as well as strengthening referral services for women at higher risk of depression. Identifying potential sources of stressors or reasons for depression after screening could be part of the interventions for those who have depression symptoms. The cause of depression could be associated with economic hardship, an unplanned pregnancy, the simple fear of delivery or pregnancy outcome, or other concerns. Screening and identifying potential areas for discussion and counselling or providing psychological support could help to reduce maternal stress and depression.

The evidence from the qualitative study (Chapter seven) showed that health literacy about perinatal depression was low among the health administrators. Strengthening mental health governance and building the capacity of health administrators working at various levels of the healthcare system is crucial. Ethiopian health policy and the recently developed mental health strategy have not fully addressed issues of maternal mental health. As a result, health structures at various levels of the Ethiopian health system do not have plans or strategies to screen and intervene in perinatal depression. This is far from the WHO mhGap action program goals, where integration of mental health services is highly recommended, following the declaration of mental health as a primary health care component. It is very important to consider integrating maternal mental health with the routine maternal health services to deal with the screening for, and intervention in, perinatal depression.

A further issue for consideration is the development and testing of a perinatal depression screening tool, which needs to be brief and valid. Introducing a brief screening tool is very important because qualitative participants identified patient loads as a major area of concern in regard to introducing screening activities. Furthermore, the development of a screening tool should account for symptoms that indicate the severity and chronicity of depression rather than symptoms for which natural remission is possible. A further locally developed stepped care approach could be introduced in the current healthcare system by which women with minor and severe depression could be followed up using a range of intervention modalities to reduce health

system burden. Women with severe depression symptoms could be referred to health facilities with established mental health clinics for further diagnosis and treatment. Furthermore, a system for the referral for women with minor depression symptoms to community or peer support groups could be established in the community. It is advisable for health extension workers to make repeated visits to women with minor depression to ensure symptom remission or monitor whether further intervention be required.

In the AND causal model (Chapter 5), financial stress and unplanned pregnancy both directly and indirectly increased the risk of AND. Dealing with economic hardship might not be achieved in the short term because depression is a deep-rooted problem in low-income countries, but it might be advisable to consider short-term interventions for those with a severe problem. Strengthening youth-friendly reproductive health services, improving access and quality of family planning services, increasing education and decision-making power in women, and supporting gender equality would help to minimise unplanned pregnancy. In pregnancy, it is important to discuss these issues with women and provide support in order to overcome any associated stress.

In this thesis, social resources such as good marital agreement, partner and social support were found to buffer the effect of stressors. This raises the importance of establishing and using community support groups, and of discussing maternal mental health issues and the supports required with families, close friends, and partners. Enhancing partner involvement throughout the pregnancy and childbirth would also help to increase sharing and co-operation between partners and to improve support. This could also be done by health extension workers who are trusted by all households in the communities wherein they are working. Health extension workers are also trained in mediation skills that could help them in negotiating disagreements. Interventions taken to improve maternal support would enhance the stress coping ability and resilience of women and, in turn, help to reduce the risk of LBW and preterm birth associated with AND. All interventions taken to reduce AND would also help to reduce the risk of stillbirths and PND.

In the PND causal model, self-reported labour complications and LBW, which had a positive association with AND, were found to increase the risk of PND. All the interventions proposed to

reduce AND would also help to reduce the risk of LBW and labour complications and ultimately help to reduce the risk of PND. Screening postnatal women as early as possible could also help in identifying and intervening those with a high risk of depression.

Bearing in mind the limitations stated in chapter eight of this thesis, it is important to recommend further studies that would help to support conclusive evidence. One limitation that was discussed was the use of a screening test to identify women with depression. Screening tools tend to overestimate depression compared with diagnostic tests and so further study using diagnostic tests could help to validate findings. A finding from one of the systematic reviews presented in chapter four showed that the effect of AND on LBW and preterm birth was found to be consistent in studies using the EPDS and diagnostic tests. However, repeating the study in the context of Ethiopia would be helpful to be sure about the effect of AND on adverse birth and infant health outcomes.

Furthermore, the relatively low prevalence of antenatal and postnatal depression among women studied for this thesis may have masked their real effect on adverse birth outcomes and further study with a larger sample size would be recommended to address this issue. Another limitation was related to excluding women with severe depression and further studies should consider looking at high-risk women. This is also vital to see whether effects are different across the severity of depression. Previous studies conducted into the effects of perinatal depression on childhood developmental outcomes that considered the severity and chronicity of symptoms found a strong association. It would be helpful to consider depression chronicity and trajectories by screening at different time across the perinatal period to investigate effects on birth and infant health.

The proposed potential causal models for antenatal and postnatal depression presented in chapters five and six could have been affected by the omission of potentially important confounders such as violence and history of childhood abuse, and complications such as hypertension and diabetes mellites. Therefore, it is again helpful to consider further studies that account for these factors to develop a more precise and replicable causal model in order to develop specific, targeted and effective interventions. Measurement bias from the use of MUAC

for measuring infant nutritional status might be best confirmed by conducting further studies using standard indices such as wasting and stunting.

Limitations associated with the limited experience of qualitative study participants in the Ethiopian healthcare system, and potential social desirability biases associated with the information participants provided, could be reduced by repeating the study among participants with a broader range of experience. The qualitative study addressed health system issues, however, exploring the lived experience of women with depression symptoms would be of importance to identify common contextual factors that exacerbate the development of depression. This could help in development of a list of risk factors that might identify perinatal women at higher risk of depression in the local community. Furthermore, potential maternal factors that enhance or deter health services access need to be investigated in more detail to inform planning and implementation of further intervention activities.

In summary, the findings from this thesis have clear implications for how, when, and by whom perinatal women at higher risk of depression should be identified and targeted for intervention. Similarly, the developed causal model has highlighted the most important intervention modalities that should be targeted to significantly reduce the risk of perinatal depression and its consequences. This also highlighted areas where policy and health system interventions are required and the knowledge gaps that future research should address to further develop comprehensive knowledge about perinatal depression and its consequences. Finally, the findings and recommendations generated from this thesis would help Ethiopia and other low-income countries by providing evidence to develop and implement local perinatal mental health services.

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Annexes

Annex 1. Supplementary information on the systematic reviews

Annex 1.1. Supplementary information on a systematic review of AND and its association with adverse birth outcomes in low- and middle-income countries.

PRISMA checklist

Section/topic	#	1. Checklist item	Reported on page #
2. **TITLE**			
Title	1	3. Identify the report as a systematic review, meta-analysis, or both.	1
4. **ABSTRACT**			
Structured summary	2	5. Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
6. **INTRODUCTION**			
Rationale	3	7. Describe the rationale for the review in the context of what is already known.	4
Objectives	4	8. Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
9. **METHODS**			
Protocol and registration	5	10. Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	11. Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	12. Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	13. Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	14. State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5 & 9
Data collection process	10	15. Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	16. List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	17. Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6

Summary measures	13	18. State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	19. Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-12 & 17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Appendix p 7-13
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-12 & 17
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-14 18-19 Appendix p 15-20
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5 Appendix 9-13
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12-13,16,19
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	20-24
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	24
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	24
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	24

Literature search strategy

#	Database	
	Search strategy for prenatal depression and factors	
	PubMed	Search ((((((Pregnant mothers*) OR (antenatal mothers*) OR (pregnant women*) OR (antenatal period*) OR pregnancy* OR (antepartum women*)) AND ((depression* OR (clinical depression*) OR (depressed mood*) OR(major depressive disorder*) OR (depressive symptom*) OR (psychological morbidity*) OR (major depression*) OR (unipolar depression*)) AND((exposure* OR (risk factor*) OR correlates* OR (associated factors*) OR predictors*) AND (((cross sectional*) OR (crosssectional*) OR survey* OR(case control*) OR (nested case control*)) Sort by: PublicationDate Filters:Publication date from 2007/01/01 to 2017/12/31; Humans; English;MEDLINE; Field: Title/Abstract
	Scopus	(TITLE-ABS-KEY (pregnan* OR "antenatal mothers" OR "antepartum wom?n")) AND(TITLE-ABS-KEY (depress* OR "clinical depression" OR "major depressive disorder" OR "depressive symptom" OR "major depression")) AND (TITLE-ABS-KEY (exposure* OR"risk factor*" OR correlates* OR "associated factors" OR predictors)) AND (TITLE-ABSKEY("cross sectional" OR survey* OR "case control" OR "nested case control")) AND(LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR ,2015) OR LIMIT-TO (PUBYEAR , 2014) OR LIMIT-TO (PUBYEAR , 2013) OR LIMITTO(PUBYEAR , 2012) OR LIMIT-TO (PUBYEAR , 2011) OR LIMIT-TO (PUBYEAR , 2010)OR LIMIT-TO (PUBYEAR , 2009) OR LIMIT-TO (PUBYEAR , 2008) OR LIMIT-TO (PUBYEAR ,2007)) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re") OR LIMITTO(DOCTYPE , "sh")) AND (LIMIT-TO (SUBJAREA , "MEDI") OR LIMIT-TO (SUBJAREA ,"NURS")) AND (LIMIT-TO (EXACTKEYWORD , "Human") OR LIMIT-TO (EXACTKEYWORD ,"Female") OR LIMIT-TO (EXACTKEYWORD , "Pregnancy") OR LIMIT-TO (EXACTKEYWORD ,"Humans") OR LIMIT-TO (EXACTKEYWORD , "Article")) AND (LIMIT-TO (LANGUAGE ,"English")) AND (LIMIT-TO (SRCTYPE , "j"))
	Search strategy for adverse birth outcome	
	CINAHL(EBSCO)	Depression during antenatal period)OR (antenatal depression) OR (depressionduring pregnancy) OR (low mood) OR(feeling sad) OR (depressed mood) OR(depressive symptom) OR (depressivedisorder with peripurum onset) OR (antipartum depressive onset) AND ((adverse birth outcome*) OR (preterm birth) OR (stillbirth) OR (small birth) OR (small for gestational age) OR (low birth weight) OR (fetal or infant death) OR (congenital anomaly) OR (infant birth outcome) OR (birth defect) OR macrosomia OR (neonatal outcomes) AND (prospective cohort) OR(retrospective cohort) OR (Follow up study) OR(longitudinal study) OR (case control study)OR (nested case control study) AND (exposure* OR (risk factor*) OR correlates* OR (associated factors*) OR predictors* Sort by: PublicationDate Filters:Publication date from 2007/01/01 to 2017/12/31; Humans; English;MEDLINE; Field: Title/Abstract

NOS quality assessment checklist

I. Prenatal depression

1.1. Cross-sectional studies

	Selection (max. 5 points)				**Comparability** (max. 2 points)	**Assessment of the outcome** (max. 3 points)		**Total Score**
List of studies	representativeness of the sample	Sample size	Non-respondents	Ascertainment of the risk-factors	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.	Ascertainment of the outcome	Stastical test	
Abdelhai R et al. 2015	1	1	1	1	2	1	1	8
Abujilban SA et al. 2014	1	0	1	1	2	1	1	7
Adewuya, A. et al. 2007	1	0	1	1	1	1	1	7
Ajinkya, S., et al. 2013	1	1	1	1	2	1	1	8
Actas, S. et al. 2014	1	1	1	1	2	1	1	8
Alvarado-Esquivel, C., 2016	1	1	1	1	2	1	1	8
Assefa Gemta, W. 2015	1	1	1	1	2	1	1	8
Ayele, Tadesse Awoke, 2016	1	1	1	1	2	1	1	8
Barrios, Y. V. 2015	1	0	1	1	2	1	1	7
Bavle, A. D.	1	1	1	1	2	1	1	8
Biratu, A. 2015	1	1	1	1	2	1	1	8
Bisetegn, T. A. 2016	1	1	1	1	2	1	1	8

Bitew, T et al. 1016	1	1	1	1	2	1	1	8
Bindt C et al. 2013	1	1	1	1	1	1	1	7
Coll CVDN et al. 2017	1	1	1	1	1	1	1	7
de Jesus Silva, Monica Maria, 2016	1	1	1	1	2	1	1	8
de Moraes, E. V, 2016	1	1	1	1	2	1	1	8
de Oliveira Mariana, et al. 2015	1	1	1	1	1	2	1	8
Dibaba, Y. 2013	1	1	1	1	1	2	1	8
Dmitrovic, BK et al. 2013	1	0	1	1	2	1	1	7
Esimai, O. 2008	1	0	1	1	1	2	1	7
Fadzil, A. 2013	1	0	1	1	2	1	1	7
Faisal-Cury, A. 2012	0	1	1	1	1	2	1	7
Gausia, K 2009	1	1	1	1	2	1	1	8
Gelaye, Bizu, 2017	1	0	1	1	2	1	1	7
Gemta A et al. 2013	1	1	1	1	1	1	1	7
George, C. 2016	1	1	1	1	1	1	1	8
Golbasi, Zehra, 2010	1	1	1	1	1	1	11	8
Hartley, Mary, 2011	1	1	1	1	2	1	1	8
Heyningen, T. V. 2016	1	0	1	1	2	1	1	7
Huanging H et al. 2017	1	1	1	1	1	1	1	7
Hu, H. Q. et al. 2017	1	0	1	1	1	2	1	7
Jeong, Hyun-Ghang, et al. 2013	1	1	1	1	1	1	1	8
Kamalak, Z. et al. 2016	1	0	1	1	1	1	1	6
Kaaya SF et al. 2009	1	1	1	1	1	1	1	7

Lara, M. A. et al. 2012	1	1	1	1	1	1	1	7
Lau, Ying, et al. 2013	1	0	1	1	1	1	1	6
Lau, Y. et al. 2007	1	0	1	1	1	1	1	6
Lau, Ying, et al. 2011	1	1	1	1	2	1	1	8
Li, Yingtao, 2016	1	1	1	1	1	1	1	7
Luna Matos M.L, 2009	1	1	1	1	1	1	1	7
Mahenge, B., 2015	1	1	1	1	1	1	1	7
Målqvist, M., 2016	1	0	1	1	2	1	1	7
Manikkam, L. 2012	1	1	1	1	1	1	1	7
Melo Jr, E. F. 2012	1	1	1	1	1	1	1	8
Mitsuhiro, S. S. 2009	1	1	1	1	1	1	1	7
Mohammad, K. I., 2011	1	1	1	1	2	1	1	8
Moshki, M. et al. 2016	1	1	1	1	1	1	1	8
Mossie, T. B, 2017	1	1	1	1	1	1	1	8
Nasreen, H. E., 2011	1	1	1	1	1	1	1	7
Pereira, P. K. 2009	1	1	1	1	1	1	1	8
Rochat, T. J. et al. 2011	1	1	1	1	1	1	1	7
Rwakarema, M. et al. 2015	1	1	1	1	1	1	1	8
Sahile, M. A. et al. 2017	1	1	1	1	1	1	1	8
Senturk, V. et al. 2011	1	1	1	1	1	1	1	8
Shakya, R. 2008	0	1	1	1	1	1	1	6
Shidhaye, P. 2017	1	1	1	1	1	1	1	7
Silva, Ricardo Azevedo da, 2012	1	1	1	1	2	1	1	8

Srinivasan, N. 2015	0	1	1	1	1	1	1	6
Stewart, Robert C. 2014	1	1	1	1	1	1	1	7
Thompson, O. 2016	1	1	1	1	2	1	1	8
Waqas, A. 2015	1	1	1	1	2	1	1	8
Weobong, B. 2014	1	1	1	1	1	1	1	8

1.2. Longitudinal studies

	Selection (score)				**Comparability** (score)		**Outcome** (score)			**Total Score**
List of studies	Representative of exposed cohort	Selections of non-exposed cohort	Assessment of exposure	Absence of outcome at start of study	Control for age or obesity or smoking or exercise	Control for other variables (second important variables)	Assessment of outcome	Follow-up period	Adequacy of follow-up	
Coll, C. D. V. N. 2017	★	★	★	★	★	★	★	★	★	8
Guo, N. 2013	★	★	★	★	★	★	★	0	0	7
Fisher, J. 2013	★	★	★	★	★	★	★	0	0	7
Pottinger, Audrey M. 2009	★	★	★	★	★	★	★	0	0	7
Padmapriya, N. 2016	★	★	★	★	★	★	★	★	0	8
Silva, Ricardo, 2012	★	★	★	★	★	★	★	★	0	8
Tsai, A. C. 2016	★	0	★	★	★	★	0	★	0	6
Vilela, A. A. F. 2014	★	0	★	★	★	★	0	★	0	6

II. AND and adverse birth outcomes

2.1. Longitudinal studies

	Selection (maximum four stars, one for each)				**Comparability** (maximum two stars, one for each)		**Outcome** (maximum three stars, one for each)			**Total Score**
List of studies (author, date)	Representative of exposed cohort	Selections of non-exposed cohort	Assessment of exposure	Absence of outcome at start of study	Control for age or obesity or smoking or exercise	Control for other variables (second important variables)	Assessment of outcome	Follow-up period	Adequacy of follow-up	
Rahman A et al. 2007	★	★	★	★	★	★	★	★	0	8
Niemi M et al. 2013	★	★	★	★	★	★	★	★	★	9
Sanchez SE et al. 2013	★	★	★	0	★	★	★	★	0	7
Chang Hy et al. 2014	★	★	★	★	★	★	★	★	★	9
Husain N et al. 2014	★	★	★	★	★	★	★	★	0	8
Rao D et al. 2015	★	★	★	★	0	★	★	★	0	7
Bindt C et al. 2013	★	★	★	★	★	★	★	★	0	8
Wado WD et al. 2014	★	★	★	★	★	★	★	★	★	9
Nasreen HE et al. 2010	★	0	★	★	★	★	★	★	0	7

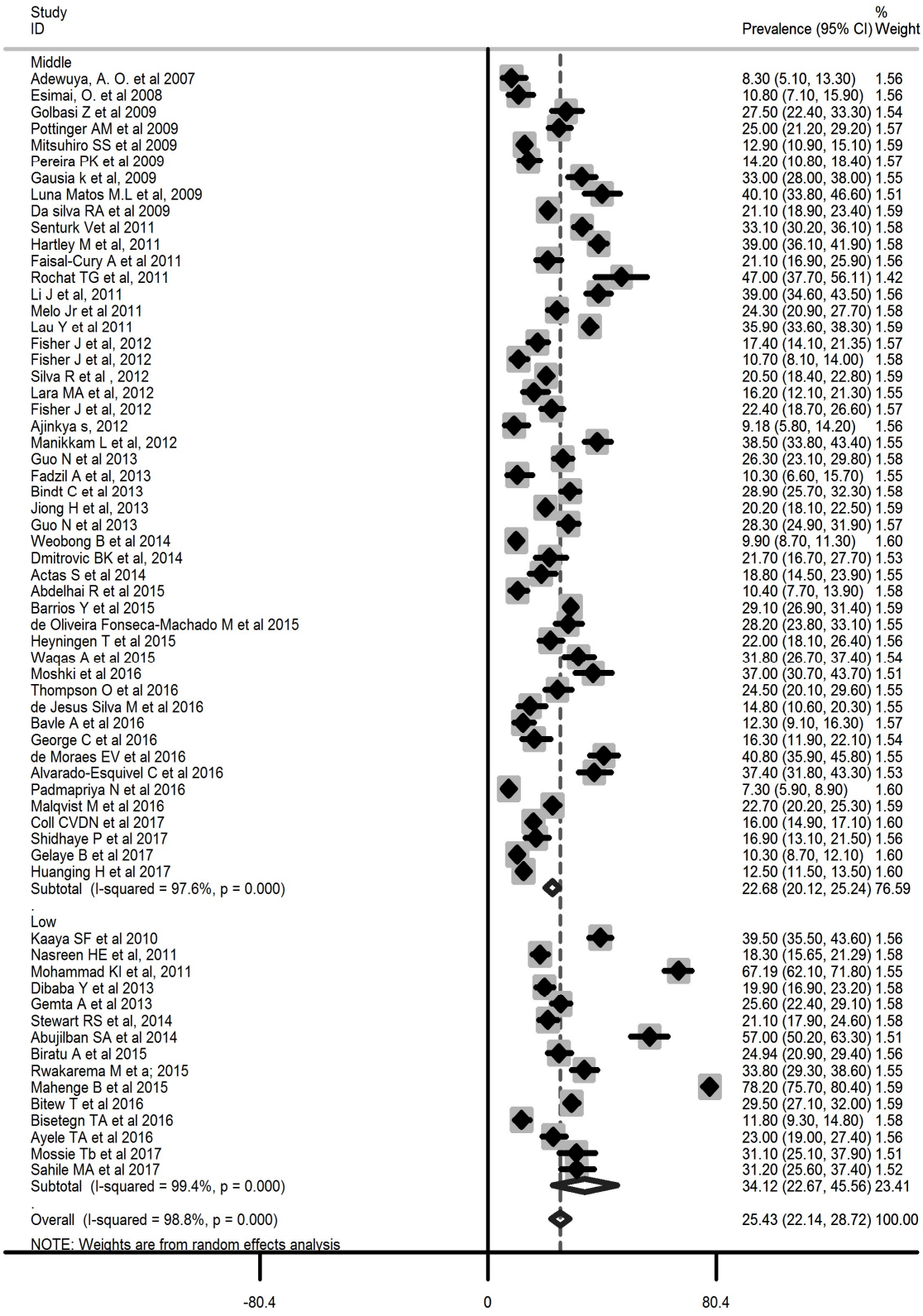


Figure 1: Meta-analysis of AND prevalence sub-analysed by country income

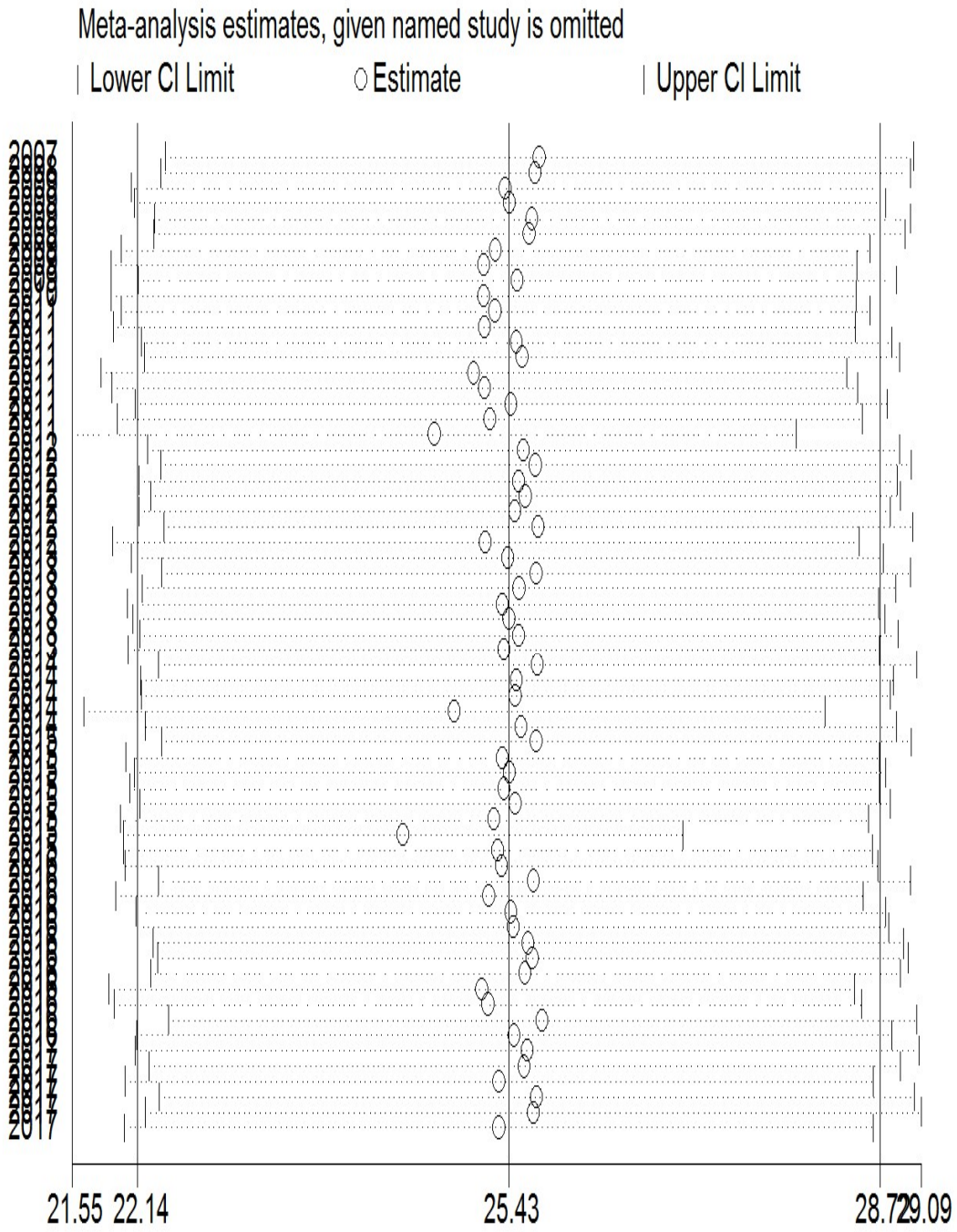


Figure 2: Sensitivity analysis for AND prevalence

Egger's test for small-study effects

Number of studies = 64 Root MSE = 8.311

Std_Eff	Coef.	Std. Err.	t	P>|t|	[95% Conf. Interval]
slope	.1015521	.0314174	3.23	0.002	.0387496 .1643545
bias	7.879764	2.171573	3.63	0.001	3.538852 12.22068

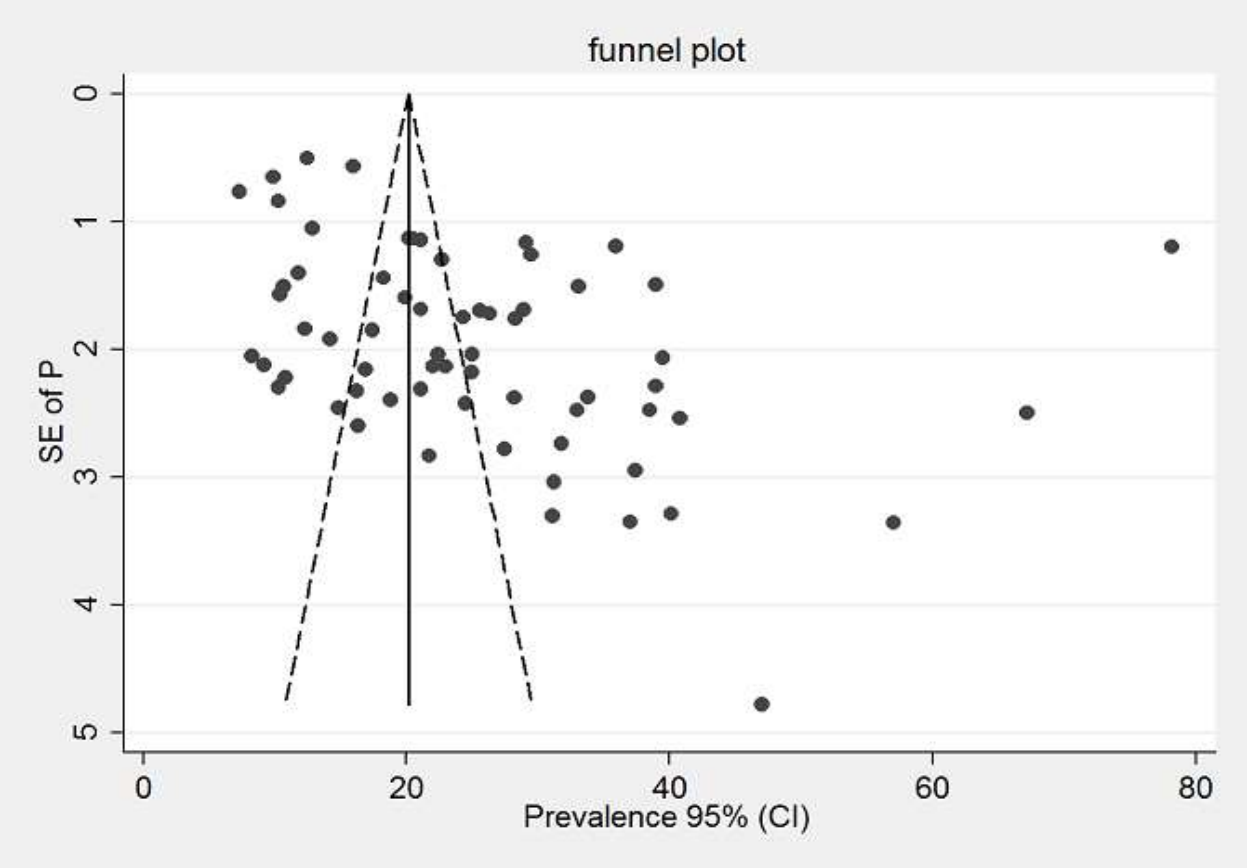


Figure 3: Funnel asymmetry for testing publication bias on studies of AND prevalence

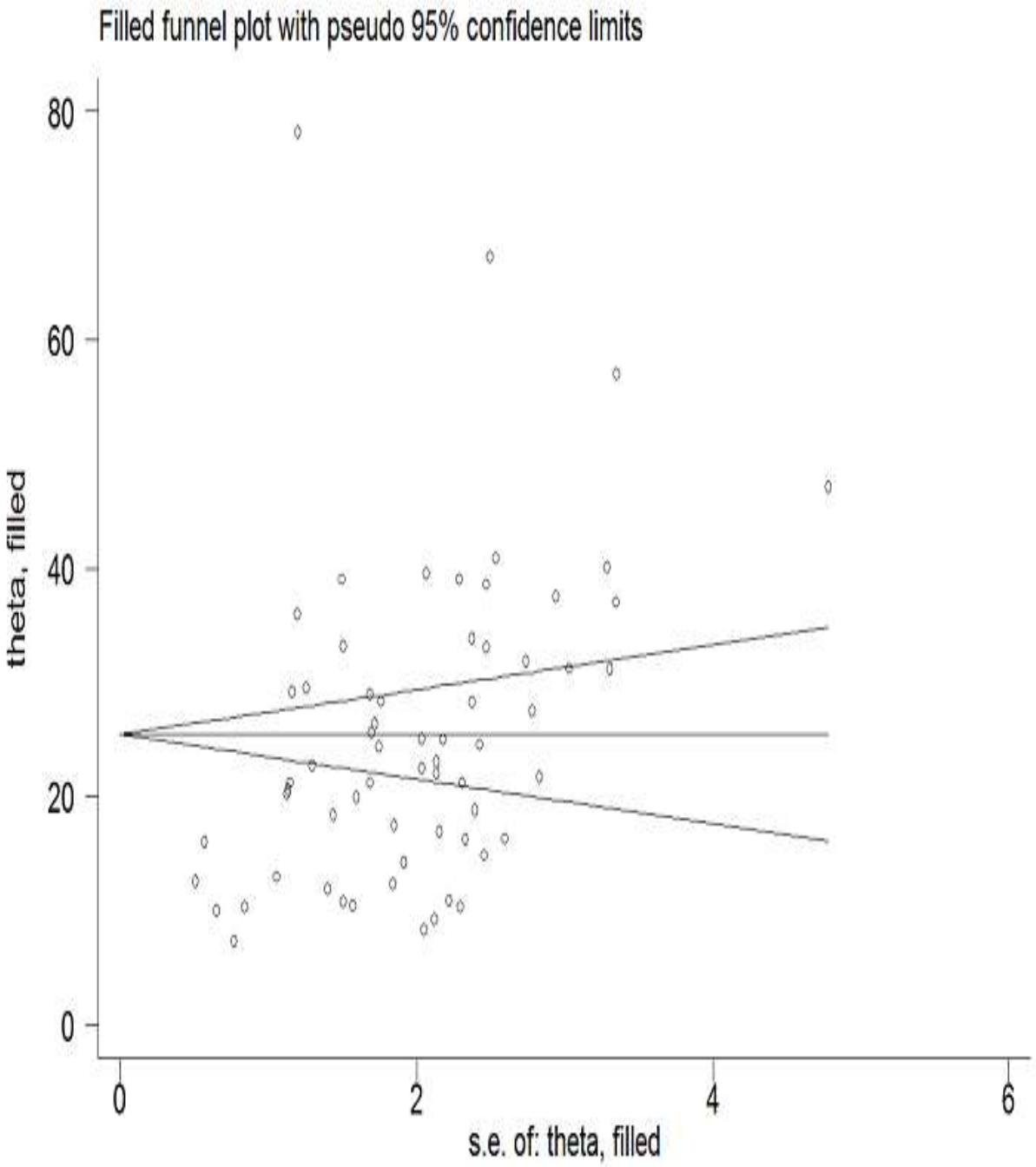


Figure 4: Filled funnel plot for AND prevalence

Meta-analysis of factors associated with AND

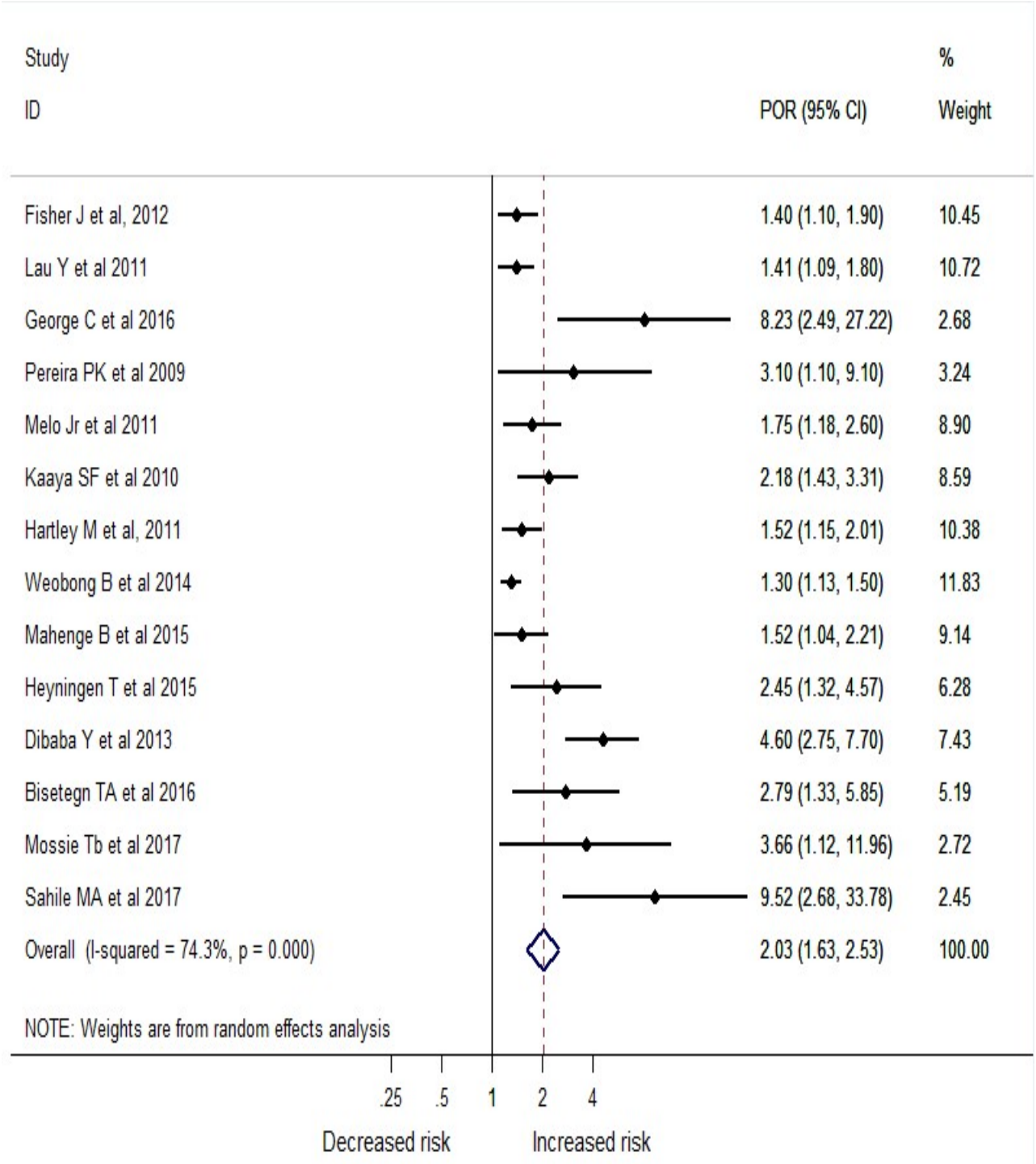


Figure 5: Economic difficulty as a factor for AND forest plot

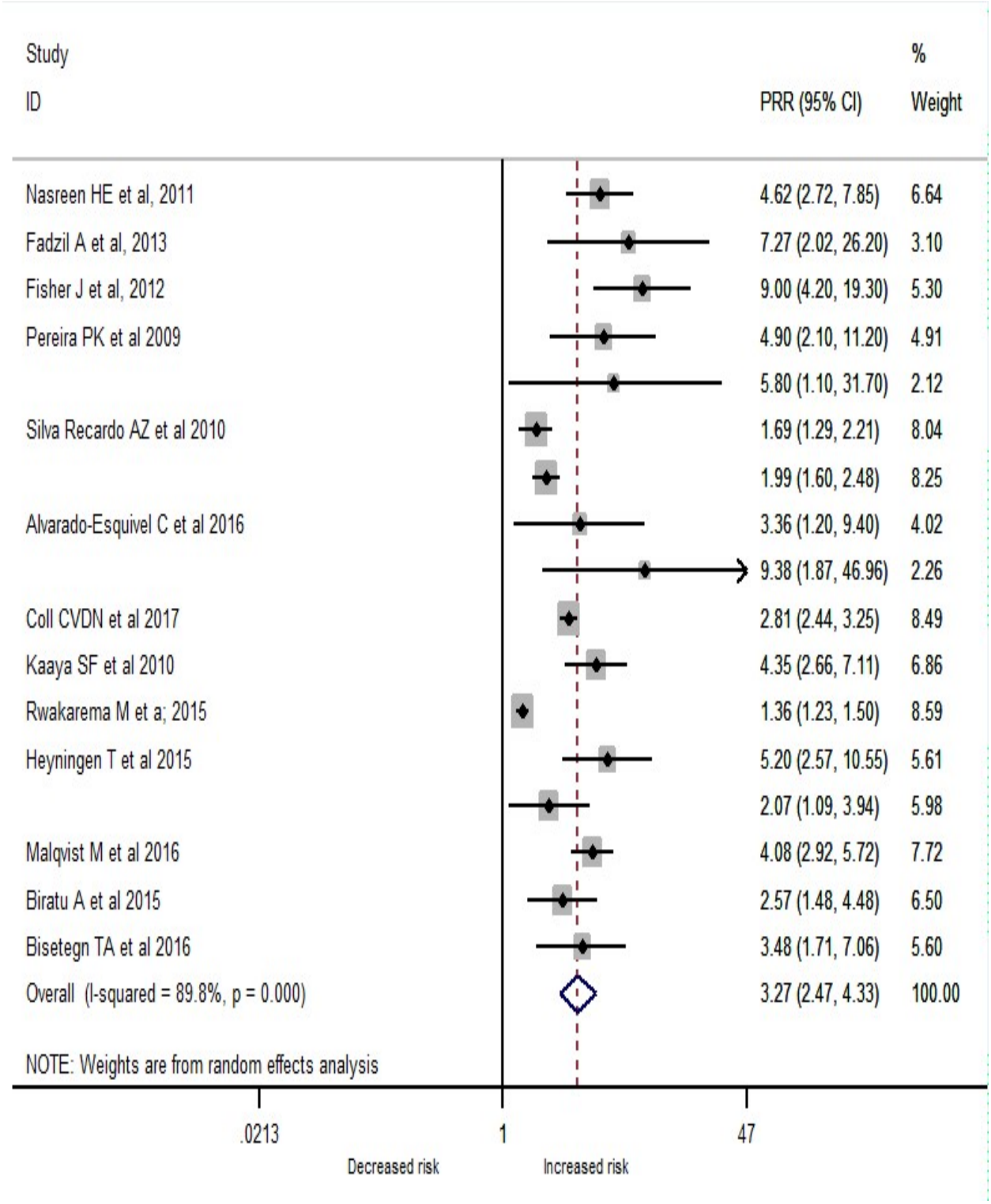


Figure 6: History of CMD (*depression, anxiety, stressful life event*) as a factor for AND, forest plot

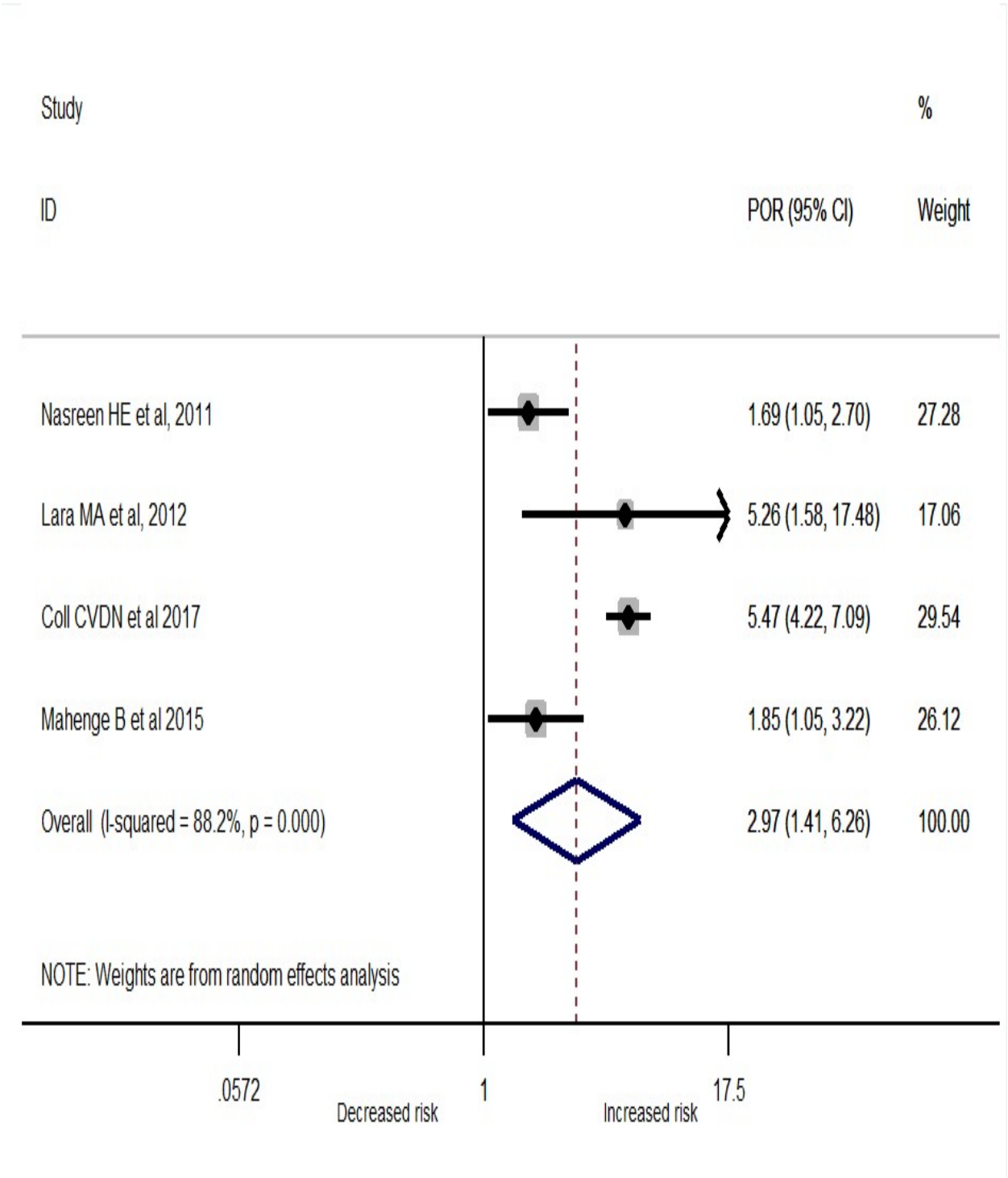


Figure 7: Male preference in the current pregnancy as a factor for AND, forest plot

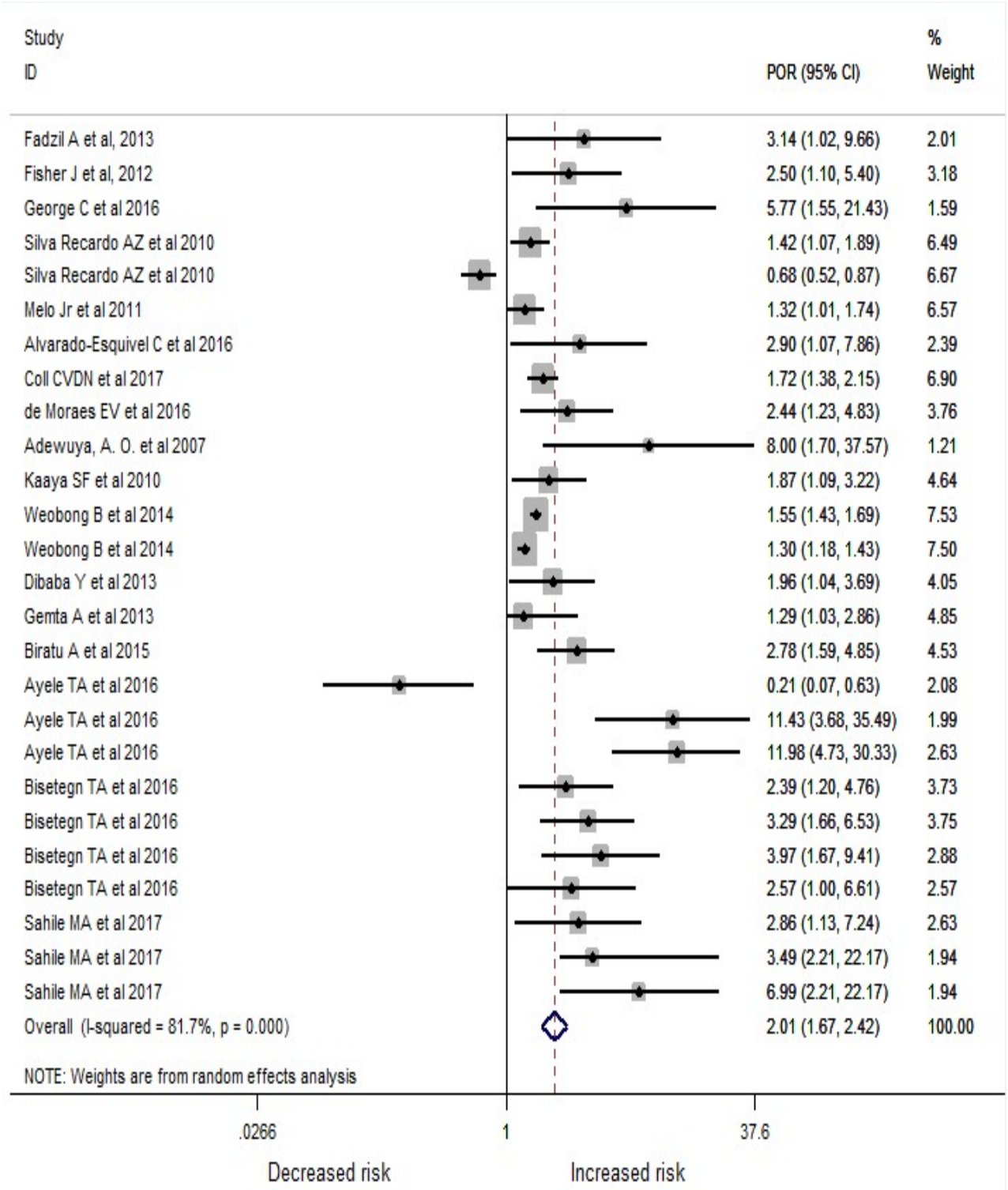


Figure 8: Bad obstetric history (*unplanned pregnancy, GDM, GHP, labor complication, history of emesis, multiparty*) as a factor of AND, forest plot

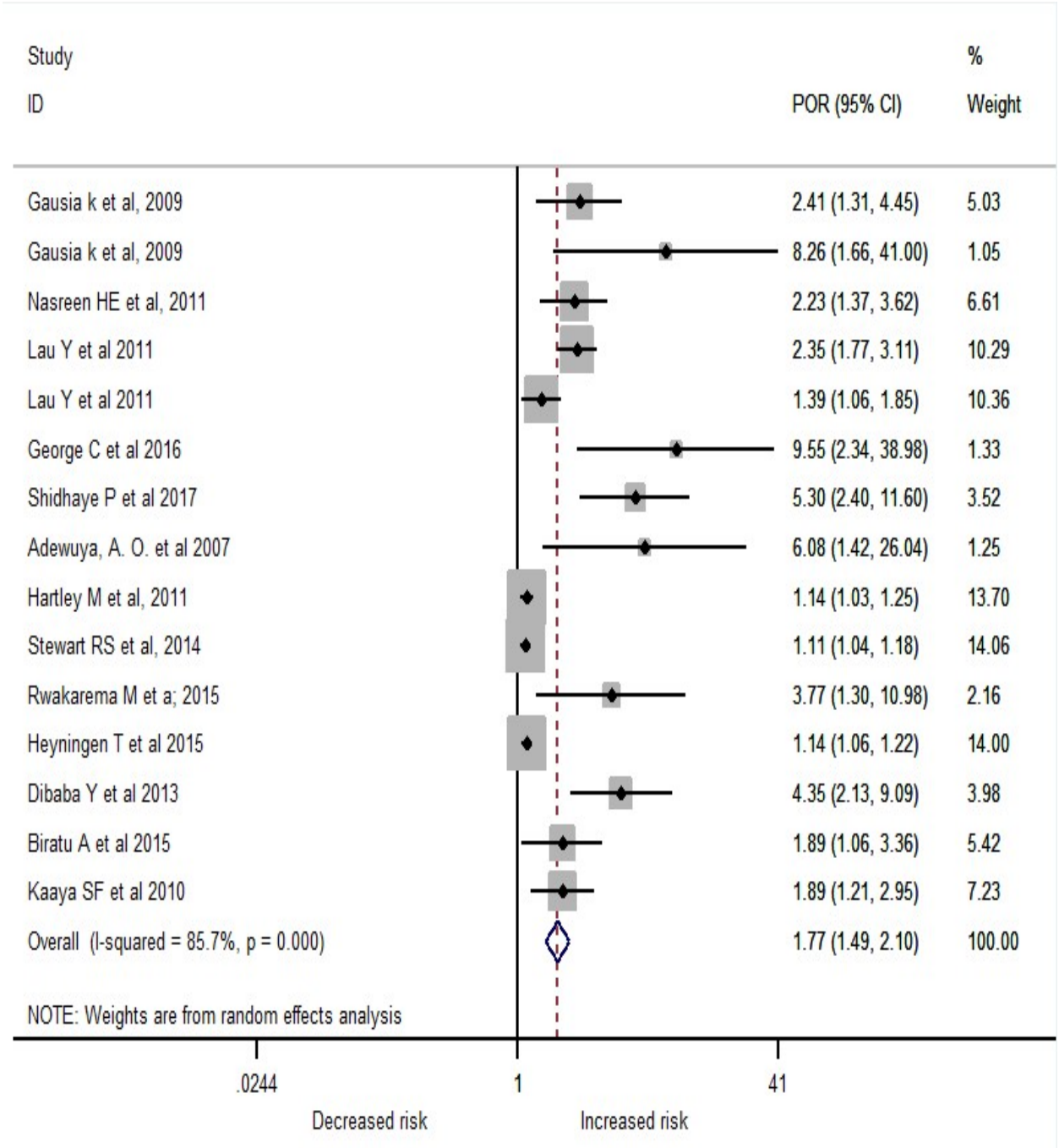


Figure 9: Poor social support as a risk factor of AND, forest plot

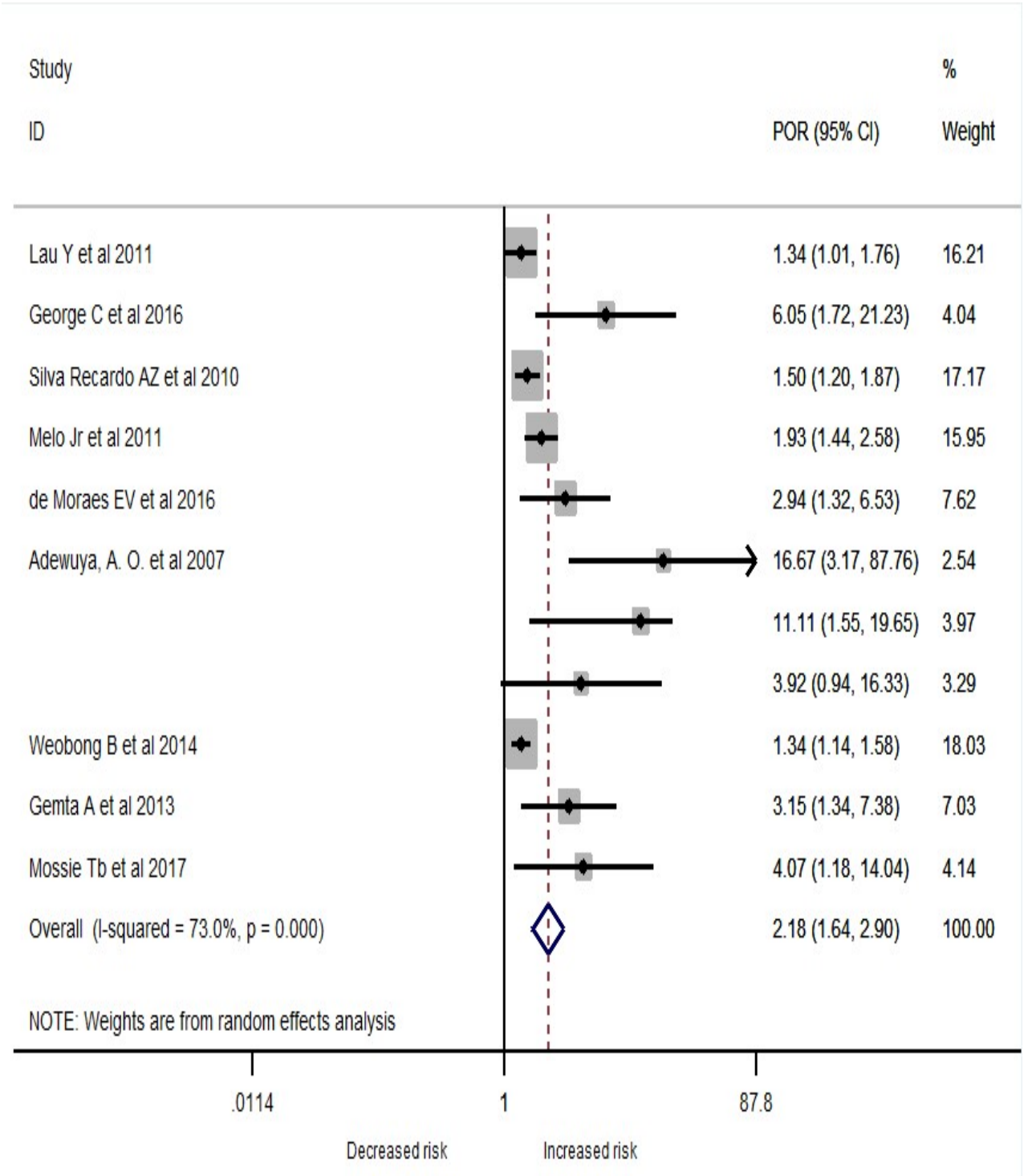


Figure 10: Unfavourable marital condition as a risk factor for AND, forest plot

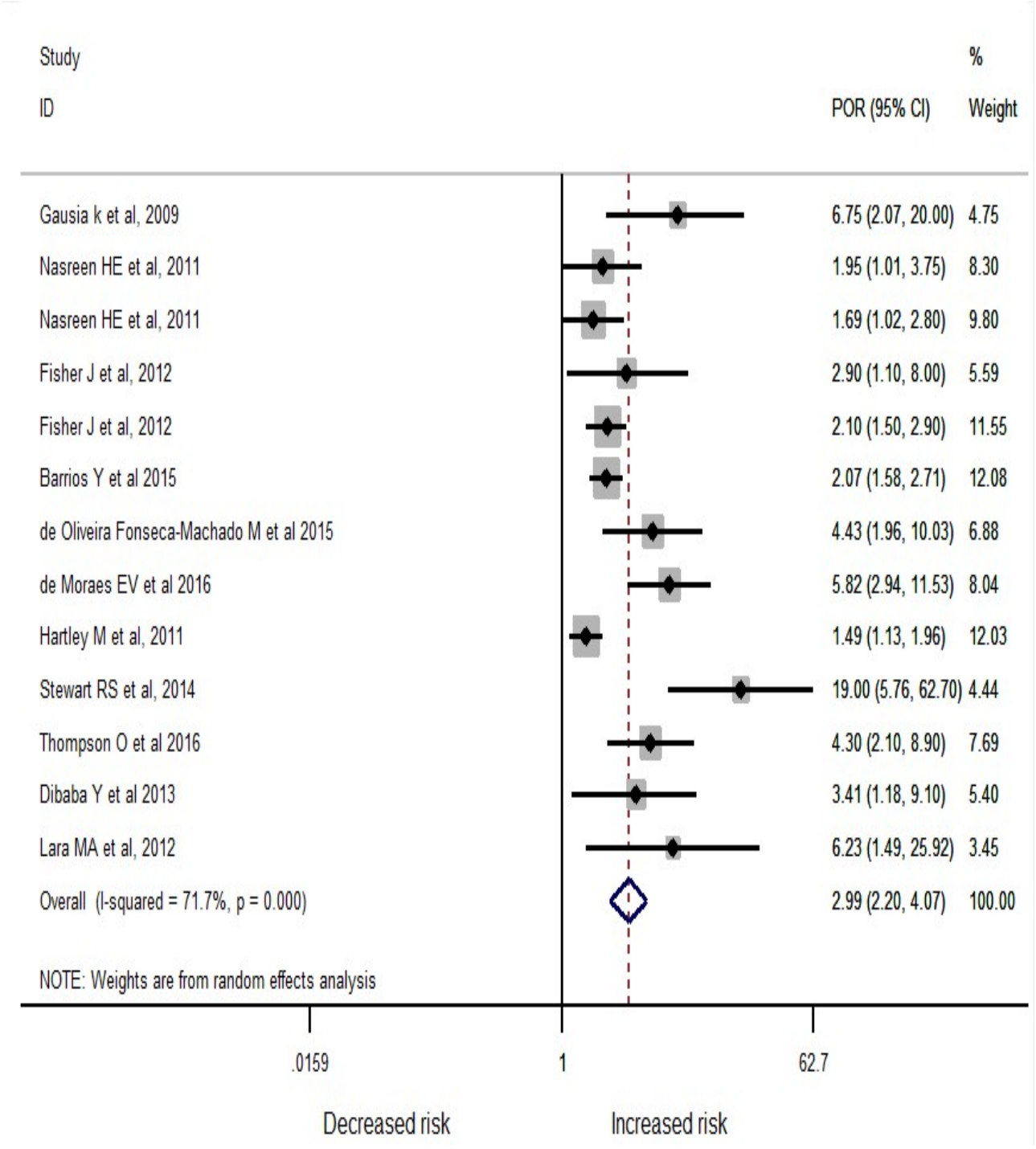


Figure 11: History of IPV as a risk factor for AND, forest plot

Annex 1.2. Supplementary information of a systematic review of PND and its association with adverse infant health outcomes in low-and middle-income countries.

PRISMA checklist

Table 1: Prisma check list for the systematic review of PND and its effect on adverse birth and infant health outcomes in low- and middle-income countries

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1(Title)
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4(Paragraph 2)
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4(Paragraph 2)
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6(paragraph 4)
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5(Paragraph 1)
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4(Paragraph 3)
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4(Paragraph 3) Appendix p 6-8
Study selection	9	20. State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5(Paragraph 1) & (Figure 1) Appendix 10 &11
Data collection process	10	21. Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5(paragraph 3) Appendix 18 & 32

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5(paragraph 3) Appendix 6 -8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6(Paragraph 3) Appendix 10 - 16
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5&6(paragraph 3 and 4)
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6(paragraph 2 &3)

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6(Paragraph 3)
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6(Paragraph 3)
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7&13 Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9 and 15
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6 Appendix 10 - 16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-14 Appendix p21; 25-31 & 39,
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-14 Appendix p21; 25-31 & 39,
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6 Appendix 10 - 16
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	6 Appendix 24 & 38, 25-31 & 39,
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	17(Paragraph 1)
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	20(Paragraph 3&4)

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	21(Paragraph 1)
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	22(Paragraph 4)

Literature search strategy

Table 2: Literature search strategy

#	Data base	Search builder
	1. Search strategy for postnatal depression	
1	PsycINFO	(exp POSTPARTUM DEPRESSION/) or (Depress*.tw,id.) AND (postnat* or postnatal wom?n or postpartum wom?n).tw,id.) AND ((exp Risk Factors/) or (risk*.tw,id.)) AND ((cross sectional* or case control* or nested-case contorl).mp.) : all Sort by: PublicationDate Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female; Field: Title/Abstract
2	Scopus	((Postnatal mothers) OR (Postpartum mothers) OR (mothers after birth)) AND ((Depression during postnatal period) OR (postnatal depression) OR (depression after birth) OR (postpartum depressive symptom) OR (depressive mood following birth)) AND ((risk factors) OR correlates OR (associated factors) OR predictors)) AND ((cross sectional*) OR survey OR (case control*) OR (nested case control*) OR (prospective follow up) OR (follow up) OR (retrospective follow up)) : all Sort by: PublicationDate Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female;Field: Title/Abstract
3	**Emcare**	(exp POSTPARTUM DEPRESSION/) or (Depress*.tw,id.) AND (postnat* or postnatal wom?n or postpartum wom?n).tw,id.) AND ((exp Risk Factors/) or (risk*.tw,id.)) AND ((cross sectional* or case control* or nested-case contorl).mp.) : all Sort by: PublicationDate Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female;Field: Title/Abstract
	2. Search strategy for the effect of postnatal depression on infant health outcome	
1	MEDLINE	(exp POSTPARTUM DEPRESSION/) or (Depress*.tw,id.) AND (postnat* or postnatal wom?n or postpartum wom?n).tw,id.) AND (*Neonatal Intensive Care/ or *Birth Weight/ or exp Infant Development/ or exp Morbidity/ or *Premature Birth/ or exp Neonatal Development/ or exp Neonatal Disorders/) or ((Common post neonatal illness or neonatal illnes* or malaria or pneumonia or fever or diarrhea or measle).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]) AND ((exp Psychosocial Factors/ or exp Risk Factors/) or (risk*.tw,id.)) AND ((prospective cohort* or retrospective cohort* follow up* or longitudinal* or cross sectional* or case control* or nested-case control).mp.) : all Sort by: PublicationDate Filters:Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female;Field: Title/Abstract
2	PsycINFO	(exp POSTPARTUM DEPRESSION/) or (Depress*.tw,id.) AND (postnat* or postnatal wom?n or postpartum wom?n).tw,id.) AND (*Neonatal Intensive Care/ or *Birth Weight/ or exp Infant Development/ or exp Morbidity/ or *Premature Birth/ or exp Neonatal Development/ or exp Neonatal Disorders/) or ((Common post neonatal illness or neonatal illnes* or malaria or pneumonia or fever or diarrhea or measle).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]) AND ((exp Psychosocial Factors/ or exp Risk Factors/) or (risk*.tw,id.)) AND ((prospective cohort* or retrospective cohort* follow up* or longitudinal* or cross sectional* or case control* or nested-case control).mp.) : all Sort by: PublicationDate Filters: Publication date from 2007/01/01 to 2017/12/31; Humans; English; Female; Field: Title/Abstract

NOS quality assessment checklist

I. Postnatal depression prevalence

Table 3: Quality ratings for cross –sectional studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection (max-5points)				**Comparability** (max-two points)	**Assessment of the outcome** (max-three points)		**Total Score**
List of studies	representativeness of the sample	Sample size	Non-respondents	Ascertainment of the risk-factors	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.	Ascertainment of the outcome	Stastical test	
Ahmed, H. M. 2012	1	1	1	1	1	1	1	8
Azale, Telake, 2016	1	1	1	1	2	1	1	8
Baghianimoghadam, M. H. 2007	0	1	1	1	2	1	1	7
Bottino, M. N. 2012	1	1	1	1	2	1	1	8
Correa, H. 2016	1	1	1	1	2	1	1	8
de Castro, F. 2015	1	0	1	1	1	2	1	7
Deng, Ai-Wen. 2014	1	0	1	1	2	1	1	7
Dindar, Ilknur. 2007	1	1	1	1	2	1	1	8
Dubey, C. 2012	1	0	1	1	1	2	1	7
Ege, E. 2008	1	1	1	1	2	1	1	8
El-Hachem, C. 2014	1	1	1	1	1	2	1	8
Flores-Quijano, M. E. 2008	0	1	1	1	2	1	1	7

Galeshi, M. 2016	0	1	1	1	1	1	1	6
Gao, Ling-ling. 2008	1	1	1	1	1	1	1	7
Giri, R. K. 2015	1	1	1	1	1	1	1	8
Goker, Asli. 2012	1	0	1	1	1	1	1	7
Gomez-Beloz, A. 2009	1	1	1	1	1	1	1	8
Gupta, Swapan. 2013	1	1	?	1	1	1	1	8
Hanlon, Charlotte, 2010	1	1	1	1	1	1	1	8
Hassanein, Ibrahim M. A. 2014	1	1	1	1	1	1	1	8
Hasselmann, M. H. 2008	1	0	1	1	1	1	1	7
Supriya Hegde, 2012	0	1	1	1	1	1	1	7
Ho-Yen, S. D. 2007	1	0	1	1	1	1	1	7
Iranpour, S. 2016	1	0	1	1	1	1	1	7
Iranpour, S. 2017	1	0	1	1	1	1	1	7
Johnson, A. R. 2015	0	Consecutive sampling	1	1	1	1	1	6
Kadir, Azidah Abdul, 2009	0	0	1	1	2	1	1	7
Kakyo, Tracy Alexis, 2012	1	1	0	1	1	1	1	6
Kumwar, D. 2015	0	1	1	1	1	1	1	6
Lara, M. A. 2015	1	1	1	1	1	1	1	7
Liu, S, 2017	1	1	1	1	2	1	1	8
Mathisen, S. E. 2013	0	1	1	1	2	1	1	6
Melo Jr, E. F. 2012	1	1	1	1	2	1	1	8
Mohammed, E. S. 2014	1	1	1	1	2	1	1	8
Muneer, A. 2009	0	1	1	1	2	1	1	7

Murray, L. 2015	1	1	1	1	2	1	1	8
Panyayong, B. 2013	1	1	1	1	2	1	1	8
Safadi, R. R. 2016	1	1	1	1	1	1	1	7
Serhan, Nilüfer, 2013	1	1	0	1	1	2	1	7
Shamu, Simukai, 2016	1	1	1	1	1	1	1	7
Shivalli, Siddharudha, 2015	0	1	1	1	1	2	1	7
Stellenberg, E. L. 2015	1	0	1	1	2	1	1	7
Stewart, Robert C. 2010	0	0	1	1	2	2	1	7
Tannous, Leila, 2008	1	1	1	1	1	2	1	8
Wan, E. Y. 2009	1	0	1	1	1	1	1	7
Yagmur, Y. 2010	1	1	1	1	1	2	1	8
Zainal, Nor Zuraida, 2012	1	0	1	1	2	1	1	7

Table 4: Quality ratings for case control studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection(score)				**Comparability** (score)	**Exposure** (score)			**Total Score/out of 8**
List of studies	Case definition	Representative of cases	Selections of controls	Definition of controls	Control any confounding variable	Ascertainment of exposure	Same method of ascertainment for participants	Nonresponse rate (not higher than 25%) – justifiable power maintained	
Petrosyan, Diana, 2011	1	1	0	1	1	1	1	1	7
Roomruangwong, C., 2016	1	1	0	1	1	1	1	1	6
Suhitharan, Thangavelautham, 2016	1	1	0	1	1	1	1	0	6

Table 5: Quality ratings for the cohort studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection(score)				**Comparability** (score)	**Outcome**(score)			**Total Score (out of 8)**
List of studies	Representative of exposed cohort	Selections of non-exposed cohort	Assessment of exposure	Absence of outcome at start of study	Control for any confounding variable	Assessment of outcome	Follow-up period (at least three months after birth)	Adequacy of follow-up (to clearly get the outcome of interest)	
Abdollahi et al. 2016	1	1	1	**1**	1	1	1	1	8
Abdollahi F et al. 2014	1	1	1	1	1	1	1	1	8
Khalifa DS et al. 2015	1	1	1	1	1	1	1	0	7
Mohamad Yusuff, Aza Sherin, 2015	1	1	1	1	1	1	1	1	8
Ramchandani, Paul G., 2009	1	1	1	1	1	0	1	1	7

Weobong B et al. 2015	1	1	1	1	1	1	1	0	7

II. Adverse infant health outcomes

Table 6: Quality ratings for cross –sectional studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection (max. 5 points)				**Comparability** (max. 2 points)	**Assessment of the outcome** (max. 3 points)		**Total Score**
List of studies	representativeness of the sample	Sample size	Non-respondents	Ascertainment of the risk-factors	The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.	Ascertainment of the outcome	Stastical test	
Flores-Quijano, M. E. 2008	0	1	1	1	1	1	1	6
Islam MJ et al. 2016	1	1	1	1	2	1	1	8
Madeghe BA et al. 2016	1	1	1	1	1	2	1	8
Ndokera R et al. 2008	1	1	1	1	1	1	1	7
Surkan PJ et al. 2009	1	1	1	1	1	2	1	8
Saeed Q et al. 2016	1	1	1	1	2	1	1	8
Wemakor A et al. 2016	1	1	1	1	2	1	1	8

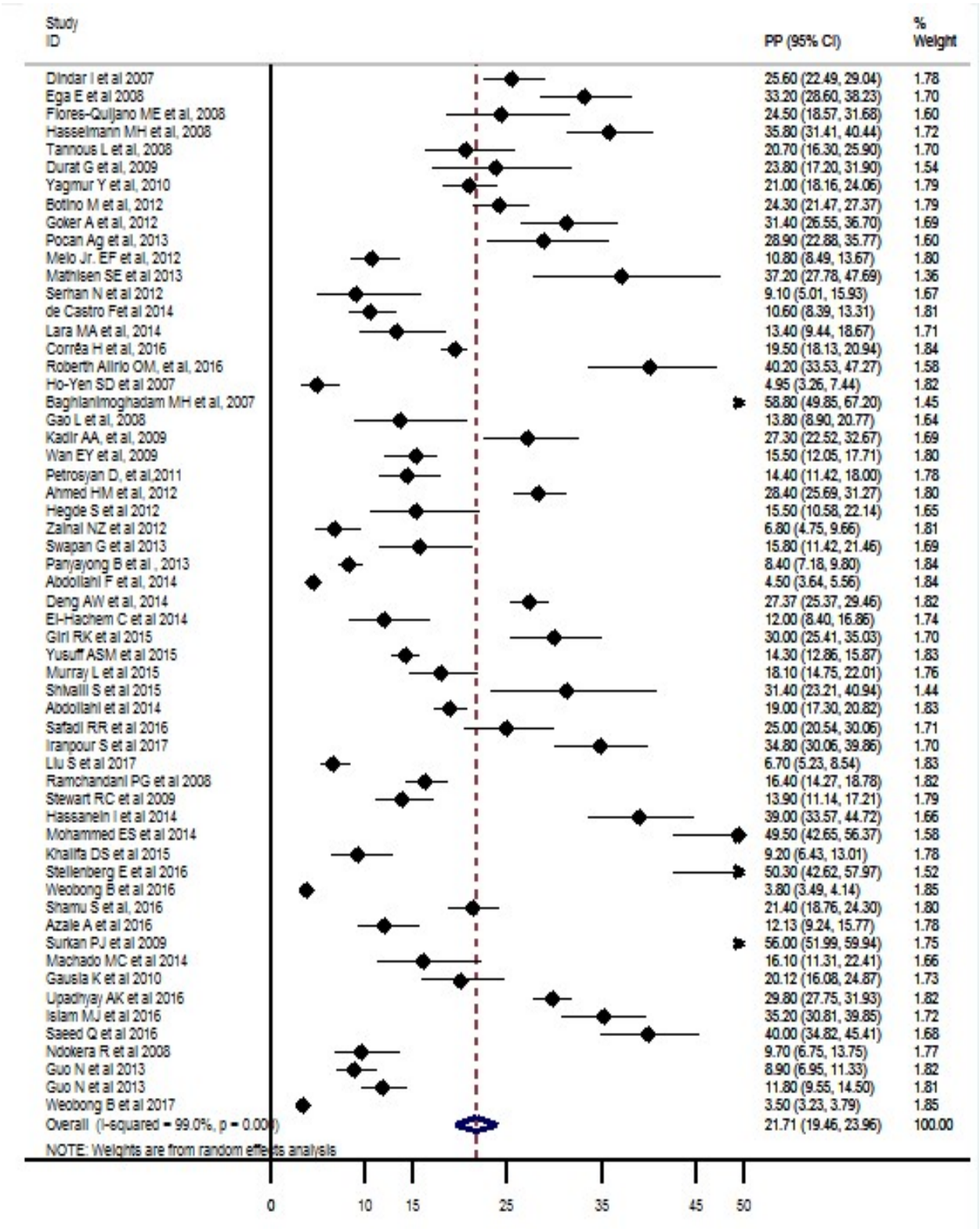
Table 7: Quality ratings for case control studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection (score)				**Comparability** (score)	**Exposure** (score)			**Total Score (out of 8)**
List of studies	Case definition	Representative of cases	Selections of controls	Definition of controls	Control any confounding variable	Ascertainment of exposure	Same method of ascertainment for participants	Non-response rate (not higher than 25%) – justifiable power maintained	
Abiodun O. Adewuya, et al. 2007	1	1	0	1	1	1	1	1	7
Ashaba, S, 2015	1	1	0	1	1	1	1	1	7

Table 8: Quality ratings for the cohort studies included on the basis of Newcastle–Ottawa quality assessment scale

	Selection(score)				**Comparability** (score)	**Outcome**(score)			**Total Score (out of 8)**
List of studies	Representative of exposed cohort	Selections of non-exposed cohort	Assessment of exposure	Absence of outcome at start of study	Control for any confounding variable	Assessment of outcome	Follow-up period (at least three months after birth)	Adequacy of follow-up (to clearly get the outcome of interest)	
Gausia, K. 1010	0	1	1	**1**	1	1	1	1	7
Guo N et al. 2013	1	1	1	1	1	1	1	0	7
Hasselmann MH et al. 2008	1	1	1	1	1	1	1	0	7
Machado MC et al. 2014	1	1	1	1	1	1	1	0	7
Rahman A et al. 2016	1	1	1	1	1	1	1	1	8
Upadhyay AK et al. 2016	1	1	1	1	1	1	1	1	8

Weobong B et al. 2017	1	1	1	1	1	1	1	1	8
Benett IM et al. 2015	1	1	1	1	1	1	1	1	8
Maureen M Black et al. 2009	1	1	1	1	1	1	1	1	8



PPD=pooled postnatal depression

Figure 1: Meta-analysis of PND prevalence (Forest plot) in low- and middle-income countries

Testing publication bias for PND prevalence

Egger's test for small-study effects:

Number of studies = 58 Root MSE = 588.3

Std_Eff	Coef.	Std. Err.	t	P>t	[95% Conf.	Interval]
slope	2.527562	.8539526	2.96	0.005	.8168894	4.238235
bias	973.746	98.58112	9.88	0.000	776.2643	1171.228

Test of H0: no small-study effects P = 0.000

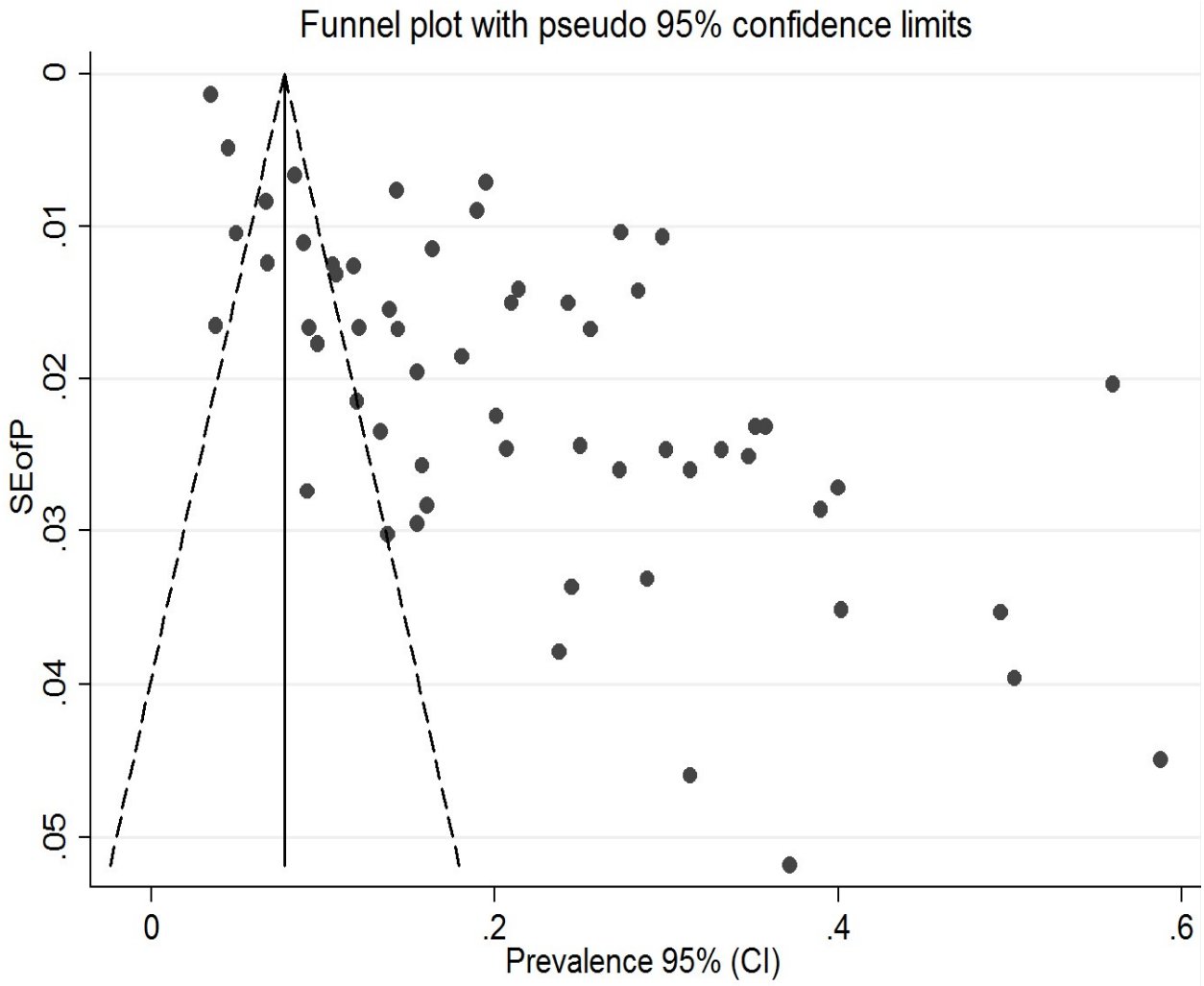


Figure 3: Funnel plot for PND prevalence in low- and middle-income countries

Meta-analysis of factors associated with PND

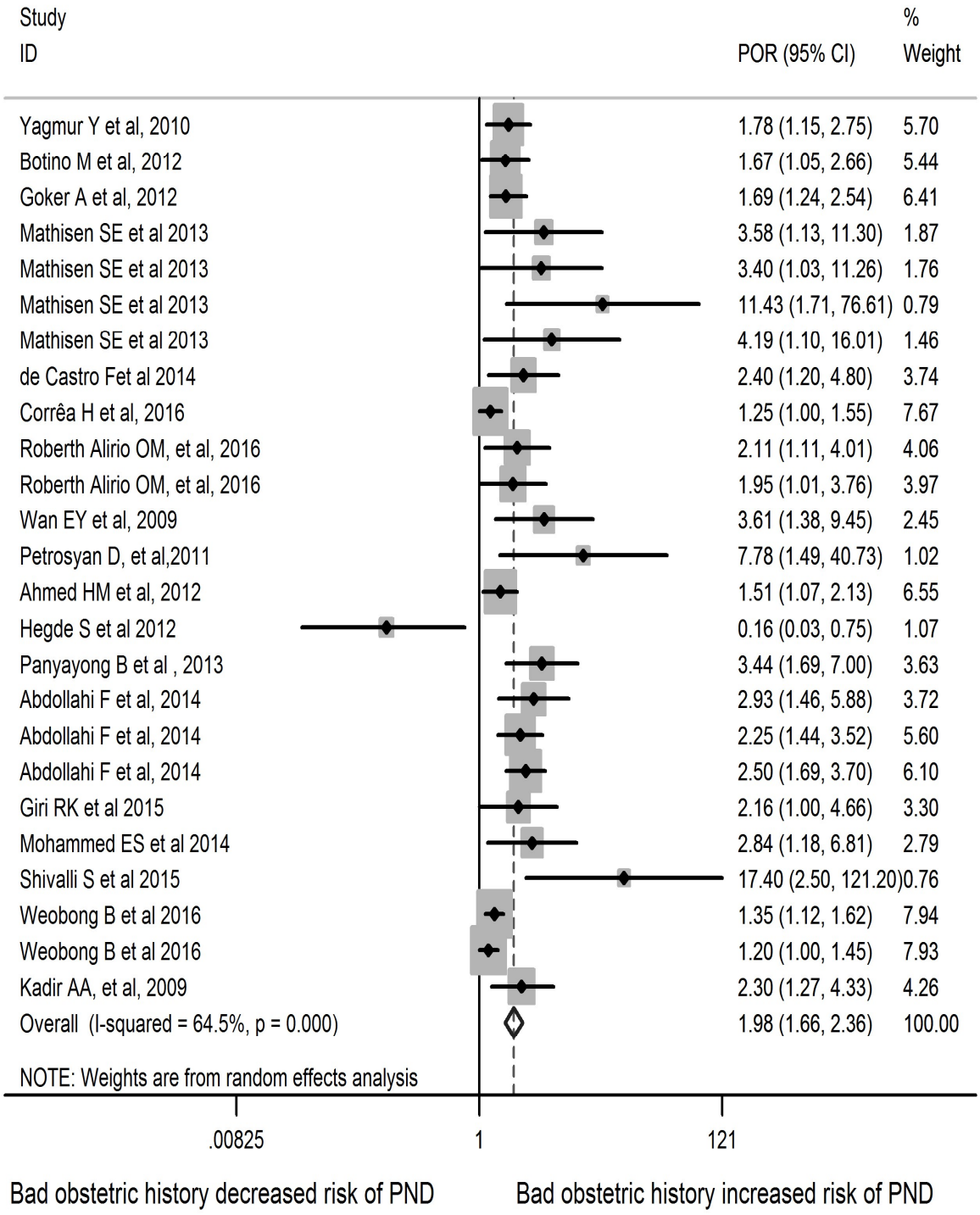


Figure 4: Bad obstetric (*unplanned pregnancy, GDM, GHP, labor complication, history of emesis, multiparity*) history as a factor for postnatal depression

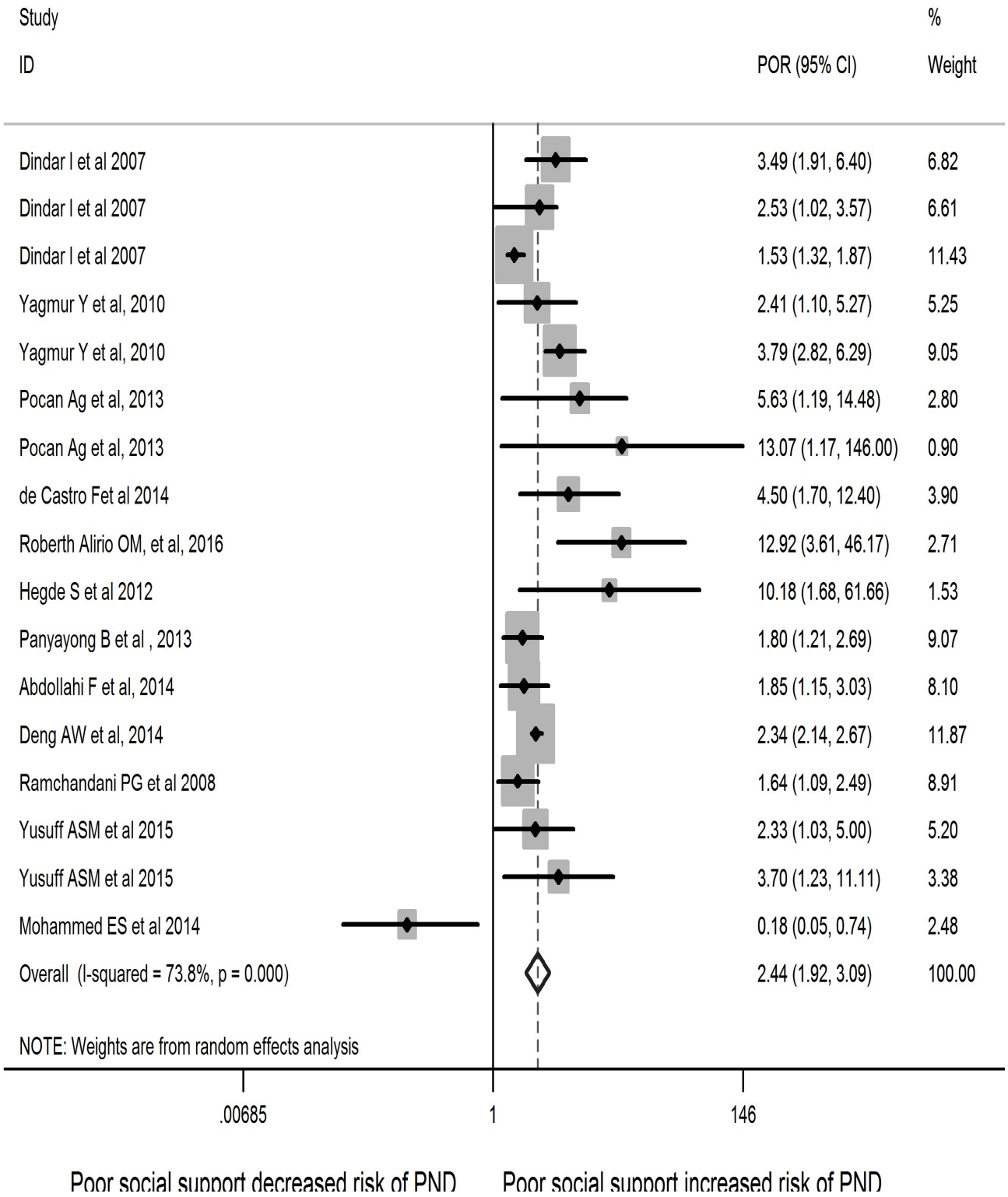


Figure 5: Poor social support as a risk factor for PND

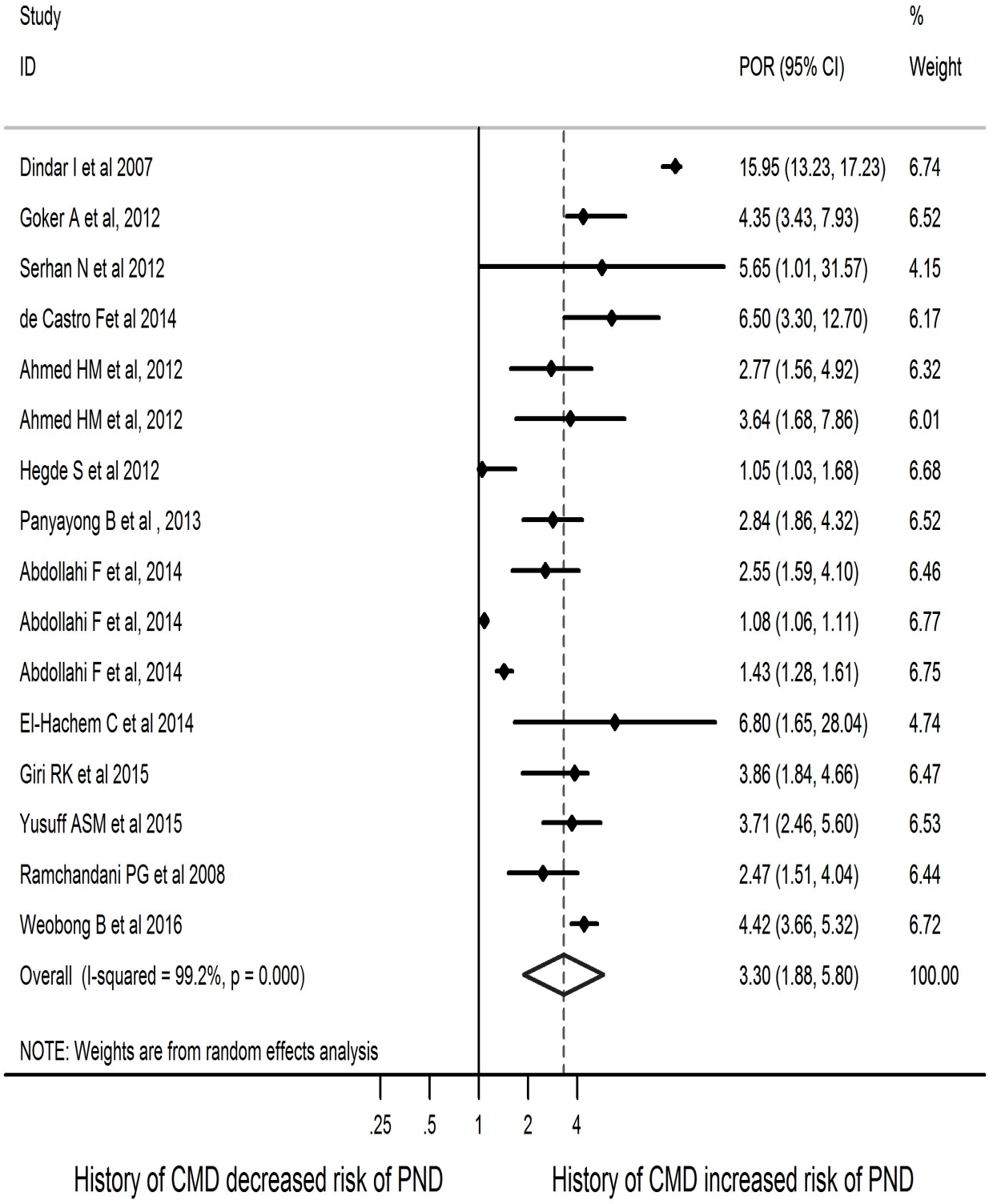


Figure 6: History of common mental disorder (*anxiety, depression, stress*) as a risk factor for PND

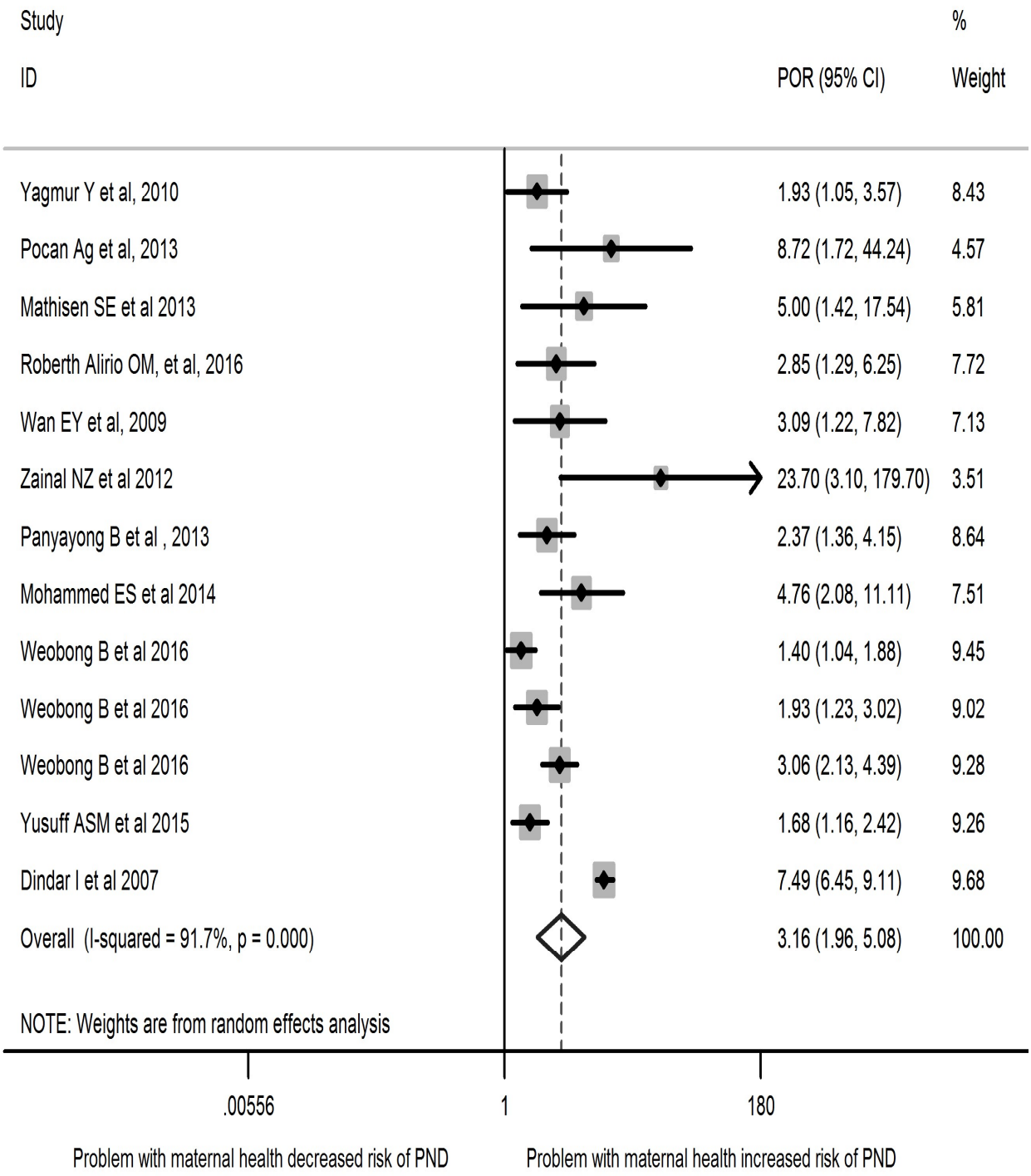


Figure 7: Maternal and newborn ill health as a risk factor for PND

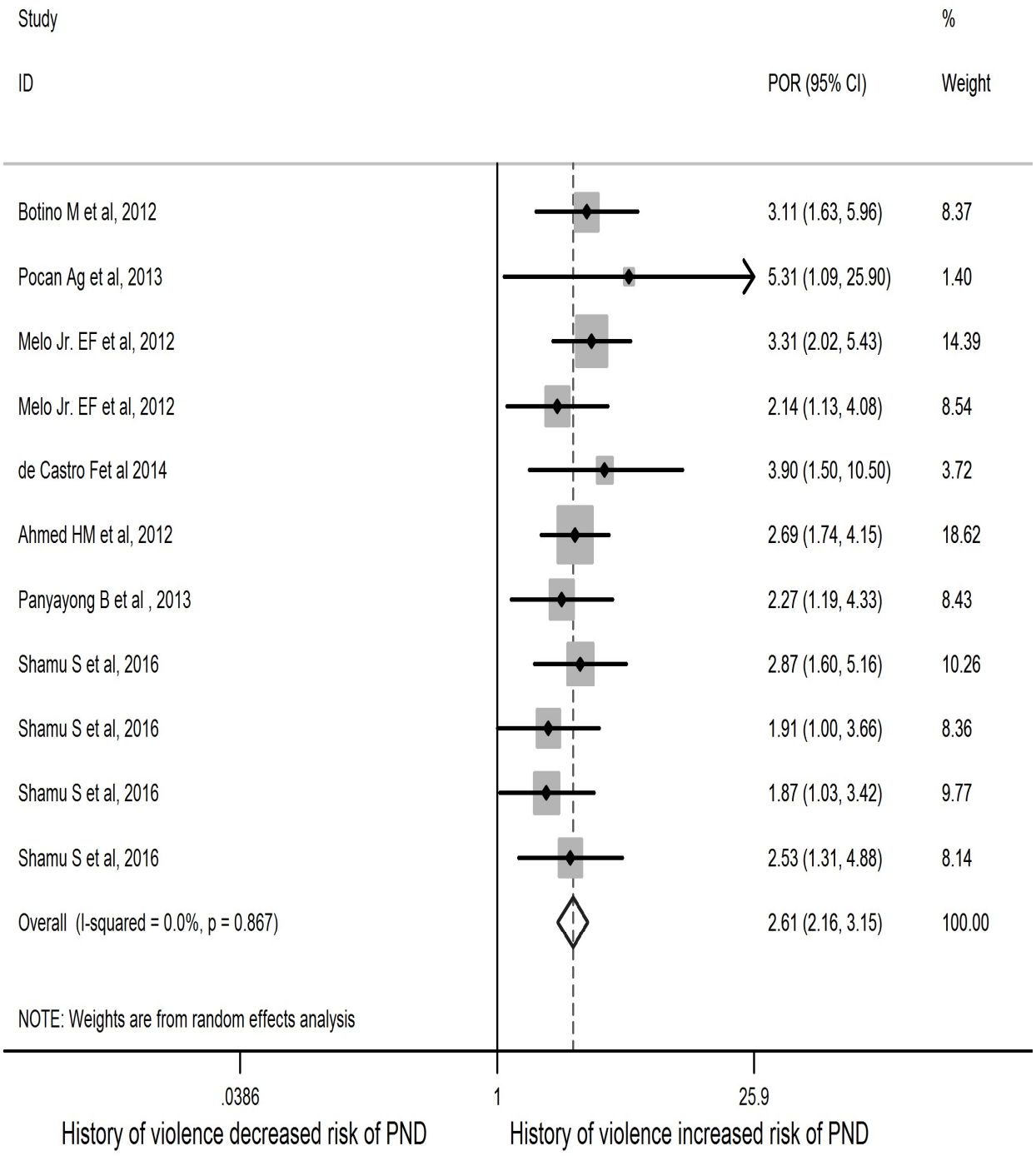


Figure 8: Exposure to any form of lifetime violence as a risk factor for PND

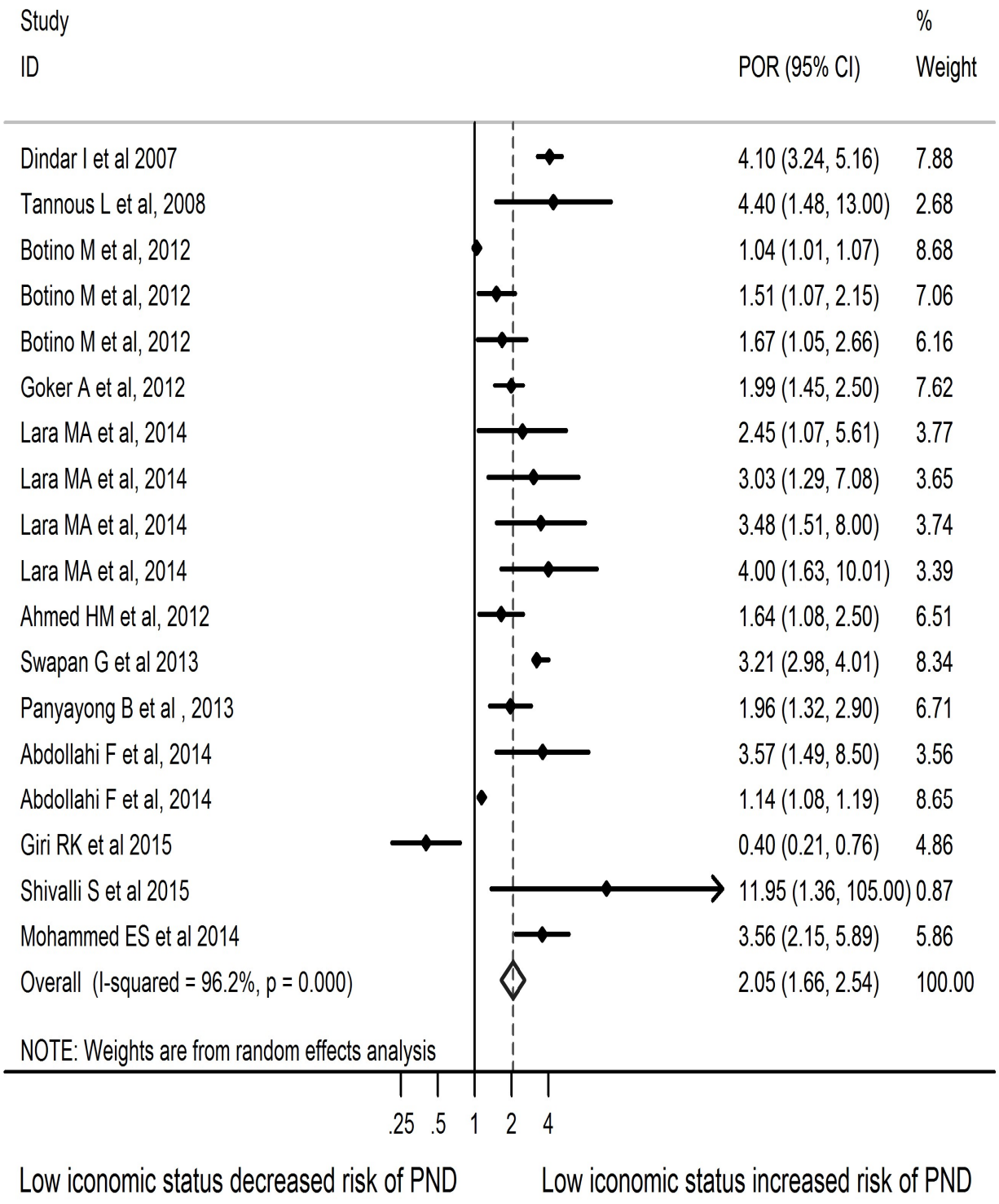


Figure 9: Low economic status as a risk factor for PND

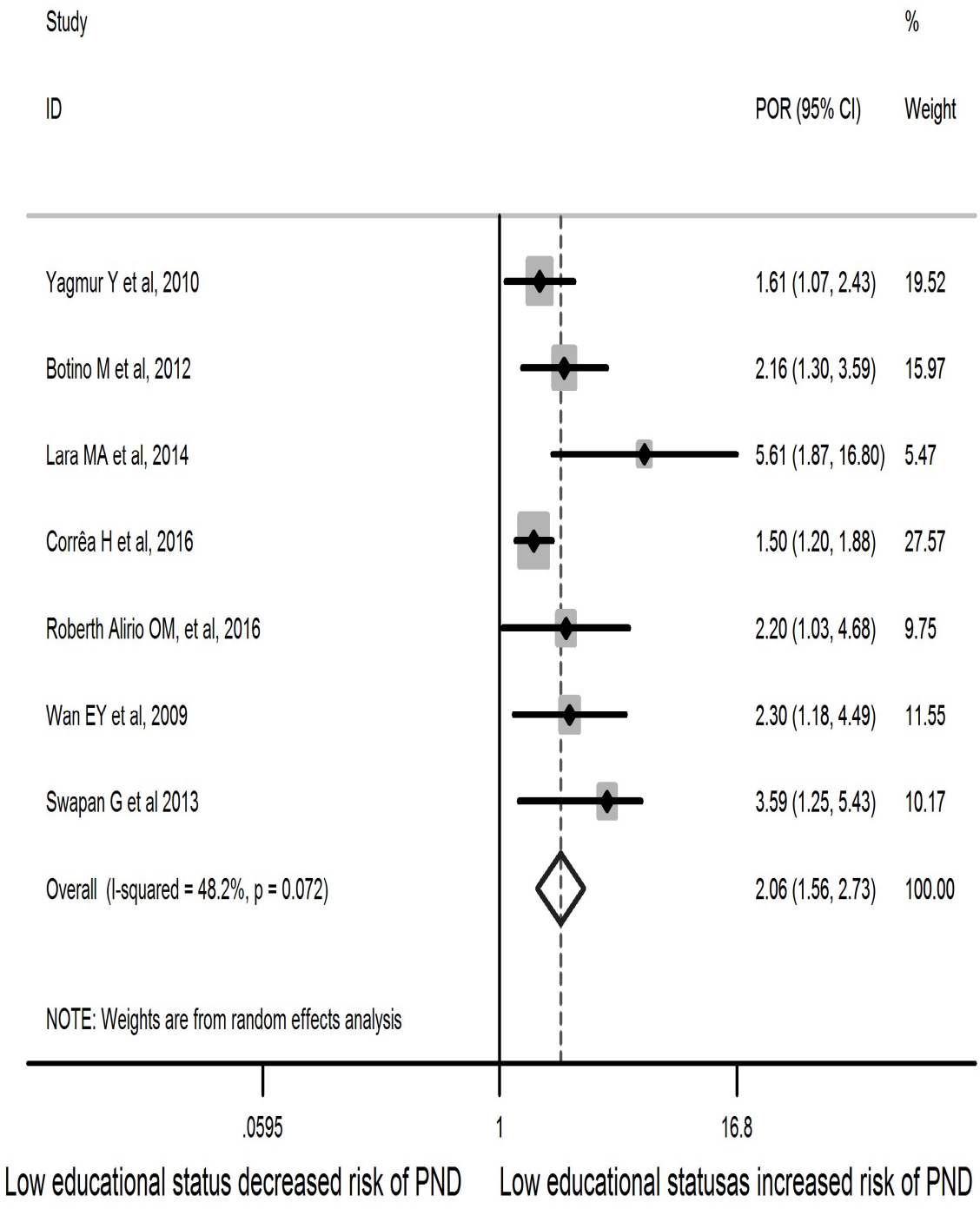


Figure 10: Low educational status as a risk factor for PND

II. Postnatal depression and adverse infant health outcome

Table 9: Trim and fill analysis for postnatal depression effect on adverse infant health outcome

Filled

Meta-analysis (exponential form)

Method	Pooled	95% CI		Asymptotic		No. of studies
	Est	Lower	Upper	z_value	p_value	17
Fixed	1.189	1.144	1.236	8.806	0.000	
Random	1.314	1.166	1.480	4.493	0.000	

Test for heterogeneity: Q=275.421 on 42 degrees of freedom (p=0.000)

Moment-based estimate of between studies variance= 0.097

Postnatal depression and adverse infant health outcomes, sub-analysis

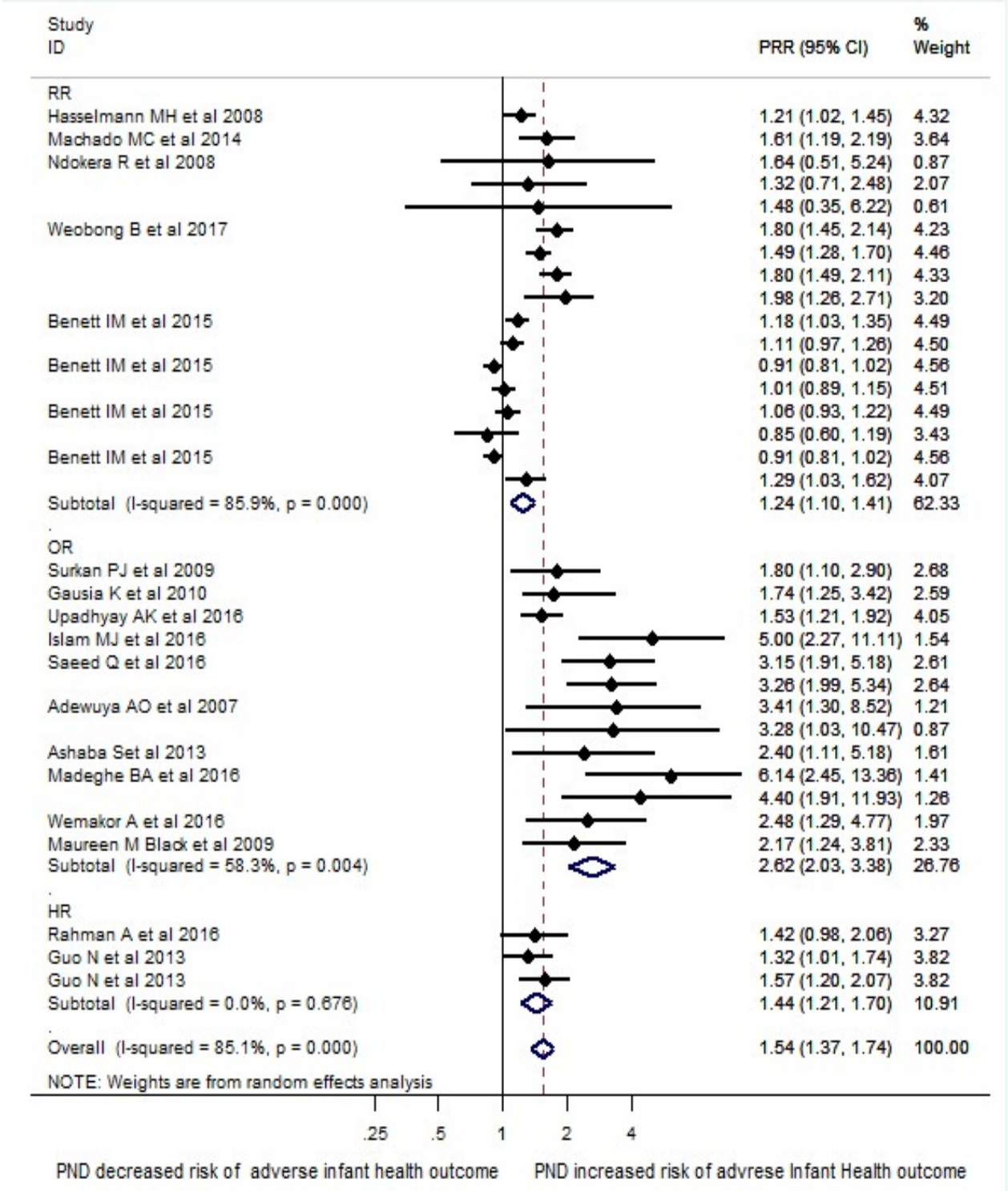


Figure 12: Effect of postnatal depression on adverse infant health outcome sub-analysed by measure of association used in primary studies

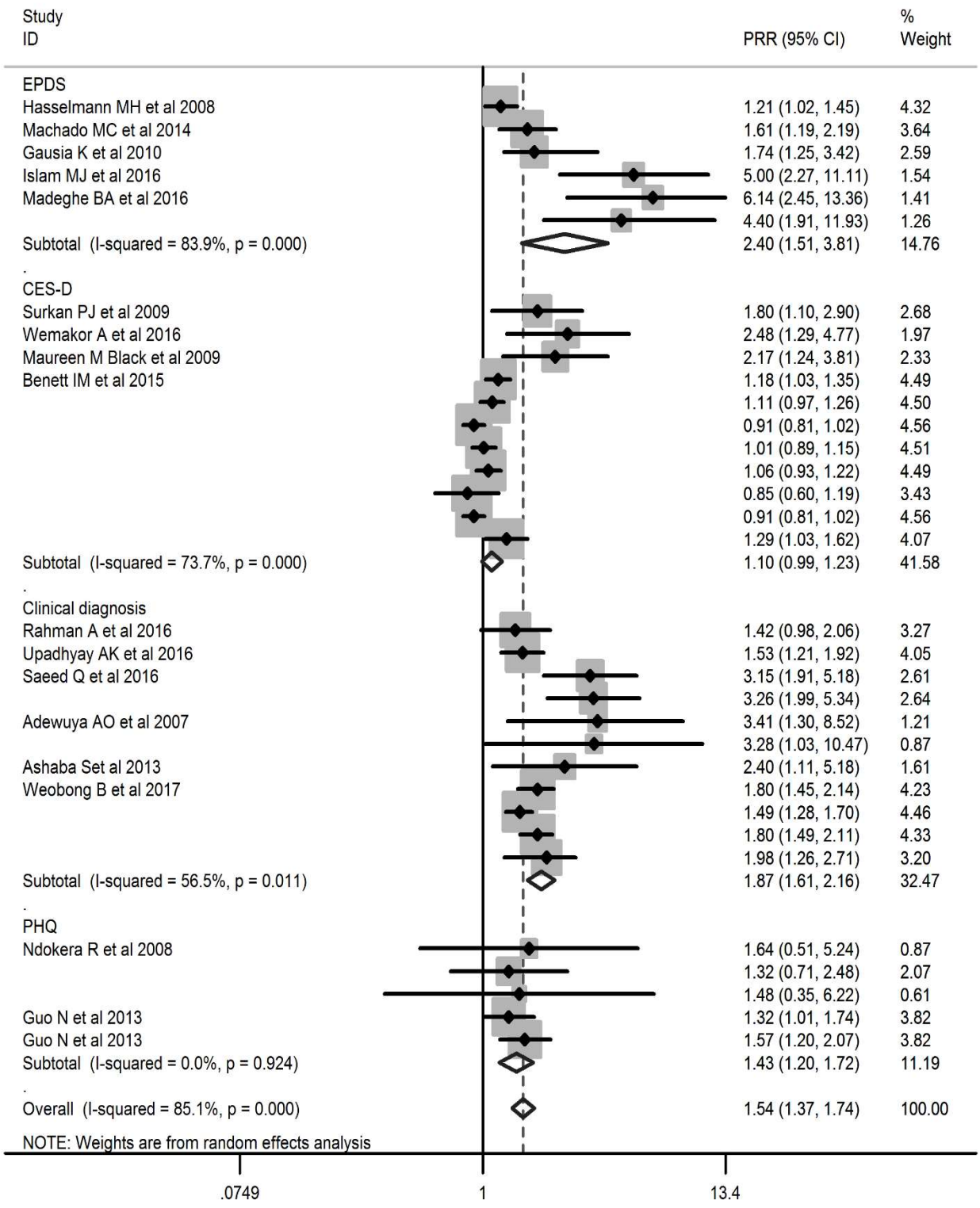


Figure 13: Effect of postnatal depression on adverse infant health outcome sub-analysed by tool used for screening depression

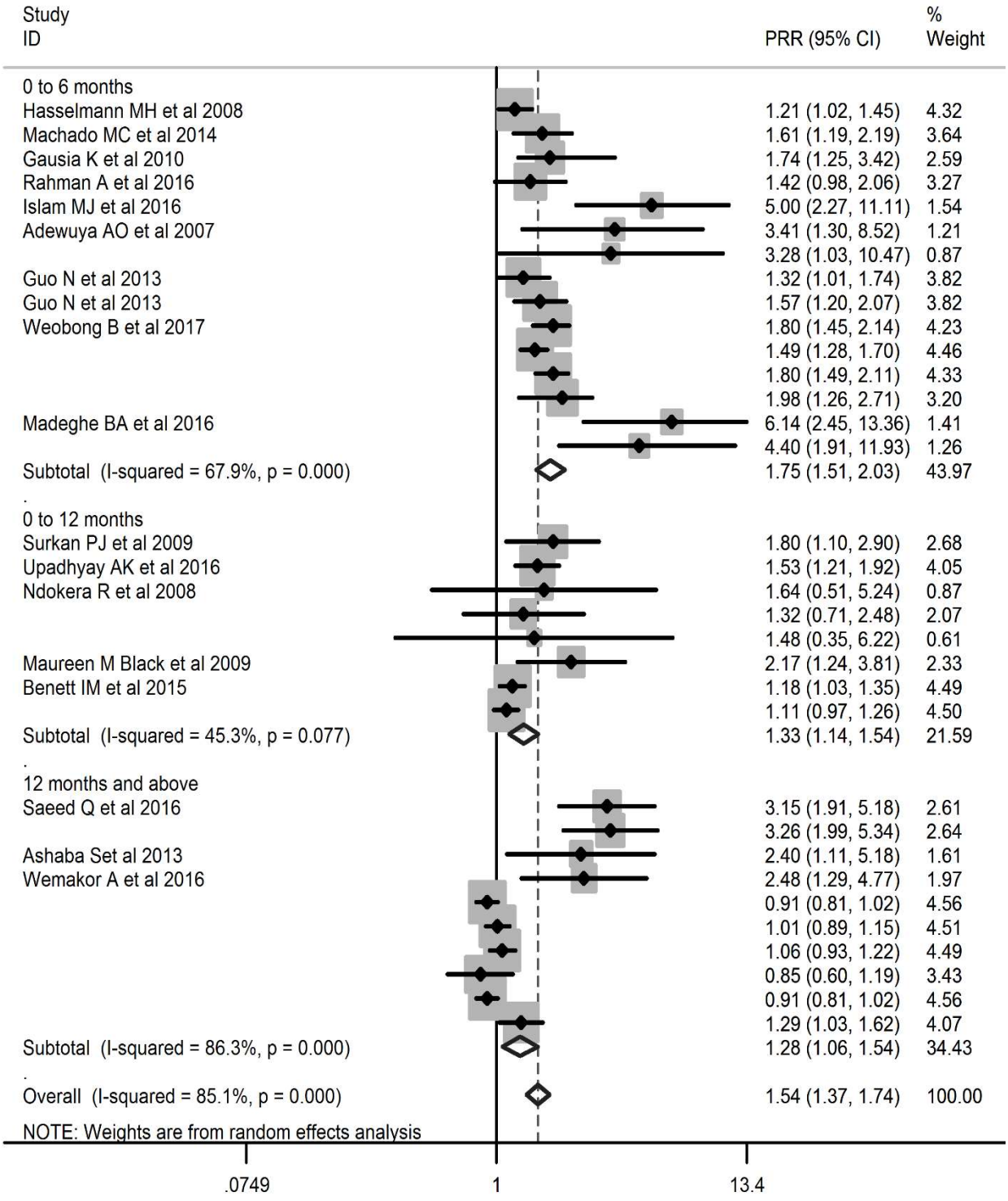


Figure 14: Effect of postnatal depression on adverse infant health outcome sub-analysed by age of the infant

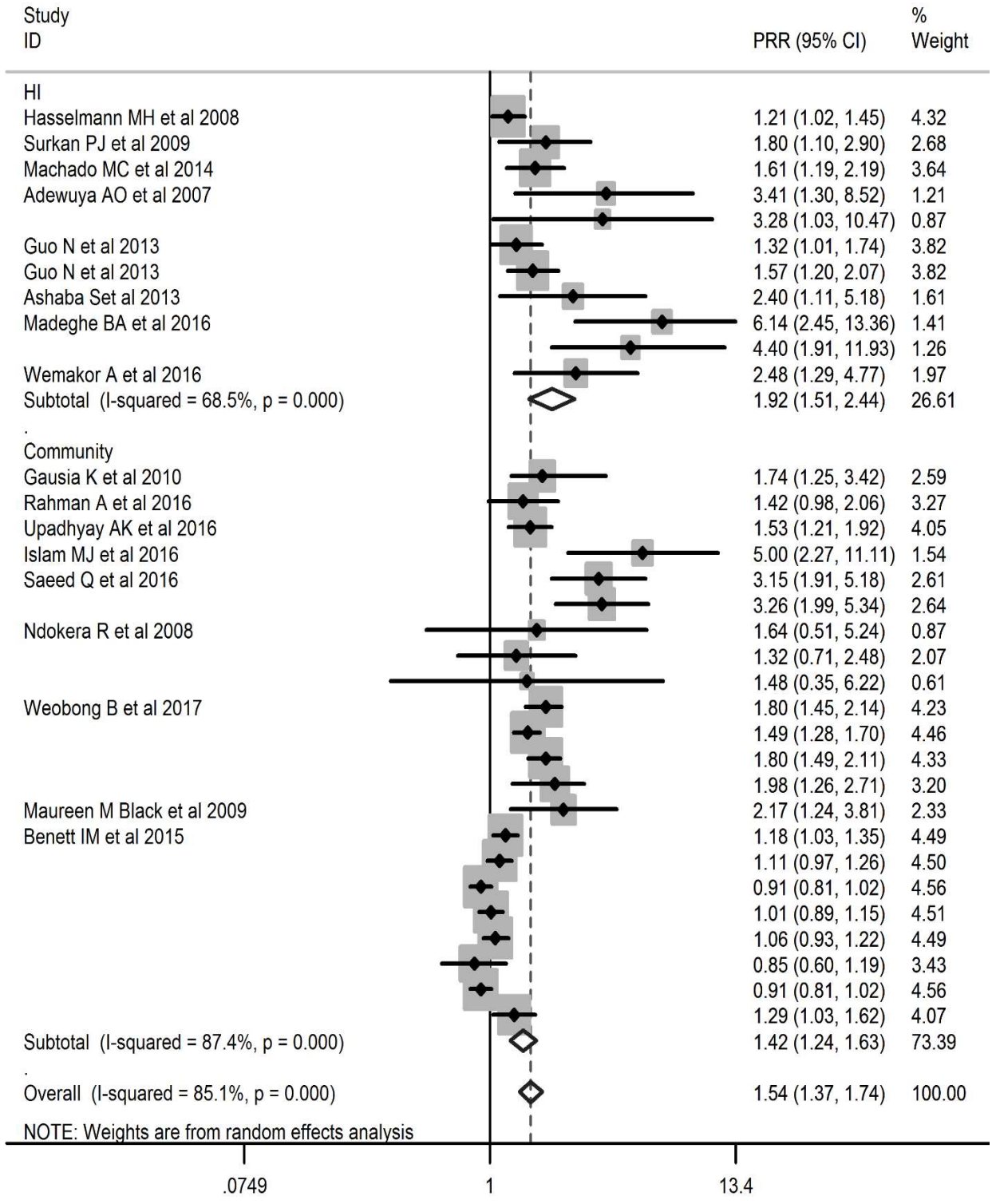


Figure 15. Effect of postnatal depression on adverse infant health outcome sub-analysed by study setting

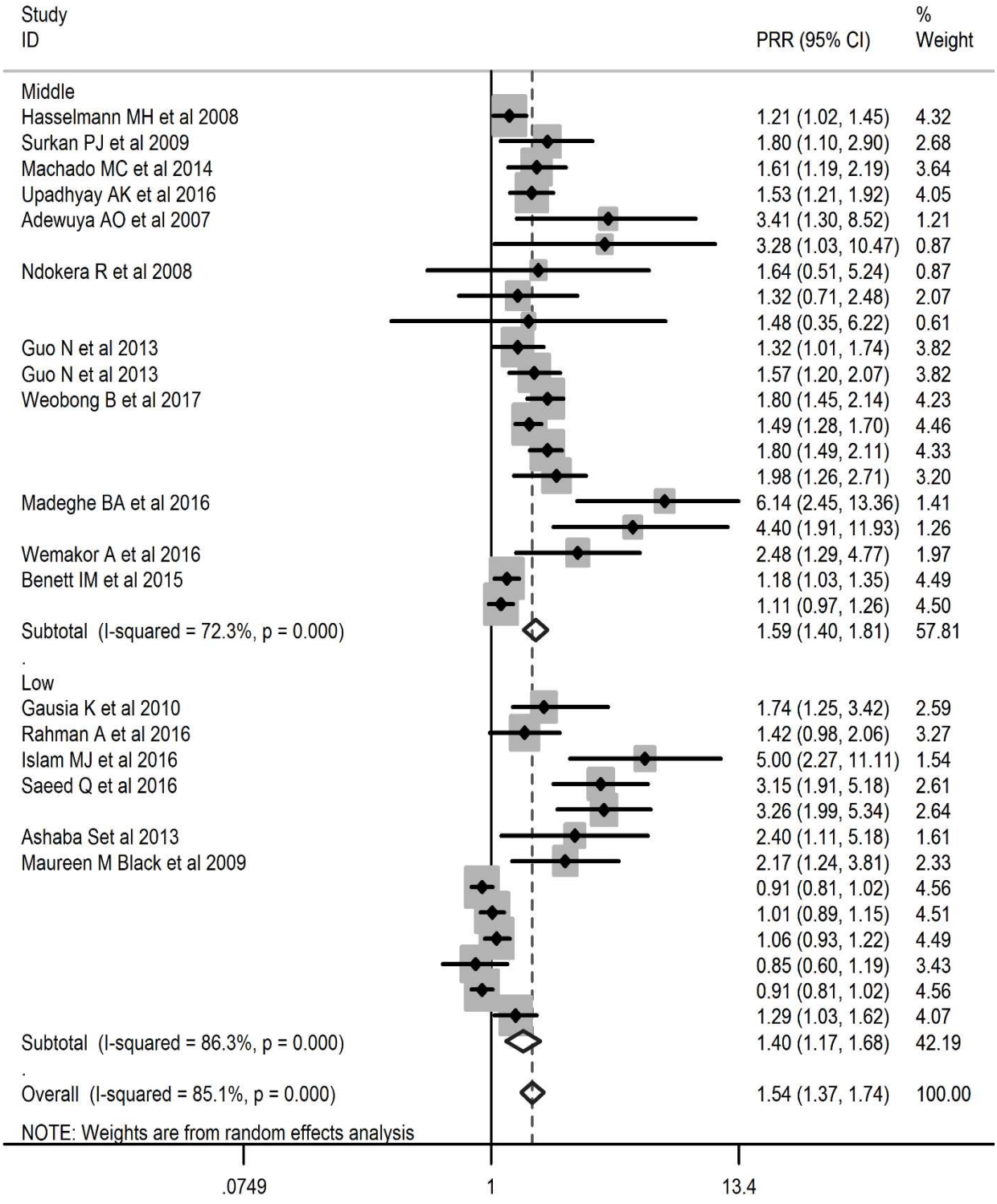


Figure 17. Effect of postnatal depression on adverse infant health outcomes sub-analysed by country income

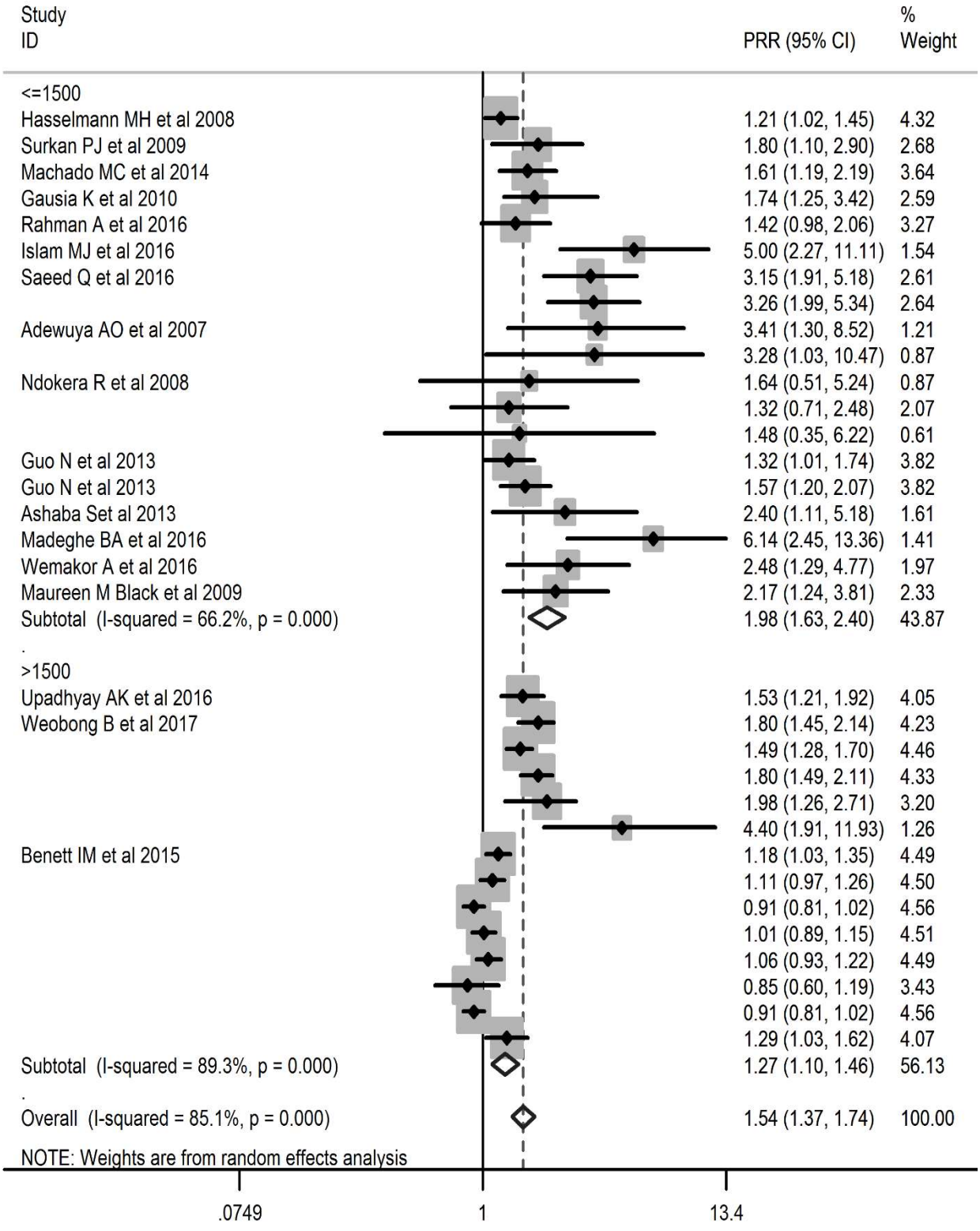


Figure 18: Effect of postnatal depression on adverse infant health outcomes sub-analysed by sample size

Annex 2. Ethics document

Annex 2.1. Letter of introduction for perinatal women participants

LETTER OF INTRODUCTION

Dear mother participants

This letter is to introduce Mr. Abel Fekadu Dadi who is a PhD student in the college of Medicine and Public Health at Flinders University, Australia. He is undertaking research leading to the production of a thesis and other publications on the subject of depression during pregnancy and after birth and its consequences. You are invited to participate in a questionnaire that newly graduated female nurse data collectors will read out to you at three consecutive visits. The first visit will take 35 - 40 minutes, the second visit will take 15 – 20 minutes and the third visit will take 10-15 minutes. While no identifying information will be published and your information will remain confidential, complete anonymity cannot be guaranteed as members of their community may know who has participated although they won't know any information that you have provided. You are entirely free to refuse or discontinue your participation at any time or to decline to answer particular questions and this will not affect your care now or in the future.

Any enquiries you may have concerning this research should be directed to me at the address: Telephone +61 87 2218417 or email lillian.mwanri@flinders.edu.au.

Thank you for your attention and assistance.

Yours sincerely

Lillian Mwanri (MD, PhD, Associate professor)

This research project has been approved by the Flinders University Social and Behavioural Research Ethics Committee (Project Number: 7959). For more information regarding ethical approval of the project the Executive Officer of the Committee can be contacted by telephone on 8201 3116, by fax on 8201 2035 or by email human.researchethics@flinders.edu.au

Annex 2.2. Information sheet for perinatal women participants

INFORMATION SHEET

(Pregnant mother participants)

Title: 'Depression during pregnancy and after birth and its consequences'

Researcher(s)

Mr. Abel Fekadu Dadi[1]: Tel: +251919782422

Supervisors

Assoc/Prof. Lillian Mwanri[1]: Tel: +61 87 2218417

Dr. Emma Miller[1]: Tel: +61 8 7221 8445

Dr. Telake Azale[2]: Tel: +251920013801

1. College of Medicine and Public Health, Flinders University, Flinders University
2. College of Medicine and Health Sciences, Institute of Public Health
   University of Gondar

Description of the study:

This study aims to explore the burden of depression and its effect on the health of pregnant mother and their newborn babies. It will be conducted among pregnant mothers and their newborn living in Gondar town. Data will be collected from June 2018 to June 2019. The study has been approved by Flinders University Social and Behavioural Ethics Committee (Australia), and University of Gondar College of Medicine and Health Sciences Ethical Review Board. The permission has also been sought from Gondar Town Health Office.

Purpose of the study:

This study aims to assess if depression in pregnancy and after delivery is a significant public health problem for pregnant mothers and their newly born babies. The overall goal is to provide information that can help address health issues that are associated with depression and its outcomes in women who are pregnant or have new babies in Ethiopia.

What will I be asked to do?

You are invited to participate in a questionnaire that newly graduated female nurse data collectors will read out to you. You will be visited three times as follows; once when pregnant and twice during a three-month period after delivery. During the first visit you will be asked about your socio-demographic and obstetric details and any depressive symptoms you might have. This visit will take about 35-40 minutes. We will visit you a second time to ask you questions about your health, how you went during the birth, any support that you are receiving after delivery, and any depressive symptoms you might have had in the period after the birth, which will take 15-20 minutes. We will also visit you for a third time to ask you about the health of your baby, how you are going with breast feeding and caring for the baby that will take 10-15 minutes. All three visits will take place in any place you choose that is convenient to you, if your home is not where you would prefer to have these done.

What benefit will I gain for my involvement in the study?

We are not able to provide any direct payments to you, but if you participate in this research project, it may help to identify any health issues that might occur in you or your baby early, so that we can direct you to any services that might be required. We are happy to reimburse you for any transport costs or other charges that might occur if you choose to be interviewed somewhere other than your own home. Sharing your valuable perspectives should help us develop better maternal health programs that will help all pregnant mothers and their babies in future.

Will I be identifiable by being involved in this study?

So that we can meet you again, we will give you a special secret ID number that will be used throughout your follow up period. Only the data collectors will know both your ID number and your name and this information will be kept in a password-protected computer. Complete anonymity may not be guaranteed as members of your community may know who has participated, however they will not know about any information you provide. The questionnaire will be discarded once the information you have provided has been coded and entered into a computer and ready for analysis. The researcher will only know your special ID number and will not record your name. Your information will be treated with the strictest confidence and no identifying information will be published or shared with any party without your knowledge or consent. As a matter of policy, while all information will be treated with the strictest confidence, it is important to note that any illegal activities, including child abuse, of which we become aware will need to be reported to the relevant authorities.

Are there any risks or discomforts if I am involved?

Some people may get a bit upset about some of the questions or may find out they may have depression or other health problems when doing the survey. If this happens to you, remember that you may stop at any time and you do not have to answer any questions that make you feel uncomfortable. Please make sure you let the data collector know you are feeling upset. If you experience such feelings please contact the counsellor (Name: Firnos Berihun) in the Psychiatry Department, room number (TBA) in Gondar University Specialised Hospital free of charge.

How do I agree to participate?

Your participation is voluntary and you can tell us your decision after reading this information sheet and discussing with your family. You can let us know your decision in a weeks' time by calling the number of your data collector. If you are willing to participate, please sign and return the consent form accompanying this information sheet to the data collector.

How will I receive feedback?

After each interview, your data collector will let you know about your mental health status, the level of your nutrition and that of your baby, and how well your baby is doing health wise. At the end of the study, if you wish, you will be able to access a summary report about the project at your health post and Gondar Town health Office. This report will tell you how all the participants did collectively throughout the study and there will be no information of a particular person. Please note that the report will have the information summarising the findings of the research only.

Any enquiries you may have concerning this research should be directed to Associate Professor Lillian Mwanri (telephone +61 87 2218417 or email lillian.mwanri@flinders.edu.au) or Mr. Abel Fekadu (+251919782422) in the first instance. If you have any complaints about how the research is being conducted, you may contact the Social and Behavioural Research Ethics Committee (SBREC) directly.

Thank you for your time and commitment.

This research project has been approved by the Flinders University Social and Behavioural Research Ethics Committee (Project number: 7959). For more information regarding ethical approval of the project only, the Executive Officer of the Committee can be contacted by telephone on (08) 8201 3116, by fax on (08) 8201 2035, or by email to human.researchethics@flinders.edu.au

Annex 2.3. Verbal script for perinatal women participants

Revised copy of verbal script for mother participants

I ---------- am contacting you on behalf of Mr. Abel Fekadu Dadi, who is a student undertaking his PhD research on maternal depression and its effects. I have newly graduated in nursing and am collecting data on the behalf of Mr Fekadu Dadi. You are invited to participate in a questionnaire that I will read out to you during three consecutive contacts. The first questionnaire will take 35 - 40 minutes, the second questionnaire will take 15 – 20 minutes and the third questionnaire will take 10-15 minutes. Please note that your participation is voluntary. If you decide to participate, you can stop at any time, even during the questionnaire process if you wish to do so. If you decide to not participate, this will not affect the service that you will get now or in the future. While you may not directly benefit from your participation, it is hoped that this research will lead to better care for pregnant mothers and their babies in the future. You are not required to decide now as I will provide you an information sheet to read to get a full picture of the research and to call me back with your decision (my phone number ----------). You can call me in about one week once you have had a chance to think about it.

Annex 2.4. Consent form for perinatal women participants

CONSENT FORM FOR PARTICIPATION IN RESEARCH

(Consent form for interviews of women participants)

Depression during pregnancy and after birth burden and its consequences

I, being an age of 18 and above years, hereby consent to participate as requested in the letter of introduction for the research project on “Depression during pregnancy and after birth burden and its consequences"

1. I have read the information provided; or have had the information read to me.
2. Details of procedures and any risks have been explained to my satisfaction
3. I agree to paper documentation of my information
4. I should retain a copy of the Information Sheet and Consent Form for future reference
5. I understand that:
    I. I may not directly benefit from taking part in this research
    II. I will be interviewed in three occasions
    III. Whether I participate or not, or withdraw after participating, will have no effect on any service that is being provided to me.
    IV. I may ask that the interview be stopped at any time and I may withdraw at any time from the research without any harm or disadvantage
    V. Any information provided will be treated with the strictest confidence and no identifying information will be published.
    VI. While no identifying information will be published and my information will remain confidential, complete anonymity cannot be guaranteed as members of their community may know who has participated.
6. I agree to the information being made available to other researchers who may not be members of this research team, but who the research team deem to be doing related research, on condition that my identity is not revealed.

I certify that I have explained the study to the volunteer and consider that she understands what is involved and freely consents to participate.

Researcher’s name ----------

Researcher’s signature----------Date----------

Participant’s signature……Date……..

Annex 2.5. Letter of introduction for healthcare administrator participants

LETTER OF INTRODUCTION

Dear administrators

This letter is to introduce Mr. Abel Fekadu Dadi who is a PhD student in the college of Medicine and Public Health at Flinders University, Australia. He is undertaking a research leading to the production of a thesis or other publications on the subject of knowledge, practice and your opinion about the health care system in relation to perinatal depression. He would like to invite you to assist with this research by agreeing to be involved in an interview. No more than 50 minutes on interview will be required. While no identifying information will be published and your information will remain confidential, anonymity may not be guaranteed due to the location and small number of study participants. You are entirely free to discontinue your participation at any time or to decline to answer particular questions.

Since he intends to make a tape recording of the interview, he will seek your consent, on the attached form, to record the interview, to use the recording or a transcription in preparing the research report or publication, on condition that your name or identity is not revealed, and to make the recording available to other researchers on the same conditions (or that the recording will not be made available to any other person). It may be necessary to make the recording available to secretarial assistance (or transcription service) for transcription, in which case you may be assured that such persons will be asked to sign a confidentiality agreement which outlines the requirement that your name or identity not be revealed and that the confidentiality of the material is respected and maintained.

Any enquiries you may have concerning this research should be directed to me at the address: Telephone +61 87 2218417 or email lillian.mwanri@flinders.edu.au.

Thank you for your attention and assistance.

Yours sincerely

Lillian Mwanri (MD, PhD, Associate professor)

This research project has been approved by the Flinders University Social and Behavioural Research Ethics Committee (Project Number: 7959). For more information regarding ethical approval of the project the Executive Officer of the Committee can be contacted by telephone on 8201 3116, by fax on 8201 2035 or by email human.researchethics@flinders.edu.au.

Annex 2.6. Information sheet for healthcare administrator participants

INFORMATION SHEET

(Health system administrators)

Title: 'To explore knowledge, practice and health system administrators' view towards health care system in relation to perinatal depression'

Researcher(s)

Mr. Abel Fekadu Dadi[1]: Tel: +251919782422

Supervisors

Assoc/Prof. Lillian Mwanri[1]: Tel: +61 87 2218417

Dr. Emma Miller[1]: Tel: +61 8 7221 8445

Dr. Telake Azale[2]: Tel: +251920013801

3. College of Medicine and Public Health, Flinders University, Flinders University
4. College of Medicine and Health Sciences, Institute of Public Health
   University of Gondar

Description of the study:

This study aims to explore knowledge, practice and health system administrators' view towards health care system in relation to prenatal depression. It will be conducted among health system administrators working at different levels of health care system in Ethiopia. Participants will be drawn from the lowest level in Gondar town to national level in Ethiopia. Data will be collected from June 2018 to June 2019. The study has been approved by Flinders University Social and Behavioural Ethics Committee (Australia), and University of Gondar College of Medicine and Health Sciences Ethical Review Board. The permission has also been sought from Gondar Town Health Office.

Purpose of the study:

This study aims to explore knowledge, practice and health system administrators' view towards health care system in relation to perinatal depression.

What will I be asked to do?

You are invited to attend a one-to-one interview with the researcher who will ask you a few questions about your knowledge, views about the health care system in relation to perinatal depression. The interview will be audio recorded using a digital voice recorder to lastly make analysis. The interview will take about 50 minutes and will take place in your private office or any other place convenient to you.

What benefit will I gain for my involvement in the study?

We are not able to provide any direct payments to you, but sharing of your perspectives will improve the planning and implementation of future programs that address issues of depression in perinatal period and improve the health of the people. We are happy to reimburse you for any transport costs or other charges that might occur if you choose to be interviewed somewhere other than your own office.

Will I be identifiable by being involved in this study?

The interview will be voice recorded into a voice file using a tape recorder. The voice file will be transcribed into interview scripts. The interview script will be assigned a code and your name will not be recorded. After transcription, the voice file will be discarded. The coded interview script will be entered on to the computer software for analysis and will be protected by a password known to researchers only. However, because of the small number of participants and the location where the interview is taking place, in some cases your anonymity may not be fully guaranteed. Your information will be treated with the strictest confidence and no identifying information will be published or shared to any party without your knowledge or consent.

Are there any risks or discomforts if I am involved?

Some people may get a bit upset about some of the questions. If this happens to you, you can stop at any time and you do not have to answer any questions that make you feel uncomfortable. Please make sure you let the interviewer know that you are feeling upset. If you experience such feelings please contact a counsellor (Name: Firnos Berihun) in psychiatry department, room number (TBA) in Gondar University Specialised Hospital free of charge.

How do I agree to participate?

Your participation is voluntary. If you are willing to participate, please let us know and send us a text message at (+251919782422). If you do not want to participate you may say “No I do not want to participate”. Upon receiving the message, an interviewer will contact you to arrange the meeting for

interview. Before the interview, you will then be required to sign the consent form for your willingness to participate. During the interview, you can refuse to answer any questions and you are free to withdraw from the interview at any time without any effect or consequences.

How will I receive feedback?

We can discuss any issues that you may encounter during the interview. At the end of the study, if you wish, you will be able to access a summary report about the project at your health post and Gondar Town health Office.

Any enquiries you may have concerning this research should be directed to Associate professor Lillian Mwanri at the address: Telephone +61 87 2218417 or email lillian.mwanri@flinders.edu.au or Mr. Abel Fekadu on +251919782422. Only complaint about how the research is being conducted should be directed to Social and Behavioural Research Ethics Committee (SBREC).

Thanks for taking the time to read this information sheet and we hope that you will accept our invitation.

This research project has been approved by the Flinders University Social and Behavioural Research Ethics Committee (Project Number:7959) For more information regarding ethical approval of the project only, the Executive Officer of the Committee can be contacted by telephone on (08) 8201 3116, by fax on (08) 8201 2035, or by email to human.researchethics@flinders.edu.au

Annex 2.7. Consent form for healthcare administrator participants

CONSENT FORM FOR PARTICIPATION IN RESEARCH

(Consent form for interviews of health care system administrators)

To explore knowledge, practice and health care system administrators' view towards health care system in relation to perinatal depression

I, being an age of 18 and above years, hereby consent to participate as requested in the letter of introduction for the research project on "To explore knowledge, practice and health professional's view towards health care system in relation to perinatal depression in Gondar town, Northwest Ethiopia".

1. I have read the information provided
2. Details of procedures and any risks have been explained to my satisfaction
3. I agree to audio recording of my information
4. I should retain a copy of the Information Sheet and Consent Form for future reference
5. I understand that:
    I. I may not directly benefit from taking part in this research
    II. Whether I participate or not, or withdraw after participating, will have no effect on my employment and/or work arrangements
    III. I may ask that the recording be stopped at any time and I may withdraw at any time from the research without any harm or disadvantage
    IV. Any information provided will be treated with the strictest confidence and no identifying information will be published.
    V. While no identifying information will be published and my information will remain confidential, anonymity cannot be guaranteed due to the location of interviews and small number of participants.
6. I agree to the information being made available to other researchers who may not be members of this research team, but who the research team deem to be doing related, on condition that my identity is not revealed.

I certify that I have explained the study to the volunteer and consider that she/he understands what is involved and freely consents to participate.

Researcher's name ----------

Researcher's signature----------Date----------

Participant's signature……Date……..

Annex 2.8. Ethical approval from Social and Behavioural Research Ethics Committee of the Flinders University

Dear Abel,

The Chair of the Social and Behavioural Research Ethics Committee (SBREC) at Flinders University considered your response to conditional approval out of session and your project has now been granted final ethics approval. This means that you now have approval to commence your research. Your ethics final approval notice can be found below.

FINAL APPROVAL NOTICE

Project No.:7959

Project Title: The prevalence of Perinatal Depression and its Effect on Birth and Infant Health Outcomes amount a cohort of pregnant mothers in Gondar town, Ethiopia

Principal Researcher: Mr. Abel Fekadu Dadi

Email: dadi0001@flinders.edu.au

Approval Date: 11 May 2018

Ethics Approval Expiry Date: 20 March 2022

The above proposed project has been approved on the basis of the information contained in the application, its attachments and the information subsequently provided with the addition of the following comment(s):

Additional information required following commencement of research:

1. **Permissions**

Please ensure that copies of the correspondence granting permission to conduct the research from the Gondar town Health Office are submitted to the Committee on receipt. Please ensure that the SBREC project number is included in the subject line of any permission emails forwarded to the Committee. Please note that data collection should not commence until the researcher has received the relevant permissions (item D8 and Conditional approval response – number 11).

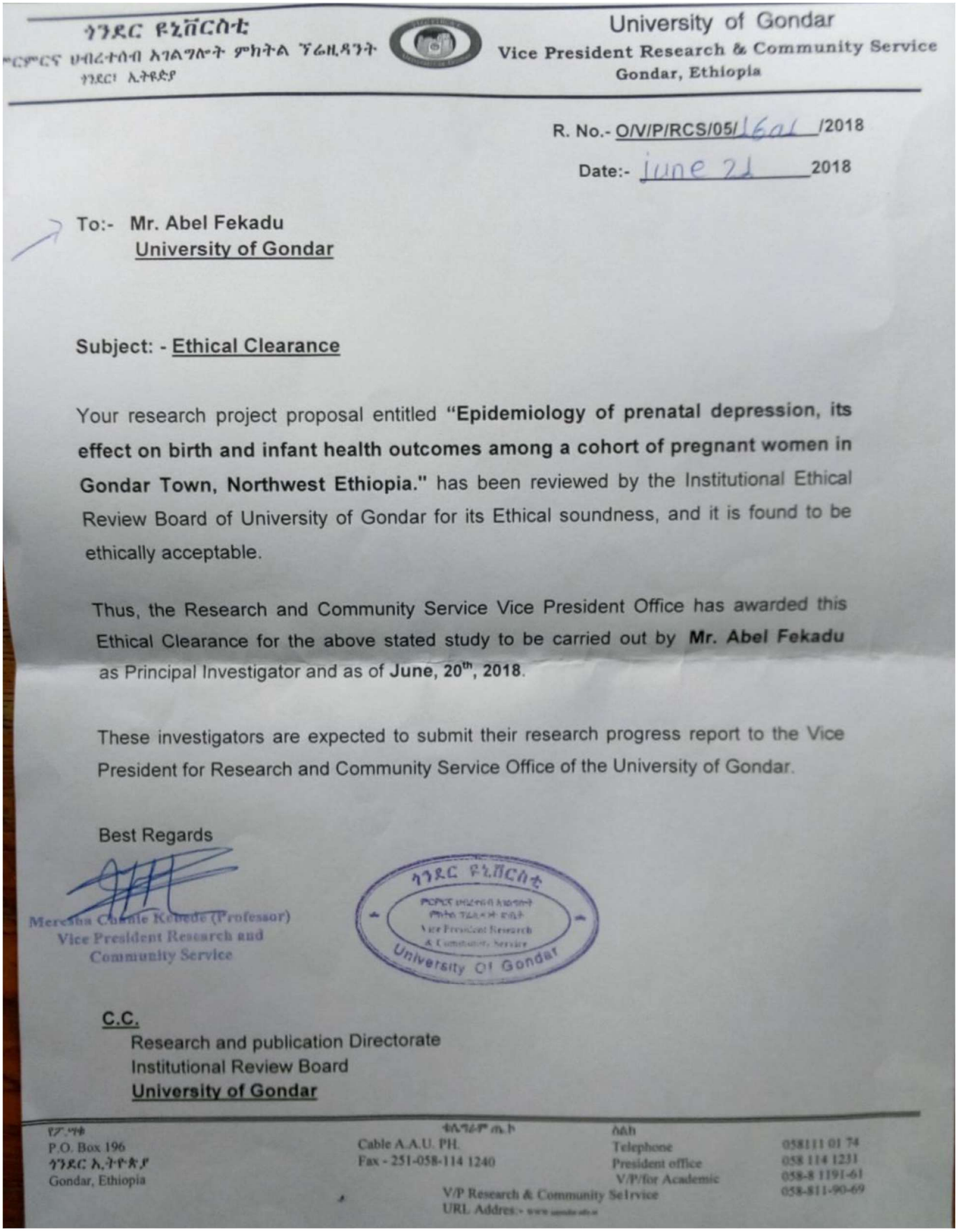
2. **Other Ethics Committees**

Please provide a copy of the ethics approval notice from the Institutional Review Board of University of Gondar on receipt. Please note that data collection should not commence until the researcher has received the relevant ethics committee approvals (item G1).

3. **Translations**

Please provide a copy of the translation of the questionnaire to the Committee. Please note that data collection should not commence until the researcher has provided the translation of these documents.

Annex 2.9. Ethical approval from the Institutional Review Board (IRB) of the University of Gondar



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University of Gondar
Vice President Research & Community Service
Gondar, Ethiopia

R. No.- O/V/P/RCS/05/1601/2018

Date:- June 21 2018

To:- Mr. Abel Fekadu
University of Gondar

Subject: - Ethical Clearance

Your research project proposal entitled **"Epidemiology of prenatal depression, its effect on birth and infant health outcomes among a cohort of pregnant women in Gondar Town, Northwest Ethiopia."** has been reviewed by the Institutional Ethical Review Board of University of Gondar for its Ethical soundness, and it is found to be ethically acceptable.

Thus, the Research and Community Service Vice President Office has awarded this Ethical Clearance for the above stated study to be carried out by **Mr. Abel Fekadu** as Principal Investigator and as of **June, 20th, 2018**.

These investigators are expected to submit their research progress report to the Vice President for Research and Community Service Office of the University of Gondar.

Best Regards

Mereshu Cabule Kebede (Professor)
Vice President Research and
Community Service

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Vice President Research & Community Service
University Of Gondar

C.C.
Research and publication Directorate
Institutional Review Board
University of Gondar

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Fax - 251-058-114 1240

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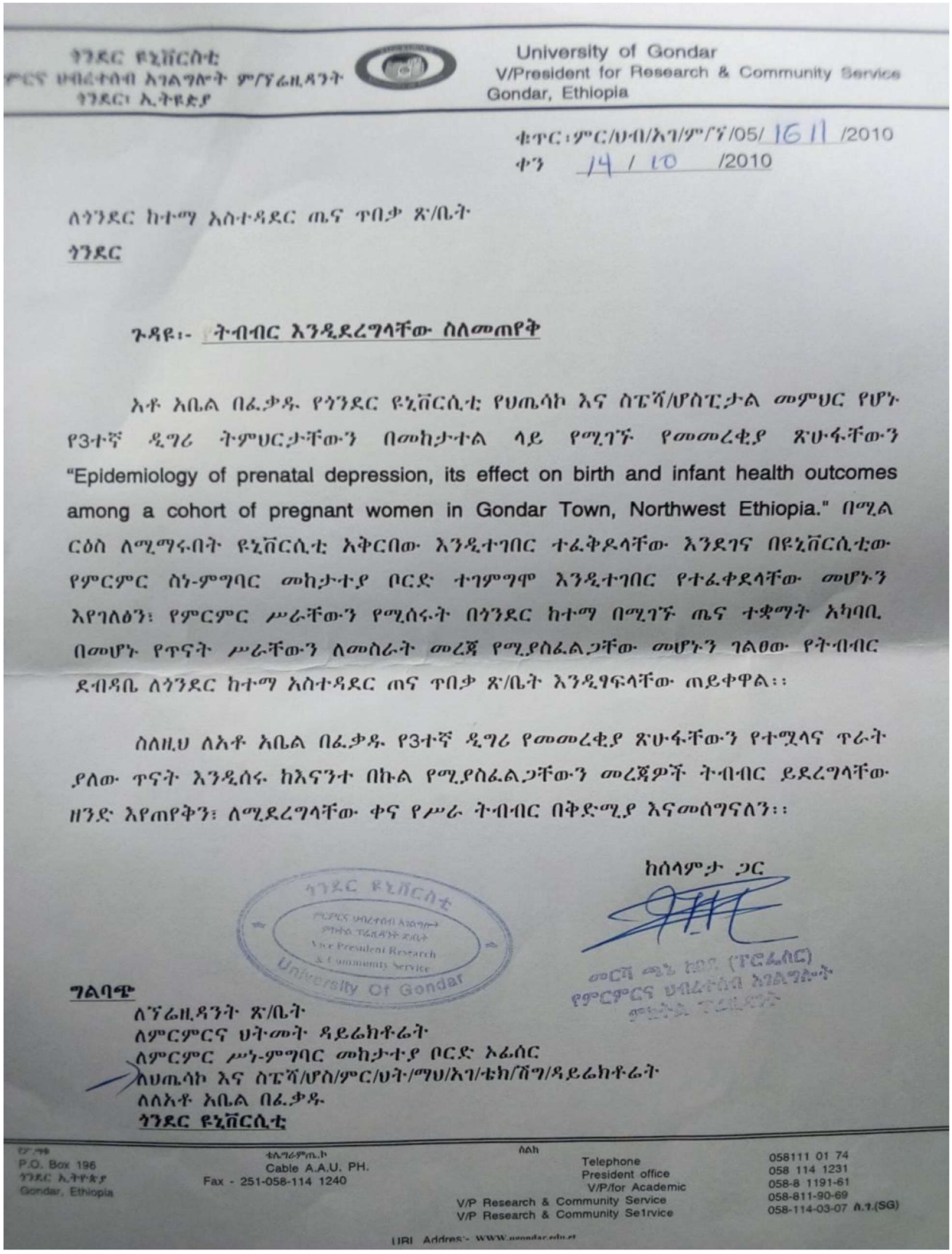
Telephone
President office 058111 01 74
V/P/for Academic 058 114 1231
V/P Research & Community Service 058-8 1191-61
URL Addres:- 058-811-90-69

Annex 2.10. Letter of support from University of Gondar to Gondar Town health office



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University of Gondar
V/President for Research & Community Service
Gondar, Ethiopia

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Vice President Research & Community Service
University Of Gondar

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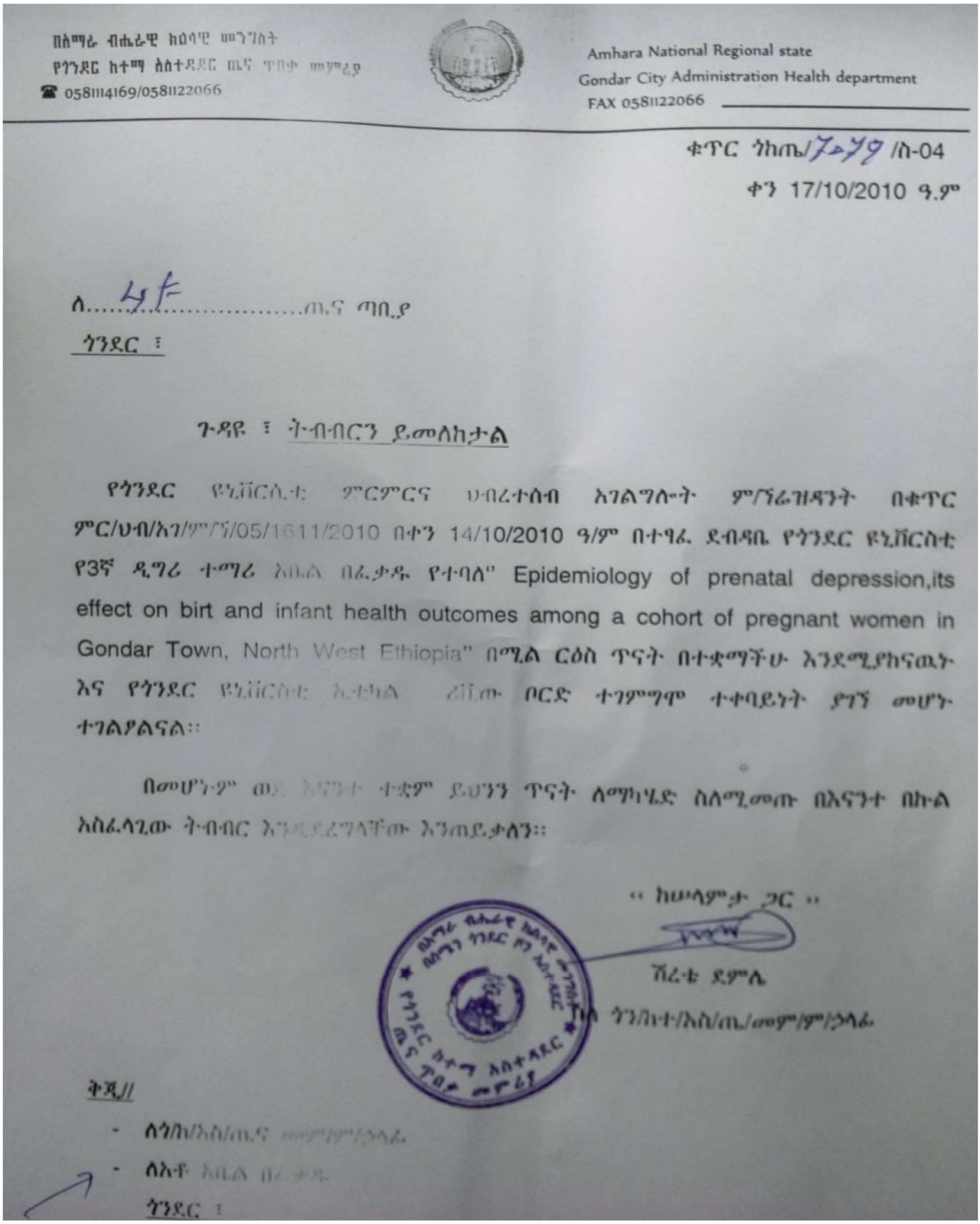
URL Address:- WWW.gondar.edu.et

Annex 2.11. Letter of support from Gondar Town health office to respective kebeles



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☎ 0581114169/0581122066

Amhara National Regional state
Gondar City Administration Health department
FAX 0581122066

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Annex 3. Data collection tool

Annex 3.1. Questionnaire for quantitative data collection

Questionnaire for collecting quantitative data (1st visit during pregnancy)

Time required: 35'-40'

Kebele name: ----------

Code of the mother: ----------

Name of the interviewer: ----------

Date of the interview: ----------

Date of appointment for next visit ----------

Direction: Please circle the response options and clearly fill open ended questions

Code	Variable	Response	Score/ explain
Part I: **Socio-demographic characteristics of the women, now I will ask you about your self**			
1.01	Age of the mother	------- years	
1.02	Educational status of the mother	1. No formal education 2. Grade 1-8 3. Grade 9-12 4. Diploma and above	
1.03	Occupation of the mother	1. Housewife 2. Student 3. Government employee 4. Self-employee	
1.04	Marital status of the mother	1. Single 2. Married 3. Divorced 4. Widowed 5. Separated	
1.05	How you can explain your marital condition in general?	1. Very good 2. Good 3. Bad 4. Very Bad	
1.06	How often you discuss and agree with your husband on day to day life?	1. Most of the time 2. Sometimes 3. Rarely 4. Never	
1.07	Are you an active follower of any religion?	1. Orthodox 2. Muslim 3. Catholic 4. Protestant	

		5. Other	
1.08	In the last three months, have you ever worried that your household would not have enough food?	1. Yes 2. No	
1.09	Your monthly income in Ethiopian birr	----------	
Part II: Fertility: Now, I would like to ask you about the births that you have had in your life.			
2.01	How many children do you have?	---------- children	
2.02	Is your current pregnancy a planned pregnancy?	1. Yes, I wanted a child at this time 2. No, but I did want a child - later 3. No, I did not intend to have a child at all	
2.03	How many months pregnant are you now?	---------- weeks	
2.04	Did you have difficulty in getting pregnant this time (e.g. used any fertility medication/waited long time to get pregnant?	1. Yes 2. No	
2.05	Mid upper arm circumference (MUAC) of the mother	----------mm	
Part III. Feelings of depression (EPDS). **Tell us the way you have been feeling in the past (1) week including today. In the past seven days,**			
3.01	In the last week, have you been able to laugh and see the funny side of things?	As much as I always used to Not as much as I used to Certainly not as much as I used to Not at all	0 1 2 3
3.02	In the last week, have you looked forward with enjoyment to things?	As much as I always used to Rather less Certainly less Never looked forward	0 1 2 3
3.03	In the last week, have you blamed yourself unnecessarily when things went wrong?	Most of the time Sometimes Rarely Never	3 2 1 0
3.04	In the last week, have you been anxious or worried for no good reason?	Most of the time Sometimes Not often Never	0 1 2 3
3.05	In the last week, have you felt scared or panicky for no good reason?	Most of the time Sometimes Rarely Never	3 2 1 0

3.06	In the last week, have things been getting on top of you?	Most of the time unable to cope Sometimes unable Mostly able Coping as usual	3 2 1 0
3.07	In the last week, have you been so unhappy that you have had difficulty sleeping?	Most of the time Sometimes Rarely Never	3 2 1 0
3.08	In the last week, have you felt sad or miserable?	Most of the time Sometimes Occasionally Never	3 2 1 0
3.09	In the last week, have you felt so unhappy that you have been crying?	Most of the time Sometimes Occasionally Never	3 2 1 0
3.10	In the last week, has the thought of harming yourself occurred to you?	Frequently Sometimes Not often Never	3 2 1 0
3.11	Have you felt these symptoms before being pregnant?	1. Yes 2. No	
Part IV. Oslo Social Support Scale (OSSS-3) to assess pregnant women social support, Now, we would like to ask you questions about the support you get from different people			
4.01	How many people are so close to you that you can count on them if you have serious personal problems?	None 1 or 2 3 to 5 6 or more	1 2 3 4
4.02	How much concern do people show in what you are doing?	A lot of concern and interest Some concern and interest Uncertain Little concern and interest No concern and interest	5 4 3 2 1
4.03	How easy is it to get practical help from neighbours if you should need it?	Very easy Easy Possible Difficult Very difficult	5 4 3 2 1
4.04	My husband helps me a lot	Always Most of the time Some of the time Rarely Never	5 4 3 2 1
Part V. Obstetric related factors, now I would like to ask you questions related to your current pregnancy			

5.01	After you knew that you are pregnant, did you go anywhere to receive antenatal care?	1. Yes 2. No	
5.02	Including this pregnancy, for how many times have you been pregnant and give birth	1. For the first time 2. Two and above	If "1" got Q. No 5.05
5.03	Have you ever given birth to low weight baby?	1. Yes 2. No	
5.04	Have you ever given birth to preterm?	1. Yes 2. No	
5.05	Have you ever had a baby by cesarean delivery	1. Yes 2. No	
5.06	Do you have any fear of giving to this birth?	1.Yes 2.No	
5.07	Are you and your husband interested in the sex of your current pregnancy?	1.Yes 2.No	
5.08	Have you practice physical activity such as brisk walking, dancing, gardening, and usual housework for at least three hours/week	1. Yes 2. No	
5.09	How do you rate your daily health condition?	1. Very good 2. Good 3. Bad 4. Very bad	
5.10	Is there anybody who smoke near to you in your home or in your work place?	1. Yes (exposure to second hand smoking) 2. No	
5.11	How often are you drinking coffee during this pregnancy?	1. Daily 2. Sometimes 3. Never	
Part VI. Stress coping ability of the women by Perinatal Coping Inventory (PCI-4)			
6.01	Planned how you will handle the birth	Frequently Sometimes Not often Never	3 2 1 0
6.02	Felt that being pregnant has enriched your life	Frequently Sometimes Not often Never	3 2 1 0
6.03	Prayed that the birth will go well	Frequently Sometimes Not often Never	3 2 1 0
6.04	Avoided being with people in general	Frequently Sometimes	0 1

		Not often Never	2 3

Questionnaire for collecting Birth outcome and postnatal depression (2nd visit, after delivery)

Time required: 15- 20"

Code	Questions	Response category	comment
Part I. Adverse Pregnancy Outcome assessment questions			
1.01	Birth weight of the new born	---------- grams	
1.02	Gestational weeks of the delivery	----------weeks. days	
1.03	Stillbirth event	1. Yes 2. No	
1.04	Mode of delivery	1. Cs 2. Vaginal delivery	
1.05	Type of delivery	1. Single 2. Twin	
1.06	Labor complication	1. Yes 2. No	
1.07	How many weeks since you have given birth?	----------weeks	
1.08	After you give birth, did you go anywhere to receive postnatal care?	1. Yes 2. No	
1.09	In the past 15 days, how many days you were unable to perform your usual home activities?	----------days	
1.10	Weight of the mother	---------- kg	
1.11	MUAC of the mother	----------cm	
Part II. Feelings of depression (EPDS). Tell us the way you have been feeling in the past (1) week including today. In the past seven days,			
2.01	In the last week, have you been able to laugh and see the funny side of things? For example: can you laugh at things which normally make you laugh?	As much as I always used to Not as much as I used to Certainly not as much as I used to Not at all	0 1 2 3
2.02	In the last week, have you looked forward with enjoyment to things? Another example is, are you able to look forward to market day? Or to something like this?	As much as I always used to Rather less Certainly less Never looked forward	0 1 2 3
2.03	In the last week, have you blamed yourself unnecessarily when things went wrong? For example, if your child gets ill do you blame yourself? Or, for example, if the crops fail? Or something like this?	Most of the time Sometimes Rarely Never	3 2 1 0
2.04	In the last week, have you been anxious or worried for no good reason?	Most of the time Sometimes	0 1

		Not often Never	2 3
2.05	In the last week, have you felt scared or panicky for no good reason?	Most of the time Sometimes Rarely Never	3 2 1 0
2.06	In the last week, have things been getting on top of you?	Most of the time unable to cope Sometimes unable Mostly able Coping as usual	3 2 1 0
2.07	In the last week, have you been so unhappy that you have had difficulty sleeping?	Most of the time Sometimes Rarely Never	3 2 1 0
2.08	In the last week, have you felt sad or miserable?	Most of the time Sometimes Occasionally Never	3 2 1 0
2.09	In the last week, have you felt so unhappy that you have been crying?	Most of the time Sometimes Occasionally Never	3 2 1 0
2.10	In the last week, has the thought of harming yourself occurred to you?	Frequently Sometimes Not often Never	3 2 1 0
Part III. Oslo Social Support Scale (OSSS-3) to assess women social support after birth, Now, we would like to ask you questions about the support you get from different people			
3.01	How many people are so close to you that you can count on them if you have serious personal problems?	None 1 or 2 3 to 5 6 or more	1 2 3 4
3.02	How much concern do people show in what you are doing?	A lot of concern and interest Some concern and interest Uncertain Little concern and interest No concern and interest	5 4 3 2 1
3.03	How easy is it to get practical help from neighbours if you should need it?	Very easy Easy Possible Difficult Very difficult	5 4 3 2 1
3.04	My husband helps me a lot	Always Most of the time Some of the time Rarely Never	5 4 3 2 1

Questionnaire for collecting data on infant health outcome (3rd visit)

Time required: 10'-15'

Code	Questions	Response category	comment
Part I. Environmental factors			
1.01	What is the age of the infant?	--------- months	
1.02	Who is caring the infant most of the time?	1. Mother 2. Father 3. Grand mother 4. Sister/brother 5. Home maid	
1.03	My breasts seem to have enough milk	1. Strongly agree 2. Agree 3. No idea 4. Disagree 5. Strongly disagree	
1.04	My baby generally appears satisfied after breast feedings	1. Strongly agree 2. Agree 3. No idea 4. Disagree 5. Strongly disagree	
Part II. Adverse Infant health outcome assessment questions			
2.01	Breast feeding	1. Exclusively breast fed 2. Non-exclusive breast fed	
2.02	Malnutrition assessment	MUAC ---------- mm Weight of the infant ------grams	
2.03	Infant illness assessment	Diarrhea symptoms (three or more loose of stools in 24 hours) 1. Yes 2. No	
		ARI symptoms (cough/cold accompanying fever/or fast breathing) 1. Yes 2. No	
2.04	How do you rate your infant daily health condition?	1. Very good 2. Good 3. Neutral 4. Bad 5. Very bad	

Annex 3.2. Interview guide for qualitative study

Time of the interview: 45'-50'

Date of the interview ----------

Code of the interviewee ----------

Part I: Demographic information

a. Age ----------years
b. Total experience as health worker and health system administrator ---------- years
c. Profession 1. Clinical nurse 2. Midwifery 3. Health officer 4. Medical doctor
d. Marital status 1. Never married 2. Married (living together) 3. Separated 4. Widowed
e. Monthly income: ----------ETB
f. Religion 1. Orthodox 2. Catholic 3. Muslim 4. Protestant

Part II: Interview guide

1. **Knowledge and practice about perinatal depression**

- How would you describe a mother of good mental health? Probe
    - They feel good, can do their usual work, they can come for service, can understand what they told
    - What do you think perinatal depression is? Probe, Mental illness, mood disorder,
    - Who is at risk of depression? Probe,
      Everybody, pregnant women, postnatal women, adolescents
- What are the sign and symptoms the women with depression could show? Probe
    - Dissatisfaction, think of worthlessness, hate to do their usual activity, think of suicide, feeling sad, feeling tired
- What do you think about the cause of depression? Probe
    - Poverty, pregnancy, lack of support, fear of birth
- When would the mother develop depression? Probe

- Immediately after pregnancy, 1st trimester, 2nd trimester, 3rd trimester, after birth

- What do you think should be done for the mother with severe depression? probe
    - Nothing, refer to hospital, counseling
- What would happen if depressed women cannot gate appropriate intervention? Probe
    - Effect on birth outcome, service uptake, maternal health consequence, may die, may suicide

2. Health system administrator's opinion about health care system concerning perinatal depression

- How our country policy looks about perinatal depression as a problem?
- Do our health system have plan, strategy, and initiative to screen depression during perinatal period?
- What activities have been undertaken to facilitate screening for perinatal depression? Mainstreaming the problem, training health professionals, including in a plan, evaluating the performance of planned activities
- Would you tell me how could health professionals identify women with depression? Probe
    - Sign and symptom, from their complain,
- When do you think it is favorable to screen women with depression? Probe
    - During ANC, PNC, during vaccination time, during delivery
- Where do you think it is favorable to screen women with depression? Probe
    - At health facility, at their home, during campaign
- What could health professionals use to identify women who have depression sign? Probe

  Observation, screening tool, laboratory,
- If health professionals want to screen and treat depressed women who come to their department, can they do? What do they need to do so?
- Is the condition/set up of the health facility initiate you/them to do so? Probe

    - Facility to treat women with depression, trained professionals, time to screen
- What do you think is a barrier for screening and treating women with depression/ for health professionals? Probe
    - No way in place for screening, no guideline for treatment, no system emplaced to do this, I don't know how to identify and treat

I thank you very much again for your participation in the interview and providing responses, and will strictly be kept confidential.